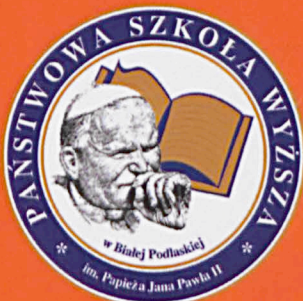


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in Białą Podlaską,
Sidorska 95/97, 21-500 Białą Podlaską
e-mail: p.rynkiewicz@pswbp.pl
tel. +48 83 344 99 00, extension 271
Contact: Paulina Rynkiewicz

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TREATMENT RESULTS EVALUATION IN PATIENTS WITH SEVERE SEPSIS,
CAUSED BY SEVERE TRAUMATIC BRAIN INJURY AT INTENSIVE CARE UNIT
OF TERNOPIL UNIVERSITY HOSPITAL

OCENA WYNIKÓW LECZENIA PACJENTÓW Z CIĘŻKĄ SEPSĄ
SPOWODOWANĄ SILNYM URAZOWYM USZKODZENIEM MÓZGU
NA ODDZIALE INTENSYWNEJ TERAPII UNIWERSYTECKIEGO SZPITALA
W TARNOPOLU

Oleksandr V. Oliynyk^{1,2(A,B,C,D,E)}, Bohdana O. Pereviznyk^{2(E)}, Anna Ślifirczyk^{1(E,F)},
Oleh V. Yemiashev^{3(B,C)}, Nataliya I. Kراسiy^{3(C)}

¹Pope John Paul II State School of Higher Education in Biała Podlaska, Poland

²I.Ya. Horbachevskyi Ternopil State Medical University of Ministry of Public Health, Ukraine

³Ternopil University Hospital, Ukraine

Authors' contribution

Wkład autorów:

A. Study design/planning

zaplanowanie badań

B. Data collection/entry

zebranie danych

C. Data analysis/statistics

dane – analiza i statystyki

D. Data interpretation

interpretacja danych

E. Preparation of manuscript

przygotowanie artykułu

F. Literature analysis/search

wyszukiwanie i analiza literatury

G. Funds collection

zebranie funduszy

Summary

Background. Severe traumatic brain injury stays one of the main reasons of humans' mortality until the age of 40. Ternopil University Hospital delivers medical care to the patients with neurosurgical pathology of Ternopil region, which is comprised of 1 107 000 citizens.

Material and methods. In this paper we analyzed the treatment results of 301 patients with severe traumatic brain injury (STBI), who were treated at intensive care unit of Ternopil University Hospital during 2013-2014. Microbiological research and evaluation of results were accomplished according to generally accepted principles, based on the Bergey's classification.

Results. In 72 patients it was complicated by severe sepsis. The mortality rate in clinic reached 29.7% in 2013-2014, or equals 1.9 person per 100 000 of population. Among the intensive care unit patients with STBI, who had the surgery based on this pathological condition, sepsis developed in 23.9% of patients. Acute respiratory distress syndrome (ARDS), which complicated sepsis, was successfully cured in 73.3% of cases, by additional usage of traditional ventilation, kinesiotherapy, oxygen therapy and pulse therapy with glucocorticosteroids (GS). 22.2% of patients obtained acute renal failure, 9.72% of patients were treated by implementing hemodialysis. Concomitant polytrauma was present in 23.9% of patients.

Conclusions. The usage of pulse therapy with glucocorticosteroids additionally to traditional mechanical ventilation, kinesiotherapy, and oxygen therapy for the treatment of acute respiratory distress syndrome helps to improve the life expectancy of patients.

Keywords: severe sepsis, severe traumatic brain injury, intensive care

Streszczenie

Wprowadzenie. Silne urazowe uszkodzenie mózgu pozostaje jedną z głównych przyczyn zgonów pacjentów w wieku poniżej 40 lat. Uniwersytecki Szpital w Tarnopolu zapewnia opiekę medyczną pacjentom z patologią neurologiczną z regionu Tarnopola, który zamieszkuje 1,107,000 mieszkańców.

Materiał i metody. W tym artykule zostały przeanalizowane wyniki leczenia 301 pacjentów z silnym urazowym uszkodzeniem mózgu (STBI), którzy byli leczeni na oddziale intensywnej terapii w Uniwersyteckim Szpitalu w Tarnopolu w latach 2013-2014. Badania mikrobiologiczne oraz ocena wyników przeprowadzono zgodnie z ogólnie przyjętymi zasadami w obdarciu o klasyfikację Bergeya.

Wyniki. W przypadku 72 pacjentów komplikacją była ciężka sepsa. Śmiertelność zanonotowana przez szpital była na poziomie 29.7% w latach 2013-2014, lub też była równa 1.9 osób na 100,000 populacji. Wśród pacjentów z STBI przebywających na oddziale intensywnej terapii, którzy byli poddani operacji z powodu wystąpienia u nich tego stanu patologicznego sepsa rozwinęła się w przypadku 23.9% z nich. Zespół ostrej niewydolności oddechowej (ARDS) wraz ze skomplikowaną postacią sepsy został pomyślnie wyleczony w przypadku 73.3% pacjentów dzięki dodatkowemu użyciu tradycyjnej wentylacji, kinezyterapii, terapii tlenowej oraz leczenia pulsacyjnego glikokortykosteroidami (GS). U 22.2% pacjentów wystąpiła ostra niewydolność nerek, 9.72% pacjentów poddano leczeniu za pomocą hemodializy. Towarzystwający uraz mnogi wystąpił w przypadku 23.9% pacjentów.

Wnioski. Użycie leczenia pulsacyjnego glikokortykosteroidami stosowane dodatkowo oprócz tradycyjnej wentylacji mechanicznej, terapii tlenowej w leczeniu zespołu ostrej niewydolności oddechowej pozwala zwiększyć przeżywalność pacjentów.

Słowa kluczowe: ciężka sepsa, silne urazowe uszkodzenie mózgu, intensywna terapia

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Address for correspondence / Adres korespondencyjny: Oleksandr V. Oliynyk, Pope John Paul II State School of Higher Education in Biała Podlaska, Siderska 102, 21-500 Biała Podlaska, e-mail: alexanderoliynyk8@gmail.com, phone: +48 83 344 99 18

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Background

Severe traumatic brain injury (STBI) is one of the most prominent mortality and disability causes all over the world. STBI stays one of the main reasons of humans' mortality until the age of 40 [1]. In Great Britain STBI frequency is 1 500 people per every 100 000 of population. 9 patients out of 100 000 of population die because of traumatic brain injury [2-4].

Among the complications of STBI the prominent role is given to severe sepsis. In Germany annual mortality caused by sepsis is over 75 000 cases (equals the mortality from myocardial infarction) [6]. In general in Europe it is annually registered up to 500 000 sepsis cases. 1 per every 1 000 hospitalized patients obtains sepsis [7]. It is similar to the situation in the United States. In the USA sepsis develops in over 750 000 people annually, which is 3 cases per 1 000 of population per year. Sepsis is the cause of 20% of intra-hospital mortality, which equals 210 000 people annually [7].

The mortality rate in case of severe sepsis is still very high and equals 50-60% [5]. The highest mortality, which 80-90%, is described in patients with septic shock. All over the world 14 people per minute die because of sepsis and its annual mortality is higher than summarily of HIV, prostate and breast cancer [6].

Material and methods

We implemented the analysis of treatment results of 72 patients with STBI, followed by severe sepsis, who were treated at intensive care unit of Ternopil University Hospital. It equals 23.9% of the total amount of patients with STBI, who were treated during 2013-2014 in our hospital. Severe sepsis diagnosis was verified by determining the levels of procalcitonine and C-reactive protein.

Microbiological research and evaluation of results were accomplished according to generally accepted principles [8,9]. We used the Bergey's classification. The analysis was implemented using the semiautomatic analyzer «Vitek – 2». After the primary bacterial culture was allocated, we implemented its identification by using Kirby-Bauer disc-diffusion method. The permission for research implementation was given by Bioethics commission of Ternopil State Medical University (protocol №29 from 20.05.2015). All the experimental procedures were followed in accordance with the Helsinki Declaration of 1975.

Results

All around the worlds STBI patients' mortality equals 80 % [10]. That's why the result of 29.7% should be considered as an achievement. Among the patients of intensive care unit in Europe and USA sepsis develops in 20-40% of cases. In our clinic it is 23.9%. We should say that these 72 patients were the most complicated for us to deal with. The received result is also a kind of achievement because in 94.4% of cases sepsis was gram-negative, while it is known that its mortality is twice higher than from gram-positive [6]. The patients' characteristics are provided at *Table 1*. The results of microbiological research of 897 isolates are present in *Table 2*.

Table 1. The characteristics of the patients with STBI, followed by severe sepsis, who were treated at intensive care unit of Ternopil University Hospital during 2013-2014

Values, which characterize patients with STBI and severe sepsis	Absolute values	Relative values (%), relating to corresponding number of patients with STBI and severe sepsis
Total amount of patients with STBI, who had a surgical intervention	301	
Amount of patients with STBI, who were treated at intensive care unit	154	
Amount of patients with STBI, followed by severe sepsis, who were treated at intensive care unit	72	100.0
Amount of dead patients with STBI	21	29.17
Amount of dead patients with STBI and severe sepsis	22	30.56
Amount of patients discharged from hospital with moderate cognitive dysfunction	29	40.28
Concomitant polytrauma	19	26.3
Acute renal failure	16	22.2
Dialysis therapy	7	9.72
Acute respiratory distress syndrome (ARDS)	15	20.83
Ventilator-associated pneumonia	18	25.0

Amount of patients, who had the mechanical ventilation	72	100.0
Amount of patients with duration of mechanical ventilation over 30 days	13	18.05
Amount of patients with duration of ventilation for 20-30 days	35	48.68
Amount of patients with duration of ventilation up to 20 days	24	33.3
Amount of patients who had hemosorbtion or plasmosorbtion	36	50.0
Total amount of hemosorbtion and plasmosorbtion procedures	126	
Amount of patients with gram-negative flora	68	94.4
The amount of patients with bedsores	4	5.55

Table 2. Antibiotic resistance of infectious agents at intensive care unit during 2013-2014 (897 isolates)

Microorganism distribution, %	Amoxicillin	Amoxiclav	Cefaperazon	Ceftazidime	Ceftriaxone	Cefotaxim	Cefepime	Imipenem	Meropenem	Amicacin	Gentamicin	Ciprofloxacin	Gatifloxacin	Levofloxacin
Escherichia coli, 6.5	100.0	100.0	80.0	50,7	37.5	100.0	25.0	66.7	66.7	33.3	33.3	33.3	25.0	25.0
Enterobacter cloacae, 3.3	100.0	100.0	100.0	100,0	100.0	100.0	100.0	40.0	33.3	40.0	100.0	60.0	66.7	100.0
Enterobacter aerogenes, 11.1	100.0	100.0	100.0	87,5	100.0	100.0	100.0	40.0	62.5	76.9	71.4	84.6	100.0	66.7
Acinetobacter baumannii, 14.3	100.0	100.0	71.4	100,0	100.0	91.4	91.4	71.4	84.6	83.3	91.7	94.1	87.5	77.8
Pseudomonas aeruginosa, 25.5	100.0	100.0	73.5	86,7	84.6	87.5	73.5	66.7	58.3	60.0	57.9	81.0	91.7	87.5
Klebsiela pneumonie, 31.4	1 00.0	100.0	97.2	100,0	100.0	100.0	97.1	53.0	54.0	65.7	88.9	92.9	83.3	88.9
Staphylococcus aureus, 7.8	30.0	30.0	00.0	00.0	50,0			66.7			00.0	00.0		50.0

Discussion

Treatment strategy equaled to the Guidelines for the Management of STBI, created by American Association of Neurological Surgeons (2007), which was modified based on our conditions [4].

- We used the following principles of intensive therapy for the patients with STBI, followed by severe sepsis.
1. The elevation of the head end of the bed at 30 degrees provides an adequate cerebral perfusion; average blood pressure should be stable at the level of no less than 90-95 mm Hg (systolic blood pressure should be no less than 130 mm Hg). The infusion of vasopressors should be carried in order to keep blood pressure stable.
 2. The compliance of adequate mechanical ventilation should be provided. Patients' staying on spontaneous breathing only in cases when the state of consciousness equals no less than 12 points according to Glasgow Coma Scale. In patients with less than 12 points (sopor-coma) the tracheal intubation should be managed. Any doubts of the need of intubation should be treated as indication for providing this manipulation. Patients with 9 or less points of Glasgow scale should have mechanical ventilation in mandatory mode. The episodes of patients' desynchronization with the respirator should be managed by the selection of right ventilation mode, because it can lead to the increase of intracranial pressure. It is obligatory to prevent the hypoxia, which can intensify brain edema. Early tracheostomy is provided to the 3rd day of staying in the intensive care unit in case of prognostication of prolonged ventilation. Analgosedation is delivered with the usage of narcotic analgesics (infusion pump of fentatyl), and following sibazone, diprofol, sodium tiopental. Mandatory ventilation modes are used only when other ones are ineffective and in case of Glasgow scale

point of 9 and higher. It is also obligatory to anticipate hyperventilation in order to prevent hypocapnia. While implementing mechanical ventilation we should be striving for normoventilation and normocapnia. The best ventilation modes to use are the ones that cause the minimal elevation of intrathoracic pressure. The optimal oxygen content of the breathing mixture is 40%. In case of worsening of neurological status because of dislocation of the brain, the oxygen content should be increased up to 100%.

3. It is needed to prevent the influence of following factors, which decrease the cerebral perfusion and oxygenation:
 - sharp increase of intrathoracic pressure;
 - hypo- and hyperosmolarity;
 - hypo- and hypercapnia;
 - hypo- and hyperglycemia;
 - hyperthermia.
4. Infusion therapy should be delivered in first hours of staying at intensive care unit and in volumes to correct hypovolemia and water-electrolyte imbalance. We prefer the infusions of crystalloids, except for 5% glucose solution. We try to manage normal osmolarity, glycemia, potassemia, sodiemia. Usually, it is possible to eliminate hypovolemia in first 12 hours after injury. Despite of surgical intervention or its absence, the most important issue to deal with is brain edema. After correction of hypovolemia it is not needed to hyperhydrate the patient and then give diuretics in order to deal with brain edema. The better option is to give the bigger amount of fluid, except for the volume that is needed for IV infusion of antibiotics, per os. The fluid balance should be corrected by check-up on diuresis and central venous pressure.
5. From the 1st day of patient's staying it is needed to make the attempts of drug stimulation of gastrointestinal tract with the usage of enteral nutrition for lowering the expectancy of gastro-intestinal insufficiency development. Enteral administration of fluids and food usually start from 2-3 day. Patients should receive a balanced mix of 2000-4000 calories and 1,5-2 grams of protein per day.
6. For hyperglycemia correction the insulin infusion with the usage of infusomat is needed. Daily doses mixtures are comprised of average 200 g of sugar. As the background for probable hyperglycemia it needs the increase in insulin dose. We use the enteral and parenteral mixtures for diabetics as it helps to decrease the need in insulin. It also led to the fact that 94.5% of our patients didn't obtain bedsores.
7. The prescription of adequate antibiotic therapy is also an important issue. As the majority of microorganisms in our department are gram-negative, the drugs of choice are meropenem, tienam, amikacin, colomycin. Over the last 3 years, we observed the increase of sensitivity of microflora to chloramphenicol, streptomycin, gentamicin (5 years ago it was 100% resistance).
8. 20.8% of patients obtained ARDS as the complication of sepsis. In treatment protocol with the level of evidence A there are mechanical ventilation, oxygen therapy, kinesiotherapy. The antibiotic and corticosteroids therapy equals to level C. Despite of this fact, we have done the pulse therapy with corticosteroids to all of our patients, who were diagnosed with this complication during first 2-3 days after its development. We also provided the continued mechanical ventilation (no less than 2 weeks) with the privilege of possible mandatory modes. 11 patients (15.3% of total amount, and 73.3% of patients with ARDS) survived.
9. In order to deal with hyperthermia we used all possible groups of drugs: non-steroidal and steroidal anti-inflammatory, non-narcotic analgesics, mechanical methods of cooling.
10. The best way to deal with intracranial hypertension is the dosed drainage of cerebrospinal fluid through ventricle catheter.
11. The monitoring of heart rate allows avoiding severe arrhythmias.

Conclusions

1. Compliance of the Guidelines for the Management of STBI, created by American Association of Neurological Surgeons (2007), significantly helps to improve treatment results in patients with following pathological condition.
2. The usage of pulse therapy with glucocorticosteroids additionally to traditional mechanical ventilation, kinesiotherapy, and oxygen therapy for the treatment of ARDS helps to improve the life expectancy of patients.

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OPTIMIZATION OF PHARMACOTHERAPY SYSTEM FOR TREATMENT OF THYROID DISEASES IN UKRAINE

OPTYMALIZACJA SYSTEMU FARMAKOTERAPII W LECZENIU CHORÓB TARCZYCY NA UKRAINIE

Yulia Vadziuk^(A,B,C,D,E,F,G)

Ternopil State Medical University

Authors' contribution

Wkład autorów:

- A. Study design/planning
zaplanowanie badań
- B. Data collection/entry
zebranie danych
- C. Data analysis/statistics
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Summary

Background. Recent years thyroid diseases are attracting considerable attention. On one hand, this is due to the fact that thyroid is actively reacts on environment, followed by appearance of various diseases. On the other hand, in current conditions population remains face to face with adverse impact of environment because an effective experience of the world community to fight against iodine deficiency is not implemented in Ukraine. Thus every year becomes more patients with thyroid pathology. So there becomes a need to optimize the system of healthcare provision for these patients.

Material and methods. We have analyzed medications listed in Ukrainian National Formulary and studied the dynamics of its formation. A comparative analysis of UNF with the British National Formulary was conducted. The compliance of UNF with the WHO Model List of Essential Medicines was checked.

Results. Comparative analysis of assortment dynamic of UNF medications for treatment and prevention of thyroid diseases showed that foreign drugs had an advantage of inclusion to formulary. The main difference between BNF and UNF is that drugs are brought in BNF only by original name. In UNF antithyroid drugs are presented by thiamazole which is absent in WHO Model List of Essential Medicines and BNF.

Conclusions. We recommend to provide arguments concerning evidence of clinical and cost effectiveness of drugs included to UNF; to include drugs in UNF exclusively by original name; to include carbimazole and propylthiouracil medications into group of antithyroid drugs in UNF; to unite subsections 7.3.2 and 7.3.3 of UNF to one general subsection "antithyroid drugs".

Keywords: marketing analysis, pharmacotherapy, thyroid diseases

Streszczenie

Wprowadzenie. Od jakiegoś czasu choroby tarczycy są obiektem znacznego zainteresowania i uwagi. Jest to z jednej strony spowodowane faktem, że tarczyca aktywnie reaguje na zmiany środowiskowe, w następstwie pojawienia się wielu chorób. Z drugiej strony w obecnych warunkach społeczeństwo staje twarzą w twarz ze szkodliwym wpływ środowiska, ponieważ na Ukrainie nikt nie stosuje się do zasad dyktowanych przez sprawne doświadczenia świata w walce z niedoborem jodu. Stąd, co roku odnotowuje się coraz większą liczbę pacjentów z patologicznymi stanami tarczycy. Dlatego też istotna jest potrzeba optymalizacji systemu służby zdrowia dostępnego dla tych pacjentów.

Materiał i metody. Przeanalizowaliśmy leki wskazane w Ukraińskim Narodowym Receptariuszu oraz zbadaliśmy dynamikę jego utworzenia. Analiza porównawcza UNR z Brytyjskim Narodowym Receptariuszem została przeprowadzona. Sprawdzona została także zgodność tego dokumentu z listą leków podstawowych Światowej Organizacji Zdrowia.

Wyniki. Analiza porównawcza dynamiki asortymentu leków zawartych w UNR w leczeniu i zapobieganiu chorobom tarczycy wykazała, że zagraniczne lekarstwa posiadały zaletę bycia włączonymi do Receptariusza. Podstawową różnicą między BNR a UNR jest fakt, że lekarstwa w ramach BNR są dostępne wyłącznie pod oryginalną nazwą. W UNR lekarstwa przeciwtarczycowe przedstawiane są poprzez tiamazol, który nie występuje na liście leków podstawowych Światowej Organizacji Zdrowia a także BNR.

Podsumowanie. Zalecamy uargumentowanie istnienia dowodów klinicznej i kosztowej efektywności leków włączonych w UNR, włączenie leków w UNR wyłącznie w formie nazwy oryginalnej, włączenie carbimazolu oraz leków na bazie propylotiouracylu do grupy leków przeciwtarczycowych UNR, połączyć podrozdziały 7.3.2 i 7.3.3 UNR w jednej ogólny podrozdział „leków przeciwtarczycowych”.

Słowa kluczowe: analiza marketingowa, farmakoterapia, choroby tarczycy

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Figures: 1
References: 10
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Address for correspondence / Adres korespondencyjny: Yulia Vadziuk, Ternopil State Medical University, m.Voli, 1, Ternopil, 46001, e-mail: yuliavadziuk@mail.ru; phone: +38 0979215225

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Background

Nowadays significant attention of world’s scientists is paid to effectiveness and safety of medicines and optimizing healthcare needs [1]. The implementation of social medical insurance in Ukraine, which the Ministry of Health plans to introduce till the end of 2016 will facilitate this [2]. The main tool to ensure proper prescribing and use of drugs is formulary system.

Formulary system is based on criteria of evidence; it provides cost efficiency, rational prescribing and use of drugs according to established standards. The process of implementation of formulary system can be seen as the optimization of drug therapy in rationalization process of drugs selection in order to increase therapeutic benefits depending on cost of their purchase [3].

It is known that the thyroid disorders are very common, affecting 750 million people worldwide by recent World Health Organization (WHO) estimates, being possibly even more prevalent than diabetes [4,5]. Analysis of official statistical data the Ministry of Health of Ukraine (2009) found a high prevalence of endocrine diseases in Ukraine. According to these criteria endocrine pathology takes one of leading places in the structure of general morbidity. There are a growing number of patients with different endocrinopathies in Ukraine, but the most common among them - thyroid disease (47% of all diseases of endocrine system) [6].

So we have identified the need for analysis of drugs for treatment of thyroid disease included to the Ukrainian National Formulary (UNF) according to international guidelines.

Material and methods

We have analyzed medications listed in UNF and studied the dynamics of its formation (2010-2014 years). A comparative analysis of UNF with the British National Formulary (BNF) was conducted. The compliance of UNF with the WHO Model List of Essential Medicines was checked.

Results

As of January 2015 in Ukraine come out six editions of UNF containing recommendations for prescribing and rational use of drugs considering efficiency, safety and economic feasibility.

We made comparative analysis of assortment dynamic of Formulary medications for treatment and prevention of thyroid disease that were included to the 2nd, 4th and 6th editions of UNF (Figure 1).

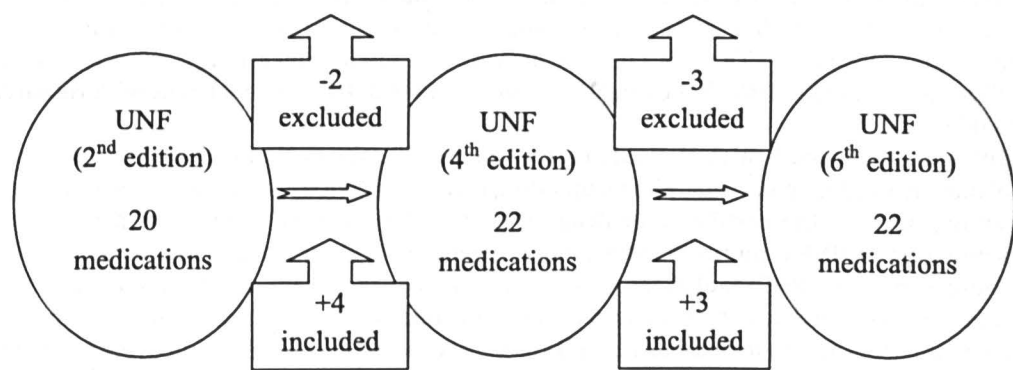


Figure 1. Dynamics of changes in lists of drugs for treatment of thyroid diseases included to different editions of UNF (by their trade names)

As we can see from figure 1, the number of medications of test group included to different editions of UNF is not significantly different. To the fourth edition of UNF 4 new foreign drugs (India, Serbia) were added and 2 domestic drugs were excluded. At inclusion of medications to 6th edition of UNF there was rotation of three foreign drugs. Inclusion and exclusion of trade names may be associated with expiry of registration certificate or registration of new drugs, because only those drugs that have active registration certificate at the time of viewing are included to Formulary.

WHO considers that 80-90% of health care needs can provide 700-800 items of drugs. Therefore, the use of high-quality and safe medicines will help reduce morbidity and mortality in many countries. WHO Model List of Essential Medicines has recommendation function and is used as a basis for drafting relevant national lists [7].

We have analyzed presence of medicines for treatment of thyroid diseases included to Ukrainian National Formulary (6th edition) according WHO Model List of Essential Medicines (18th Edition) (Table 1).

Table 1. The presence of drugs for treatment of thyroid diseases in UNF according to WHO Model List of Essential Medicines

WHO Model List of Essential Medicines	WHO recommended drug and dosage form	Presence of drugs in UNF	Presence of WHO recommended drug form	Presence of WHO recommended dosage form
Levothyroxine	Tablet: 25 micrograms, 50 micrograms, 100 micrograms	+	+	+
Potassium iodide	Tablet: 60 mg	+	+	-
Propylthiouracil	Tablet: 50 mg	-	-	-

As can be seen from table 1, among drugs for treatment of thyroid disease which are present in UNF only medications of levothyroxine are available in recommended drug form and dosage. Completely absent medications of propylthiouracil and potassium iodide drugs have no appropriate dosage form.

On the next stage we analyzed and compared British National Formulary (68th edition) and Ukrainian National Formulary (6th edition).

In UNF drugs for treatment of thyroid diseases are included to Chapter 7 “Endocrinology. Drugs”, section 3 “Medicines for treatment of thyroid disease”, which contains three subsections: 1. Thyroid hormones, 2. Antithyroid drugs, 3. Iodine drugs.

Analyzing the BNF we paid attention to the fact that drugs included here only by the original names, unlike UNF, which include both original and generic drugs. Prices of drugs in BNF indicated for full medication package, in UNF the price is calculated by defined daily dose. Drugs for treatment of thyroid diseases are included to Chapter 6 (Endocrinology), section 2 (thyroid and antithyroid drugs), subsections 1. Thyroid hormones, 2. Antithyroid drugs.

According to recommendations of BNF, thyroid hormones include levothyroxine sodium and liothyronine sodium (absent in UNF).

Antithyroid drugs of BNF contain carbimazole, propylthiouracil and iodine. Very important are recommendations for elimination thyrotoxic crisis, which added to this subsection. Also, the description of use of carbimazole drugs contain warning for doctors regarding caution of use of these medicines because of possibility of side effects (neutropenia, agranulocytosis), and provided detailed action plan for prevention of negative consequences.

Discussion

Results of comparative analysis of assortment dynamic of Formulary medications for treatment and prevention of thyroid disease that were included to the 2nd, 4th and 6th editions of UNF showed that foreign drugs had an advantage of inclusion to formulary. There is a need to provide arguments concerning evidence of clinical and cost effectiveness of drugs included in UNF, indicating the level of evidence (this is consistent with research results of Panfilova 2009 [8]).

The main difference between British National Formulary and Ukrainian National Formulary is that drugs are brought in BNF only by original name that allows updating formulary twice a year. This approach has sustainable rational foundation, because the certificate of drugs registration have time limits, which means that current principle of formulation of UNF requires constant monitoring of drugs registration and updating on daily basis. Taking into account principle of BNF regulations, validity of medicines registration and inability to update formulary on a constant basis, we consider it necessary to offer optimization of domestic formulary manual in accordance with international practices and to include drugs in Ukrainian National Formulary exclusively by original name.

In UNF antithyroid drugs are presented by thiamazole that is absent in WHO Model List of Essential Medicines and BNF. We consider it necessary to include carbimazole in this group of drugs because its use is accompanied by decrease of side effects and allergic reactions and it will allow patients to continue treatment of diffuse toxic goiter and achieve clinical and immunologic remission. Therapeutic effects of carbimazole and thiamazole are equivalent [9].

We recommend inclusion of propylthiouracil to UNF because it's included to the World Health Organization Model List of Essential Medicines. It is used only in pregnant women in first trimester and in case of thiamazole intolerance in patients who refuse other treatments [10].

We also suggest unification of subsections 7.3.2 and 7.3.3 of Ukrainian National Formulary to one general subsection “antithyroid drugs” according to British National Formulary and considering presence of only one position (potassium iodide) in subsection 7.3.3.

Conclusions

Based on research results, we recommend:

1. To provide arguments concerning evidence of clinical and cost effectiveness of drugs included to UNF, indicating the level of evidence.
2. To include drugs in Ukrainian National Formulary exclusively by original name.
3. To include carbimazole medications into group of antithyroid drugs in UNF.
4. To include propylthiouracil medications into group of antithyroid drugs in UNF.
5. To unite subsections 7.3.2 and 7.3.3 of UNF to one general subsection "antithyroid drugs".

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THE USE OF THERMOGRAPHIC CAMERA IN STROKE DIAGNOSTICS – INTRODUCTORY REPORT

ZASTOSOWANIE KAMERY TERMOWIZYJNEJ W DIAGNOSTYCE UDARÓW MÓZGU – DONIESIENIE WSTĘPNE

Jolanta Piskorz^{1(A,B,C,D)}, Gustaw Wójcik^{2,3(A,B,C,D)},
Joanna Ilzecka^{4(C,E,F)}, Włodzimierz Bulikowski^{2(C,E,F)}

¹Department of Anesthesiology and Intensive Care,

Zofia Tarnowska from the Zamoyskis Provincial Hospital in Tarnobrzeg, Poland

²Department of Rehabilitation, Physiotherapy and Balneotherapy of Medical University in Lublin, Poland

³Department of Imaging Diagnosis – Zofia Tarnowska from the Zamoyskis Provincial Hospital in Tarnobrzeg, Poland

⁴Department of Rehabilitation, Physiotherapy and Balneotherapy,

Independent Laboratory of Neurological Rehabilitation of Medical University in Lublin, Poland

Authors' contribution

Wkład autorów:

A. Study design/planning

zaplanowanie badań

B. Data collection/entry

zebranie danych

C. Data analysis/statistics

dane – analiza i statystyki

D. Data interpretation

interpretacja danych

E. Preparation of manuscript

przygotowanie artykułu

F. Literature analysis/search

wyszukiwanie i analiza literatury

G. Funds collection

zebranie funduszy

Summary

Background. Due to the serious course of most severe vascular injuries of the brain, there is a necessity to look for new diagnostic methods which are the least invasive for the patient. Objectives: the evaluation of the usefulness of thermographic camera in stroke diagnostics.

Material and methods. The research included 38 patients hospitalised due to cerebrovascular accident in the Intensive Therapy Ward and Neurology Ward. The patients were diagnosed according to EBM (evidence based medicine) by means of CT, then a series of images were taken by means of thermographic camera. The examinations were conducted on the first day of the stroke, preceded by head tomography, and next on the fourth day after the stroke.

Results. The examinations showed statistically significant ($p < 0.05$) decrease in the temperature in the brain stroke area in relation to the healthy part both on the first and the fourth day. The difference in the average temperature changes between the cerebral infarction and intracerebral hemorrhage on the first and the fourth day was not statistically significant ($P > 0.05$). The difference in the average temperature changes in the brain stroke area (irrespective of its type) between the first and the fourth day was statistically significant ($p < 0.05$). The difference in the average temperature changes between the smaller and the bigger focal areas in CT on the first and the fourth day was not statistically significant ($P > 0.05$). No significant correlation was observed between the average temperature changes and the clinical state of patients evaluated according to ESS (Epworth Sleepiness Scale) during the first day ($p > 0.05$).

Conclusion. Thermographic camera is a useful tool in brain stroke diagnostics, however it does not differentiate between hemorrhagic and ischemic strokes.

Keywords: stroke, cerebral infarction, thermal imaging camera, computer tomography

Streszczenie

Wstęp. W związku z ciężkim przebiegiem większości ostrych naczyniowych uszkodzeń mózgu istnieje konieczność poszukiwania nowych metod diagnostycznych jak najmniej inwazyjnych dla chorego. Cel pracy: ocena przydatności kamery termowizyjnej w diagnostyce udarów mózgu.

Materiał i metody. Badaniem objęto 38 pacjentów hospitalizowanych w Oddziale Intensywnej Terapii i Oddziale Neurologii z powodu udarów mózgu. Pacjentów diagnozowano zgodnie z zasadami EBM przy użyciu TK, a następnie wykonywano serię zdjęć przy pomocy kamery termowizyjnej FLIR E 30. Badania były wykonywane w I dobie udaru mózgu po diagnostyce tomograficznej głowy, a następnie w IV dobie po udarze.

Wyniki. Badania wykazały istotne statystycznie ($p < 0.05$) obniżenie temperatury okolicy objętej udarem mózgu w odniesieniu do strony zdrowej zarówno w I jak i w IV dobie pomiaru. Różnica średnich zmian temperatur pomiędzy zawałem mózgu i krwotokiem śródmózgowym w I i IV dobie nie była istotna statystycznie ($P > 0.05$). Różnica średnich zmian temperatur okolic objętych udarem (niezależnie od jego rodzaju) pomiędzy I i IV dobą badania była istotna statystycznie ($p < 0.05$). Różnica średnich zmian temperatur pomiędzy mniejszym i większym ogniskiem w TK w I i IV dobie nie była istotna statystycznie ($P > 0.05$). Nie obserwowano istotnej korelacji średnich zmian temperatur ze stanem klinicznym chorych ocenianych według skali ESS w I dobie ($p > 0.05$).

Wnioski. Kamera termowizyjna jest przydatnym narzędziem w diagnostyce udarów mózgu, jednak nie różnicuje udarów na krwotoczne i niedokrwienne.

Słowa kluczowe: udar mózgu, kamera termowizyjna, tomografia komputerowa, rezonans magnetyczny

Tables: 5

Figures: 0

References: 21

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Address for correspondence / Adres korespondencyjny: Gustaw Wójcik, Department of Rehabilitation, Physiotherapy and Balneotherapy, Medical University of Lublin, 6 Chodźki Str, 20-093 Lublin, Poland, e-mail: gustaww@tlen.pl, phone: +48 81 448 67 83

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Introduction

Stroke is one of the main reasons of morbidity and mortality in the world [1]. Every year about 4.5 ml people in the world die of cerebrovascular accident, of whom 2/3 in non-industrialised countries [2]. In Europe, every year about 1 ml people show the symptoms of stroke, of which 1/3 die, while in 1/3 there remains a disability of various degree [3]. Whereas in Poland, on the basis of epidemiological research conducted at the beginning of the 1990s, it was found that every year the symptoms of stroke occur in about 60 thousand people, half of whom die during the year, while the half who survive demonstrate permanent disability [3,4].

Ischemic strokes (cerebral infarctions) account for 80-85% of all strokes, the remaining 15-20% are hemorrhagic strokes [5]. The clinical picture differs depending on the location of the stroke and its size. The most frequent reason of ischemic strokes is thrombosis appearing locally or in consequence of an arterial embolism or heart embolism. Ischemic stroke may also be caused chemodynamically [6]. Intracerebral hemorrhage is a result of vessel damage, its rupture and bleeding into the brain tissue. It can appear due to hypertension, injury, coagulability disorder, venous malformation, amyloid angiopathy, cocaine or amphetamine abuse. Brain function becomes disturbed when the blood flow in the brain decreases below 50ml/100g/min. Irreversible damage happens when this flow is lower than 30ml/100g/min. When the blood flow through the brain tissue is blocked, the metabolism of this organ becomes disturbed already after 30 seconds. After 1 min. the function of neurons may cease. After a 5-minute blockage in the blood flow anoxia starts a chain reaction which may finally lead to cerebral infarction of the brain [7].

Stroke recognition is based on head CT. CT is a method allowing us to diagnose a hemorrhage and determine its location because, in CT, freshly extravasated blood has significantly higher density than the tissue surrounding it. In case of ischemic stroke more precise seems the examination by means of echo planar imaging technique of diffusion MRI, since early ischemic changes appear with the increased water content; then, the stroke focal area becomes well isolated in Fluid Attenuation Inversion Recovery (FLAIR) and in T2-weighted images [7]. Diffusion MRI is a more reliable method of early brain ischemia detection. This examination allows us to distinguish severe ischemic stroke from other pathological processes. Moreover, it provides additional information on the brain tissue micro-structure [8].

Visual thermography is totally non-invasive method of imaging. It consists of the evaluation of the intensity of infrared radiation in an examined body area and indicating the distribution of temperatures on its surface. In medicine thermography is used to assess heat variations in living organisms during physiological life processes and in pathological states. Because the energy of heat radiation of tissues results from the disorder in blood circulation, it carries a lot of information which can contribute to achieving better therapeutic results. Slight variations in tissue heat may precede the appearance of clinical symptoms and may signal pathologies in various organs and systems. Most pathological states are accompanied by local disturbances in blood circulation in the affected area and changes in the cell metabolism [9,10,11].

Objectives

The aim of the work is to evaluate the usefulness of thermographic camera in the diagnostics of hemorrhagic and ischemic strokes, using the temperature difference between the healthy brain tissue area and the damage-affected area.

Material and methods

The research included 38 patients (9 women and 29 men) hospitalised due to cerebrovascular accident in the Intensive Therapy Ward and Neurology Ward in Tarnobrzeg. Of all the patients included in the study, 28 patients were diagnosed with ischemic stroke (cerebral infarction) while 10 patients with intracerebral hemorrhage. The age of patients ranged from 51 to 78, the average age was 66.5. The patients were diagnosed according to EBM by means of CT, then a series of images were taken by means of the thermographic camera FLIR E 30.

Following their admission to the wards the patients were also examined by a neurologist using the ESS (European Stroke Scale). According to the above scale, the patients were assessed as 0-70 points.

The patients were divided into 2 groups: those whose CT showed a smaller stroke area – up to 5 cm (16 patients) and those with the stroke area larger than 5 cm (22 patients).

Heat was measured by means of thermographic camera in two places: the right temporal area and the left temporal area from the distance of 30 cm. The selected distance was optimal and, simultaneously, minimal to register precise temperatures of the selected surface. These examinations followed the CT diagnostics of the head on the first day of the stroke, and then on the fourth day of the stroke. An hour before the thermographic test the

patients were put in a lying position so that the areas examined did not touch the bedding, and two hours before the examination the head was not physically cooled. These actions were performed in order to achieve reliable temperature measurements.

The results of the examinations were presented as average and standard deviations. The results were developed statistically using the t-Student test for independent variables. The correlation was calculated using the Pearson's test. $P < 0.05$ was assumed as the level of statistical significance.

The research received a positive recommendation of the Board of Bioethics of Medical University in Lublin (KE-0254/84/2013)

Results

The research showed statistically significant ($p < 0.005$) temperature decrease in the stroke area in relation to the healthy area both on the first and the fourth day.

Table 1. Average temperatures of the healthy area and the stroke area and the statistical significance of temperature difference on the first and the fourth day since the onset of the illness

Day	Temperature (°C) Healthy hemisphere	Temperature (°C) Stroke hemisphere	Statistical significance (p)
I	35.55±0.76	35.06±0.77	P=0.007*
IV	35.58±0.75	35.20±0.77	P=0.03*

* Statistical significance

Source: own elaboration

The difference in average temperature changes between cerebral infarction and intracerebral hemorrhage on the first and fourth day was not statistically significant ($P > 0.05$). The data was presented in Table 2.

Table 2. Average temperature changes between cerebral infarction and intracerebral hemorrhage on the first and the fourth day

Day	Average temperature change (°C) Cerebral infarction	Average temperature change (°C) Intracerebral hemorrhage	Statistical significance (p)
I	0.46±0.17	0.54±0.25	P=0.33
IV	0.37±0.15	0.42±0.16	P=0.41

Source: own elaboration

The difference in average temperature changes in the stroke area (irrespective of its type) between the first and the fourth day of examination was statistically significant (0.48 ± 0.19 , 0.38 ± 0.16 , $p = 0.01$). Significantly lower average temperature change was observed on the fourth day of the stroke.

The difference in the average temperature changes in cerebral infarction between the first and the fourth day was statistically significant ($p < 0.05$), however the difference in the average temperature changes in the intracerebral hemorrhage between the first and the fourth day was statistically insignificant ($p > 0.05$). The data was presented in Table 3.

Table 3. Difference in average temperature changes between cerebral infarction and intracerebral hemorrhage between the first and the fourth day

Type of stroke	Average temperature change (°C) Day I	Average temperature change (°C) Day IV	Statistical significance (p)
Cerebral infarction	0.46±0.17	0.37±0.15	P=0.03*
Intracerebral hemorrhage	0.54±0.25	0.42±0.16	P=0.23

*Statistical significance

Source: own elaboration

The difference in average temperature changes between the smaller and the bigger focal area in CT on the first and the fourth day was not statistically significant ($P > 0.05$). The data was presented in Table 4.

Table 4. Difference in average temperature changes between the smaller and the bigger focal area in CT on the first and the fourth day

Day	Average temperature change (°C) Smaller focal area (<5 cm)	Average temperature change (°C) Bigger focal area (>5 cm)	Statistical significance (p)
I	0.41±0.09	0.53±0.24	P=0.07
IV	0.34±0.12	0.41±0.17	P=0.15

Source: own elaboration

The difference in average temperature changes of the smaller focal area in CT between the first and the fourth day was statistically significant ($p<0.05$), however the difference in average temperature changes of the bigger focal area in CT between the first and the fourth day was statistically insignificant ($p>0.05$). The data was presented in Table 5.

Table 5. Difference in average temperature changes of the smaller focal area and the bigger focal area in CT between the first day and the fourth day

Type of focal area	Average temperature change (°C) Day I	Average temperature change (°C) Day IV	Statistical significance (p)
Smaller focal area (<5cm)	0.41±0.09	0.34±0.12	P=0.04*
Bigger focal area (>5cm)	0.53±0.24	0.41±0.17	P=0.06

*Statistical significance

Source: own elaboration

No significant correlation was observed between the average temperature changes and the clinical state of patients in accordance with ESS on the first day ($p=0.53$).

Discussion

The temperature variations between the healthy and the damaged brain areas were analysed in the course of examinations conducted with the use of thermographic camera. These changes were due to disorders in blood perfusion, as a result of which a chain reaction started on the level of neurons, leading to cell function disturbance and, consequently, their death. The examinations showed statistically significant decrease in the temperature in the stroke affected area (irrespective of its type) in relation to the healthy part, both on the first and the fourth day of measurement. Unfortunately, this method appeared non-specific for strokes, since it does not allow us to differentiate between ischemic strokes and hemorrhagic strokes. It can be used for screening evaluation of disturbances in brain perfusion. The difference in average temperature changes in stroke areas (irrespective of its type) between the first and the fourth day of examination was statistically significant. This difference was significantly smaller on the fourth day. Probably on the fourth day of the stroke onset there appear some initial changes connected with the reorganization of the near-stroke zone, as a result of which there appears an almost 30% increase in the heat lost earlier due to brain perfusion disturbances in relation to the first day of stroke onset. The evolution of these changes refers both to disturbances connected with the damage caused by the lack of flow in brain vessels and to the damage connected with vessel rupture and intracerebral hemorrhage [12].

Clinical symptoms are not hemorrhagic stroke specific or ischemic stroke specific, therefore, the imaging examination is necessary in case of each individual patient . High attenuation blood image make possible to clinically differentiate between hemorrhage and cerebral infarction and, therefore, CT is generally used as an initial imaging examination in the ad hoc evaluation of the patient with brain stroke, particularly, if thrombotic treatment is planned [13]. Kidwell et al. [14] prove in their research that MR can also successfully exclude the presence of acute hemorrhage, and certain sequences, e.g. DWI, are sensitive in imaging the earliest ischemic changes. However, Han et al. [15] report that the DWI sequence in diffusion MRI is often unreliable and the frequency range of false negative diffusion is from 3.5% to 25% . Because of the easier access to CT in most emergency wards, this examination still continues to be the method selected in the initial evaluation of the patient, whereas the MR examination, performed later, may provide additional information. Thanks to MR, it is possible to discover small, permanent changes which would not be noticed earlier. In clinical practice, it is also of significant importance to differentiate between the stroke and a temporary ischemic attack (TIA). Traditional definition of TIA as a focal

deficit lasting up to 24 hours assumes a much longer time period than it is necessary in the MRI to appear as a stroke. It was reported that 50% of patients demonstrating a less than 24-hour neurological deficit show the symptoms of ischemia in diffusion MRI, while 50% of these patients show the symptoms of fixed infarction in the next T2-weighted images [16]. Johnston et al. [17] state that the risk of stroke and other vascular incidents is higher after the appearance of TIA than after the stroke (CVA). It contradicts the validity of the slower approach to diagnostics and treatment of patients with TIA. The risk of stroke following TIA after 90 days is about 10%, half of which happens on the first two days. 25% of patients with TIA have a stroke or other vascular incidents within the next three months. Allmendinger et al [18] describe in their work the benefits of perfusion CT as the most frequently used diagnostic tool in acute ischemic stroke evaluation. It can be performed quickly and is generally accessible. Kontas et al. [19] list the benefits of perfusion CT as the most advanced method providing important information on chemodynamics of capillaries in brain parenchyma. However, they highlight the X-ray radiation doses which the patient receives during the examination. Amar [20] also points out to the early use of CT and MR in brain perfusion evaluation and determination of the ischemic focal area. Proper, fast and correct diagnostics allows selecting patients to thrombotic treatment. Merino and Warach [21] emphasise that diffusion MRI is more precise than CT in detecting ischemic strokes. MR defines a wider range of acute and chronic vascular brain disorders than CT. Moreover, it is more sensitive in detecting acute ischemic incidents of the brain and, consequently, it can assist in taking decision on initiating correct treatment.

Using thermographic camera in early detection of brain flow pathologies may be beneficial for patients with less specific symptoms of brain strokes, yet, it does not prove itself as a diagnostic tool in differentiating between them. Therefore, it is necessary to conduct imaging examinations, such as CT, in order to determine precisely the brain pathology, even though this technique is connected with harmful effects of radiation on living organisms. Perfusion examinations carry even greater risk for the patient since they are connected with increased radiation dose and an additional intravenous injection of the contrast agent. Thermographic camera is a measuring tool which does not emit any radiation, therefore it does not pose a threat to human life. Conducting examinations using the infrared radiation is totally harmless for patients however, unfortunately, this method is characterised by very low sensitivity. Hopefully, the advance of technology will increase the sensitivity of detectors in thermographic cameras, which will improve their diagnostic possibilities.

Conclusions

1. Thermographic camera is a useful and safe tool in brain stroke diagnosis. However, this method does not offer a possibility to differentiate between hemorrhagic and ischemic strokes, which is its defect.
2. Temperature change in the stroke area does not depend on the size of the focal area in CT.
3. Temperature change in the stroke area does not correlate with the clinical state of patients.

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THE PRESENCE OF ANTI-EBV ANTIBODIES AS THE CAUSE OF FALSE POSITIVE RESULTS IN THE DIAGNOSTICS OF LYME BORRELIOSIS

OBECNOŚĆ PRZECIWCIAŁ ANTY-EBV JAKO PRZYCZYNA WYNIKÓW FAŁSZYWIE POZYTYWNYCH W DIAGNOSTYCE BORELIOZY Z LYME

Dorota Plewik^{1(A,B,C,D,E,F,G)}, Małgorzata Tokarska-Rodak^{2(A,B,E,G)}, Justyna Paszkiewicz^{2(B)}

¹Pope John Paul II State School of Higher Education in Biała Podlaska, Innovation Research Centre, Poland

²Pope John Paul II State School of Higher Education in Biała Podlaska, Institute of Health Sciences, Poland

Authors' contribution

Wkład autorów:

A. Study design/planning

zaplanowanie badań

B. Data collection/entry

zebranie danych

C. Data analysis/statistics

dane – analiza i statystyki

D. Data interpretation

interpretacja danych

E. Preparation of manuscript

przygotowanie artykułu

F. Literature analysis/search

wyszukiwanie i analiza literatury

G. Funds collection

zebranie funduszy

Summary

Background. Laboratory diagnosis of Lyme borreliosis is based on the detection of anti-*B. burgdorferi* antibodies. Mononucleosis infection can lead to false positive results in serological diagnosis of Lyme borreliosis.

Materials and methods. The experimental group comprised 60 patients diagnosed with Lyme borreliosis and 106 individuals professionally exposed to tick bites, with a positive result of ELISA anti-*B. burgdorferi* IgM test. The control group consisted of 150 healthy individuals. Immunoassay of antibodies to the Epstein-Barr viral capsid antigen (EB-VCA) in the IgM class was carried out by the means of Western blot assay.

Results. In two patients diagnosed with borreliosis the presence of IgM antibodies to EB-VCA was confirmed. In the group of individuals professionally exposed to tick bites and in the control group no anti-EB-VCA IgM antibodies were found.

Conclusions. Anti-EBV IgM antibodies can lead to obtaining false positive results in Lyme borreliosis diagnostics. In the cases when clinical symptoms are not characteristic for Lyme borreliosis, and are accompanied by a positive result of anti-*B. burgdorferi* antibodies assay only in the IgM class, one has to take into consideration the occurrence of cross-reaction in the Western blot test and carry out differential diagnosis with infectious mononucleosis.

Keywords: Lyme borreliosis, *Borrelia burgdorferi*, Epstein-Barr Virus, EB-VCA, Western blot

Streszczenie

Wprowadzenie. Diagnostyka laboratoryjna boreliozy z Lyme opiera się na wykryciu przeciwciał anti-*B. burgdorferi*. Wyniki fałszywie pozytywne w diagnostyce serologicznej boreliozy z Lyme mogą być spowodowane mononukleozą zakaźną.

Materiał i metody. Grupę badaną stanowiło 60 pacjentów z potwierdzoną boreliozą z Lyme oraz 106 osób narażonych zawodowo na pokłucia przez kleszcze z pozytywnym wynikiem testu ELISA anti-*B. burgdorferi* IgM. Grupę kontrolną stanowiło 150 zdrowych osób. Oznaczenie przeciwciał przeciwko antygenowi kapsydowemu wirusa Epstein-Barr (EB-VCA) w klasie IgM wykonano metodą Western blot.

Wyniki. U dwóch pacjentów z potwierdzoną boreliozą stwierdzono obecność przeciwciał IgM przeciwko EB-VCA. W grupie osób narażonych zawodowo na pokłucia przez kleszcze oraz w grupie kontrolnej nie wykazano obecności przeciwciał IgM anti-EB-VCA.

Wnioski. Przeciwciała anti-EBV IgM mogą powodować uzyskanie wyników fałszywie pozytywnych w diagnostyce boreliozy z Lyme. W przypadku gdy objawy kliniczne są mało charakterystyczne dla boreliozy z Lyme i towarzyszy im pozytywny wynik oznaczenia przeciwciał anti-*B. burgdorferi* tylko w klasie IgM, należy wziąć pod uwagę możliwość wystąpienia reakcji krzyżowej w teście Western blot i przeprowadzić diagnostykę różnicową z mononukleozą zakaźną.

Słowa kluczowe: borelioza z Lyme, *Borrelia burgdorferi*, wirus Epstein-Barr, EB-VCA, Western blot

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Background

Lyme borreliosis is a disease caused by *Borrelia spirochetes*, in the course of which the skin, joints, the nervous system and heart are infected. In Poland the following types occur: *B. burgdorferi sensu stricto* (s.s.), *B. afzelii*, *B. garinii*, *B. valaisiana* and *B. lusitaniae* [1]; their reservoirs are free-living animals, mainly rodents, and their vectors are *Ixodes spp.* ticks. Human infection is the result of foraging a tick attached to the skin, through its saliva or vomit. In the first phase of infection *Borrelia*

Address for correspondence / Adres korespondencyjny: Dorota Plewik, Innovation Research Centre, Pope John Paul II State School of Higher Education in Biała Podlaska, Sidorowska 105, 21-500 Biała Podlaska, e-mail: dorotaplewik@gmail.com, phone: +48 83 344 69 04

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burgdorferi sensu lato spread in the skin in the area of bite, usually causing early dermal change in the form of *erythema migrans*. Rarely, the early stage of the illness takes the form of *Borrelial lymphoma*. Thereafter the spirochetes ingress to different organs together with blood and lymph. The infection's course can involve arthritis or neuroborreliosis, rarely myocarditis. The patients with Lyme borreliosis who were wrongly diagnosed or were not properly treated can develop *acrodermatitis chronica atrophicans*, arthritis or irreversible neurological changes. The clinical course of the inflammation may be varied, which makes the proper diagnosis difficult [2]. Diagnosis of Lyme borreliosis in the case of *erythema migrans* is made on the basis of clinical symptoms, in all other clinical manifestations diagnostic tests are necessary [3]. The basic laboratory test in Lyme borreliosis diagnostics is assessing the level of anti-*B. burgdorferi* antibodies.

In order to assay the level of specific antibodies, the ELISA immunoenzymatic method, characterized by high sensitivity, is applied. However, in patients suffering from autoimmune diseases and in cases of cross-reaction with antibodies occurring in inflammations caused by other pathogens, false positive results can be obtained. Therefore, implementing a test of high specificity, enabling to detect antibodies to specific *B. burgdorferi* antigens is necessary. Currently a two-stage system of Lyme borreliosis diagnostics has to be applied. The first stage involves carrying out the ELISA test, and borderline or positive results are confirmed by more specific Western blot (Wb) test. Wb tests used in Lyme borreliosis diagnostics should be characterized by specificity not less than 95%. The most common underlying cause of false positive results is the presence of rheumatoid factor, systemic lupus erythematosus, infection with other spirochetes or infectious mononucleosis [4,5].

Infectious mononucleosis is caused by the Epstein-Barr virus (EBV, *Human herpesvirus 4*). The most common symptoms are pyrexia, pharyngitis, tonsillitis, lymphadenopathy, splenomegaly, flu-like symptoms and the presence of atypical lymphocytes in the blood. The infection often involves non-specific symptoms or does not involve any symptoms. In the diagnostics the assay of specific antibodies to capsid antigen VCA in the IgM and IgG classes, and to nuclear antigens (aEBNA), as well as to non-specific heterophile antigens is used [6].

Both Lyme borreliosis and infectious mononucleosis can have atypical clinical course, therefore in many cases laboratory tests' results are of key importance. The occurrence of cross-reactions in serological tests, and thereby obtaining false positive results, may lead to wrong diagnosis, and consequently can result in the implementation of unsuitable treatment.

The aim of work was determination of the frequency of anti-EBV IgM antibodies occurrence and their influence on Lyme borreliosis diagnostics.

Materials and methods

Three groups participated in the study:

- Group I consisted of 200 patients with suspicion of Lyme borreliosis, who were tested with serological diagnostics in the years 2007-2008. The group comprised 90 women aged 24-17, and 110 men aged 21-66. Patients with positive or borderline ELISA test results were tested with the Western blot test during the second stage of Lyme borreliosis diagnostics. From the group of patients who revealed positive results, 60 subjects were randomly chosen and tested with the Wb test including capsid antigen EBV (GenzymeVirotech GmbH).
- Group II consisted of 275 persons professionally exposed to tick bites: foresters and farmers from Lublin Voivodeship, 85 women aged 20-64, and 190 men aged 19-86. Blood samples were taken in the years 2012-2013. In all samples anti-*B. burgdorferi* antibodies assay was performed by the means of ELISA test. 106 individuals with positive or borderline ELISA test results in the IgM class underwent Wb test, involving capsid antigen EBV.
- Group III was a control group and comprised 150 healthy individuals, 101 women aged 16-35, and 49 men aged 18-34. Blood samples were taken in the years 2013-2015. All subjects underwent WB test including capsid antigen EBV.

In the examinations the *Borrelia* LINE ImmunoblotIgG/IgM (GenzymeVirotech GmbH) test was applied, which enabled to assay antibodies to the EB-VCA-gp125 antigen in the IgM class as well as to specific antigens *B. burgdorferi* (OspC, VlsE, p39, p83, BBA36, BBO323, Crasp3, pG) in the IgM or IgG classes. The test was carried out according to the manufacturer's recommendations.

The research was approved by the Bioethics Committee of the Medical University of Lublin (No. KE-0254/12/13 and KE-0254/183/2014).

Results

In the Group I two patients were diagnosed with the presence of IgM antibodies to EB-VCA-gp125. One patient revealed also antibodies to the OspC and the p39 antigens in the IgM class and antibodies to the p39 antigen in the IgG class. The second patient revealed the presence of antibodies to the p39 antigen in the IgM and IgG

classes. Both in Group II and in the control group no presence of IgM antibodies to EB-VCA-gp125 was found. Data concerning the frequency of occurrence of specific anti-*B. burgdorferi* antibodies in the groups I and II was published earlier [7, 8].

Discussion

The tests confirmed the occurrence of cross-reactions while assaying anti-*B. burgdorferi* antibodies by the means of the ELISA method. The underlying cause of cross-reactions can be other infectious diseases: syphilis, rickettsioses, mononucleosis infection, Cytomegalovirus (CMV), Varicella-zoster virus (VZV) and Herpes simplex virus-2 infections [9, 10]. In the majority of cases false positive results can be excluded upon the application of the Wb test [11,12]. Even though it is a very rare phenomenon, a false positive result can be obtained in the Western blot method. Goossens et al. examined blood samples coming from 40 patients with diagnosed infectious mononucleosis in order to determine the occurrence of anti-*B. burgdorferi* antibodies in the IgM class. A positive result in the ELISA method was obtained in 53% of samples, whereas in the WB test in 35% of samples positive result for the OspC or the p39 antigen was obtained [13]. In own research involving two patients, who in the Wb test revealed positive results for IgM anti-*B. burgdorferi*, anti-EBV IgM antibodies to capsid antigen were also present. The results confirm the possibility of cross-reactions between anti-EBV antibodies and specific *B. burgdorferi* OspC and p39 antigens.

Anti-EB-VCA IgM antibodies are present in 95% of patients infected with EBV during first several days of infection, and then disappear within 2-3 months. Therefore these antibodies can lead to obtaining false positive results in the diagnostics of different diseases only when the infection with EBV took place within the last few months. Such situations happen rarely, which is confirmed by the lack of anti-EB-VCA antibodies in the group of individuals professionally exposed to tick bites and in the control group.

False positive results for anti-*B. burgdorferi* in the IgM class can be obtained also in cases of other viral diseases. Woelfle et al. described a case of an 8-year-old boy with the facial nerve palsy in the course of meningitis and encephalomyelitis caused by Varicella-zoster virus, in whose blood anti-*B. burgdorferi* antibodies to the OspC and the p41 antigens were present in both ELISA and Wb tests [14]. In the research discussed above Goossens et al. mentions 21% of patients with acute Cytomegalovirus infection, who revealed the presence of antibodies to the OspC and the p39 *B. burgdorferi* antigens [13].

Seriburi et al. in retrospective studies on patients with possible Lyme borreliosis verified the diagnosis basing on the epidemiological and clinical data. 27.5% of patients were recognized with false positive results for Wb antibodies assay; in all cases it were IgM [15].

The number of cases of Lyme borreliosis is steadily increasing. According to the National Hygiene Institute (PZH) in 2004 in Poland 3882 cases of Lyme borreliosis were reported, whereas in 2014 the number increased to 13866 cases [16, 17]. Bearing in mind the frequency of Lyme borreliosis occurrence and the fact that the clinical picture may be diversified, it is extremely important to implement reliable laboratory diagnostics. In questionable cases, especially when the positive result is based only on the occurrence of antibodies in the IgM class, it is important to apply differential diagnostics in order to exclude the possibility of a false positive result. Literature data pointing out that in the first place infectious mononucleosis should be excluded is confirmed by own research. However, one should not forget about other infections, e.g. CMV, VZV, *T. pallidum*, especially in cases of neuroinfections with dramatical course.

Conclusions

1. Anti-EBV IgM antibodies can lead to obtaining false positive results in Lyme borreliosis diagnostics.
2. In the cases when clinical symptoms are not characteristic for Lyme borreliosis and are accompanied by a positive result of anti-*B. burgdorferi* antibodies assay only in the IgM class, one has to take into consideration the possibility of cross-reaction in the Western blot test and carry out differential diagnosis with infectious mononucleosis.

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Part II. Physical activity of social and professional groups
Dział II. Aktywność fizyczna grup społecznych i zawodowych

DIVERSITY OF PHYSICAL ACTIVITY AMONG THE SCHOOL YOUTH
DEPENDING ON THE TYPE OF PLACE OF RESIDENCE

ZRÓŻNICOWANIE AKTYWNOŚCI FIZYCZNEJ MŁODZIEŻY SZKOLNEJ
W ZALEŻNOŚCI OD RODZAJU MIEJSCA ZAMIESZKANIA

Józef Bergier^{1(A,B,C,D,E,F,G)}, Ewelina Niżnikowska^{1(A,B,D,F)}, Barbara Bergier^{1(A,B,D,F)},
Ján Junger^{2(A)}, Pongrácz Ács^{3(A)}, Ferdinand Salonna^{4(A)}

¹Pope John Paul II State School of Higher Education in Biała Podlaska, Poland

²University of Presov in Presov, Slovakia

³University of Pécs, Hungary

⁴Palacký University of Olomouc, The Czech Republic

Authors' contribution

Wkład autorów:

A. Study design/planning

zaplanowanie badań

B. Data collection/entry

zebranie danych

C. Data analysis/statistics

dane – analiza i statystyki

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interpretacja danych

E. Preparation of manuscript

przygotowanie artykułu

F. Literature analysis/search

wyszukiwanie i analiza literatury

G. Funds collection

zebranie funduszy

Summary

Background. The objective of the study was to reveal diversity of physical activity among the school youth depending on the type of place of residence (single-family house, block of flats).

Material and methods. The research conducted in 2015 covered 646 students from junior high schools and post-gymnasium schools in Biała Podlaska with an average age of $18,8 \pm 0,84$ years. The method of research which was applied was the International Physical Activity Questionnaire (IPAQ) within its full form.

Conclusions. It was indicated that the school youth, including in particular boys residing in family houses show higher level of physical activity than their peers living in blocks of flats.

Keywords: school youth, physical activity, IPAQ, place of residence

Streszczenie

Wprowadzenie. Celem pracy było ukazanie zróżnicowania aktywności fizycznej młodzieży szkolnej w zależności od rodzaju miejsca zamieszkania (dom rodzinny, blok).

Materiał i metody. Badaniami, które przeprowadzono w 2015 r. objęto 646 uczniów szkół gimnazjalnych i ponadgimnazjalnych w Białej Podlaskiej o średniej wieku $18,8 \pm 0,84$ lat. Jako metodę badań wykorzystano Międzynarodowy Kwestionariusz Aktywności Fizycznej (IPAQ) w wersji długiej.

Wnioski. Wykazano, że młodzież szkolną w tym szczególnie chłopców zamieszkających w domach rodzinnych cechuje wyższy poziom aktywności fizycznej niż ich rówieśników mieszkających w blokach.

Słowa kluczowe: młodzież szkolna, aktywność fizyczna, IPAQ, miejsce zamieszkania

Tables: 4

Figures: 6

References: 24

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Background

Nowadays we may observe that sedentary lifestyle characterized the behaviors of the youth in a large degree. Within the research conducted by HBSC [1] it was noted that almost 1/4 of the school youth conducts moderate physical activity for a minimum of 60 minutes less often than 3 times a week. The research results confirm the significant differences dependent on gender and age. Girls and the older youth are definitely less active.

Based on the results of research published by Polish authors [2, 3, 4, 5, 6] it was also observed that the Polish youth is characterized by small physical activity. These results are convergent with the world trends observed [7, 8, 9, 10, 11, 12].

Witana and Szpak [13] noted that a passive way of spending pastime is preferred by both the junior school pupils and the high school pupils and the most popular forms of spending pastime by them include watching TV, playing computer games and surfing the Internet.

Address for correspondence / Adres korespondencyjny: Józef Bergier, Pope John Paul II State School of Higher Education in Biała Podlaska, Siderska 95/97, 21-500 Biała Podlaska, e-mail: j.bergier@pswbp.pl, phone: +48 83 344 99 00

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Sedentary lifestyle dominates among the youth of most developed countries, including in particular the American youth, where this phenomenon was observed earliest [14]. Within these tests a low level of physical activity was observed which is the basic problem of public health. Particular significance is obtained by the results concerning the youth which undertakes physical activity at a moderate level of less than 3 times a week and which spends at average 5 hours a day in front of a TV. These researches are convergent with the results obtained by Piątkowska [15] who discovered that a group which spends the largest volume of time sitting are Poles below 19 years of age. The youth spends while sitting down almost 7 hours a day during a week day. According to Wojtyła et al. [16] among the boys motivation behind a significant physical effort is more often related to a wish to increase of muscles, whilst girls more often increase their physical activity during a diet. World Health Organization [17] recommends for persons at a young age at least 60 minutes of physical activity of moderate intensity for the majority of days a week. The majority of days signifies a systematic effort of moderate intensity not exceeding 130 heartbeats per minute for 4-5 days a week.

Appropriate level of physical activity at the young age positively impact motoric development, psychological and social development of a young person and reveals a need of continuing the physical activity for the entire life. Puberty period is a critical moment in which physical activity and participation in various types of its forms is very important.

The purpose of research was the assessment of physical activity of the youth as well as defining whether the type of place of residence (single family house or flat in block of flats).

Material and methods

The research covered 646 pupils from the 3rd class of junior high school and 1st and 2nd class of high schools in Biała Podlaska. The specificity of demographic features with consideration of gender, age and place of residence has been presented in table 1. Within the framework of diagnostic survey method the tool which was applied was an International Physical Activity Questionnaire (IPAQ) in its long form.

Table 1. Demographic features of the research participants

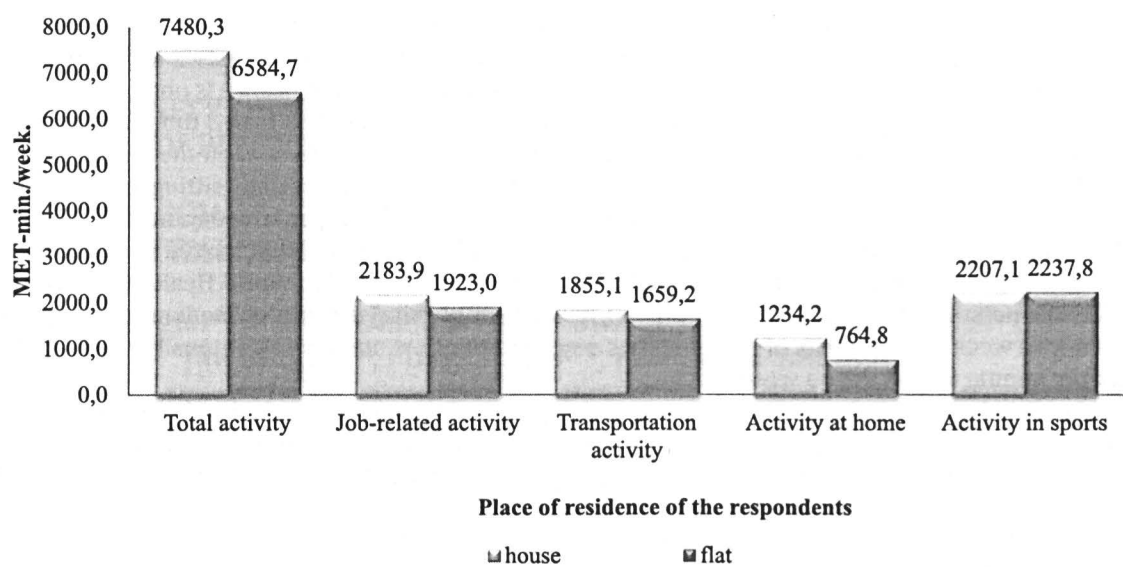
Gender		
girls	boys	
322 (49,85%)	324 (50,15%)	
Place of residence		
single family house	flat in block of flats	
423 (65,48%)	223 (34,52%)	
Class		
3rd class in junior high school	1st class in high school	2nd class in high school
215 (33,28%)	219 (33,90%)	212 (32,82%)

Results

The level of physical activity of overall number of pupils with consideration of place of residence

The tested school youth living in single family houses is characterized by higher total physical activity - 7480,3 MET-min./week than youth living in blocks of flats - 6584,7 MET-min./week, however, the difference is not statistically significant.

A statistically significant dependence occurred among the respondents residing in single family houses within the area of physical activity related to commuting and at work inside and around the house (fig. 1, table 2).



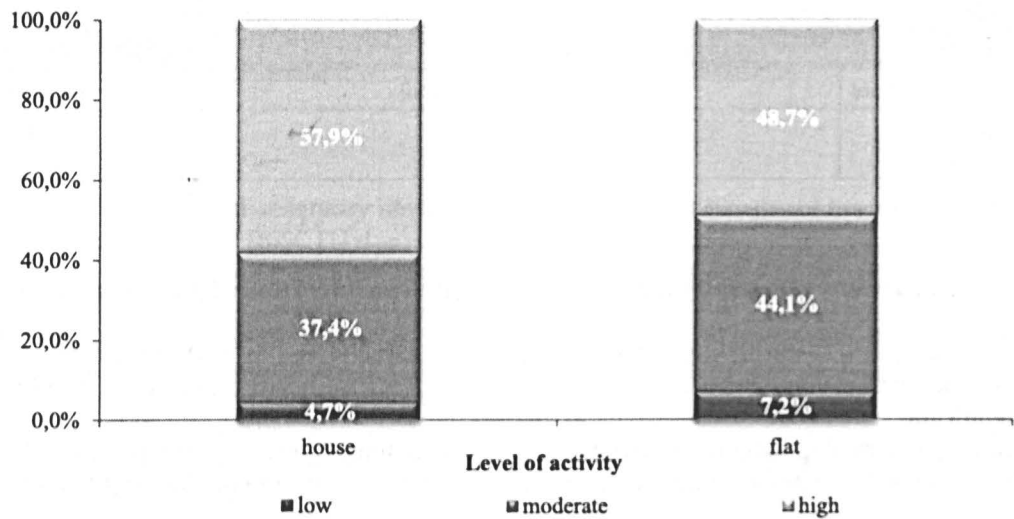
*- significant diversity at $p<0,05$
Figure 1. Areas of physical activity of pupils considering place of residence of the respondents

Table 2. Diversity of areas of physical activity of pupils considering the place of residence of respondents

U Mann-Whitney'S test				
Area of activity	Sum of ranks		Z	p
	single family house	flat in block of flats		
Total activity	139324	69012	1,20	0,2308
Activity at work	137824	70512	0,53	0,5951
Activity while commuting	141139	67197	2,01	0,0449*
Activity at home	148131	60204	5,12	0,0000*
Activity in sport	134760	73576	-0,83	0,4057

*- significant diversity at $p<0,05$

These results confirm the significant differences concerning three levels of physical activity: low, moderate, high (fig. 2).

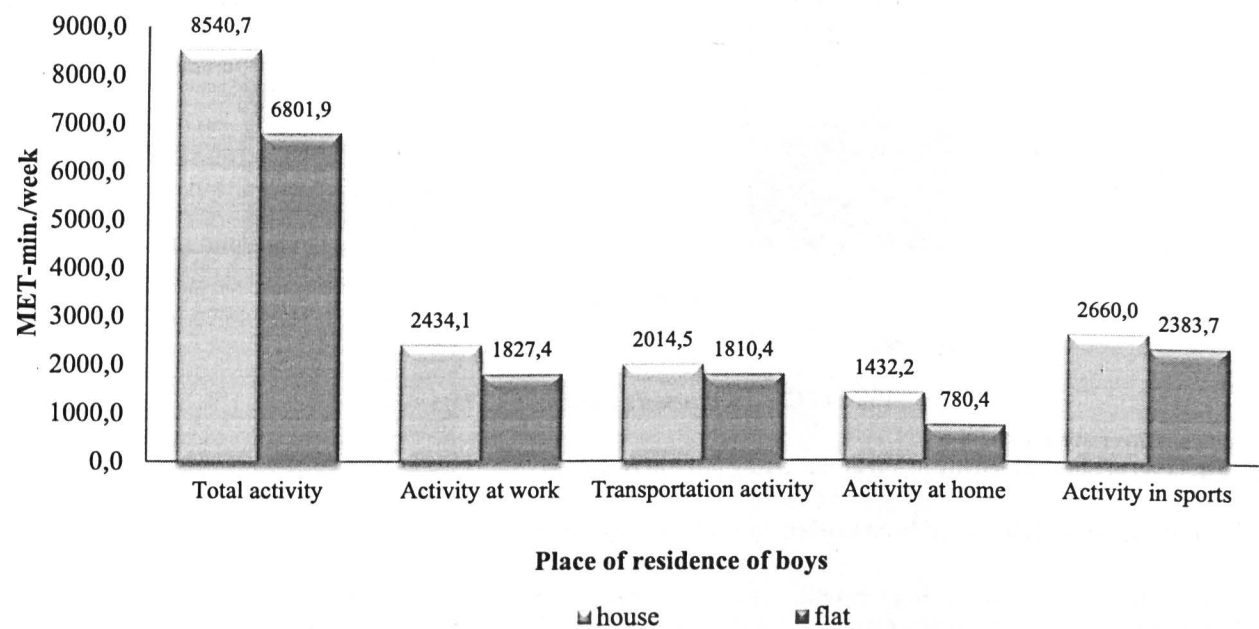


Value of Chi test Pearson's square: $\chi^2=5,58$; $p=0,0614$

*- significant diversity at $p<0,05$
Figure 2. Level of physical activity of pupils considering place of residence

Level of physical activity of boys with consideration of place of residence

The analysis of physical activity in relation to boys indicates significantly greater values among those residing at home - 8540,7 MET-min./week than those living in blocks of flats - 6801,9 MET-min./week, and activity during housework, respectively 1432,2 MET-min./week and 780,4 MET-min./week (fig. 3, table 3).



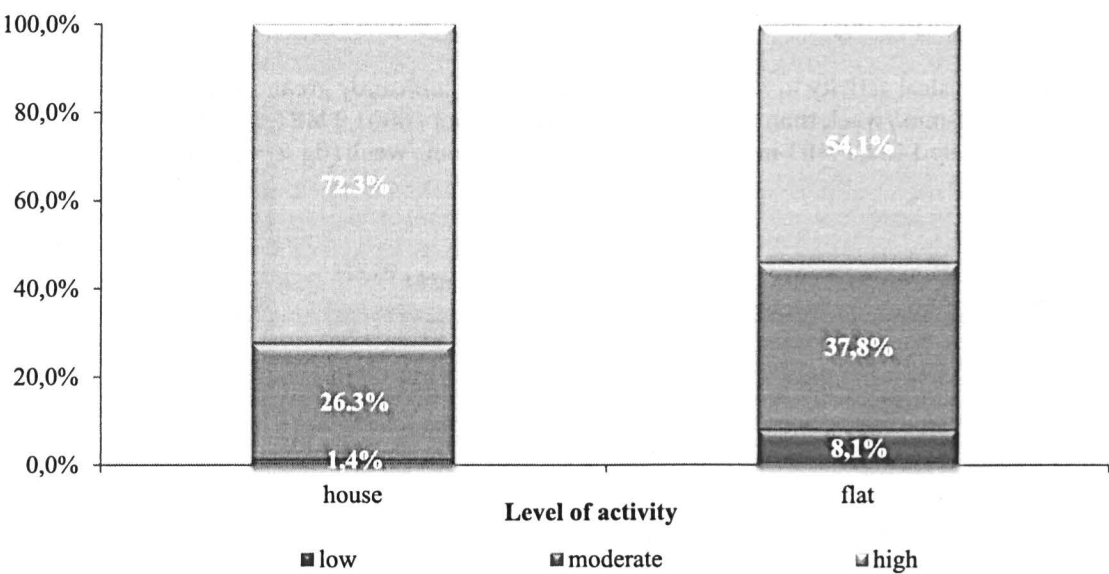
*- significant diversity at $p<0,05$
Figure 3. Areas of physical activity of boys considering place of residence of the respondents

Table 3. Diversity of areas of physical activity considering place of residence of the respondents

U Mann-Whitney'S test				
Area of activity	Sum of ranks		Z	p
	single family house	flat in block of flats		
Total activity	36251	16399	2,05	0,0407*
Activity at work	35480	17171	1,08	0,2787
Activity while commuting	36166	16484	1,94	0,0523
Activity at home	38324	14327	4,64	0,0000*
Activity in sport	35225	17426	0,76	0,4446

*- significant diversity at $p<0,05$

Results of significant differences in favor of boys residing in houses are confirmed by the collation including the level of physical activity of pupils (fig. 4).



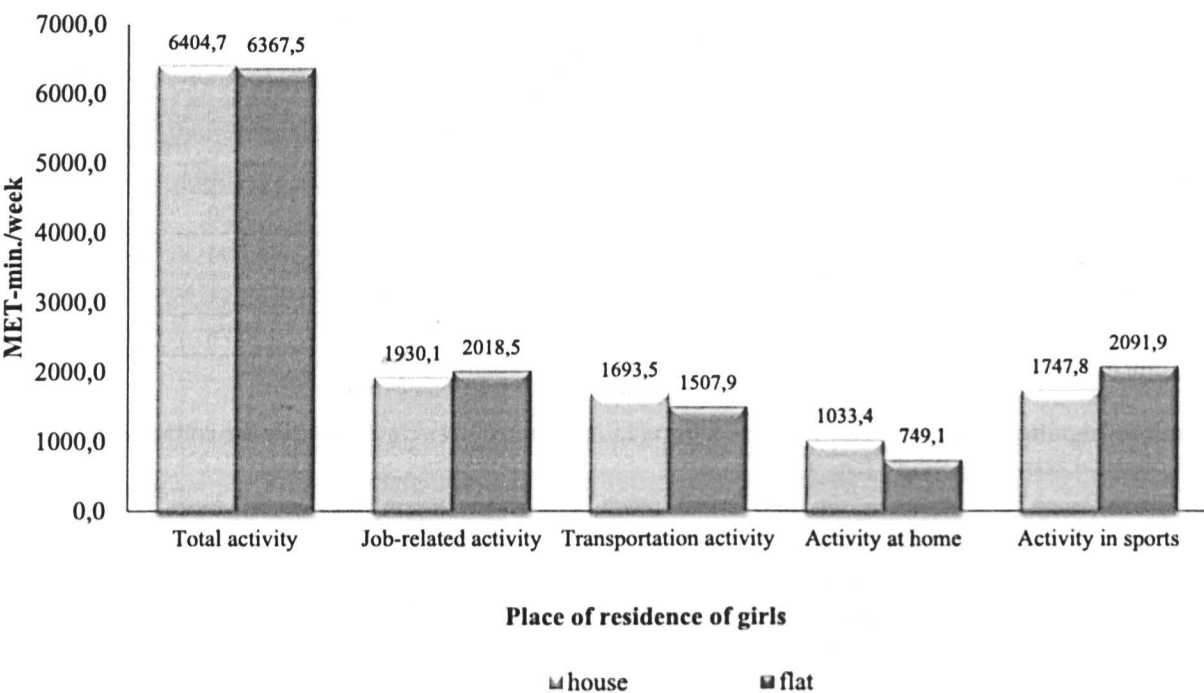
Value of Chi test Pearson's square $\chi^2=15,74$; $p=0,0004^*$

**- significant diversity at $p<0,05$*
Figure 4. Level of physical activity of boys considering place of residence

Level of physical activity of girls considering place of residence

Analysis of physical activity of girls with consideration of place of residence indicated almost identical level of total physical activity. Statistically significant differences occurred in individual areas.

Girls residing in single family houses were characterized by larger activity in housework and a significantly lower one in sports activity (fig. 5, table 4).



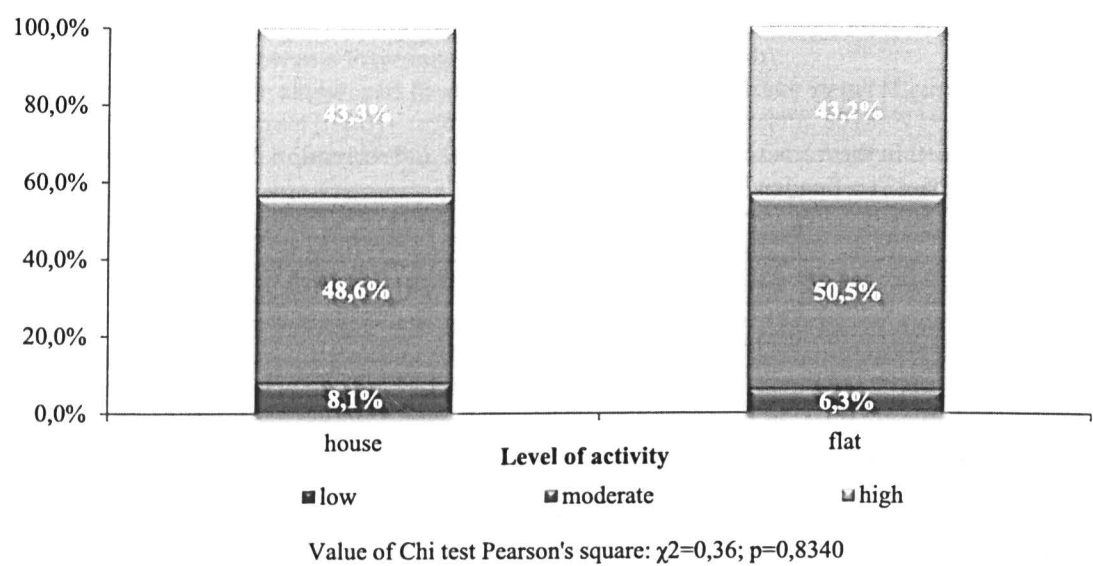
**- significant diversity at $p<0,05$*
Figure 5. Areas of physical activity of girls considering place of residence of respondents

Table 4. Diversity of areas of physical activity of girls considering place of residence of the respondents

U Mann-Whitney'S test				
Area of activity	Sum of ranks		Z	p
	single family house	flat in block of flats		
Total activity	33466	18216	-0,43	0,6636
Activity at work	33683	17998	-0,16	0,8728
Activity while commuting	34466	17216	0,83	0,4075
Activity at home	35773	15909	2,48	0,0131*
Activity in sport	32112	19569	-2,15	0,0318*

*- significant diversity at $p<0,05$

No significant differences between analyzed groups in the levels of physical activity (fig. 6).



*- significant diversity at $p<0,05$

Figure 6. Level of physical activity of girls considering place of residence

Discussion

In Poland in recent times the problem of assessment of physical activity is conducted more and more often by means of International Physical Activity Questionnaire [6, 18, 19, 20, 21]. It enables obtaining a comprehensive picture of physical activity among the respondents and not just the information on participation in sports and recreation activities. Despite multiple researches concerning physical activity factors which determine its level are still searched for.

Among the factors which determine the level of physical activity of the school youth the most frequently used test is diversity in terms of gender [19, 22, 23]. Search much less frequently concerns diversity of the level of physical activity of the school youth depending on its origins-countryside, city [3, 24]. Within the country literature there is however no place for scientific elaborations concerning diversity of physical activity in terms of place of everyday residence (single family house or block of flats).

The hereby research among the youth did not reveal any significant differences in the level of overall physical activity depending on the type of place of residence. Such differences occurred in favor of those who live in their own homes within the area of commuting and house works. It was indicated also that there is a diversity of physical activity among boys and girls depending on the type of place of their residence. It is the boys who live in houses who are characterized by greater total physical activity in the area of house works than their peers living in blocks of flats.

Other diversities occurred due to type of place of residence among girls. No significant diversities were noted in the scope of their total physical activity. Such differences were noted however within two areas of physical activity. Girls living in houses are characterized by significantly higher activity within the area of house works and a significantly lower sports activity.

To sum up, one must note that place of residence in single family house is a factor which determines higher physical activity within certain areas of physical activity, which occurs in case of boys to a larger degree.

Conclusions

Search for links between place of residence (in single family house or block of flats) in terms of physical activity of the school youth enabled the formation of the following conclusions:

1. Total number of pupils living in a single family house is characterized by significantly higher physical activity in the area of commuting and house works.
2. Boys who live in single family houses are characterized by significantly higher total physical activity and activity in house work.
3. Girls living in single family houses are characterized by significantly higher physical activity in the area of house work and lower one in recreation and sport.

Acknowledgements

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SUBJECTIVE HEALTH PROFILES AMONG UKRAINIAN STUDENTS OF MEDICAL VOCATIONAL SCHOOL

SUBIEKTYWNE PROFILE ZDROWIA WŚRÓD UKRAIŃSKIEJ MŁODZIEŻY SZKOLNEJ STUDIUM MEDYCZNEGO

Anatolii Tsos^{1(A,B,D,E,F)}, Oleksandr V. Oliynyk^{2(C,F,G)}, Adam Szepeluk^{2(C,F)}

¹Lesya Ukrainka Eastern European National University, Lutsk, Ukraine

²Pope John Paul II State School of Higher Education in Biała Podlaska, Poland

Authors' contribution

Wkład autorów:

A. Study design/planning

zaplanowanie badań

B. Data collection/entry

zebranie danych

C. Data analysis/statistics

dane – analiza i statystyki

D. Data interpretation

interpretacja danych

E. Preparation of manuscript

przygotowanie artykułu

F. Literature analysis/search

wyszukiwanie i analiza literatury

G. Funds collection

zebranie funduszy

Summary

Background. Understanding various dimensions of health is a key factor to properly identify health risks. The purpose of the research is to acquire knowledge concerning positive health and survival skills by the Ukrainian students of Medical Vocational School in Lutsk.

Material and methods. The study group comprised 467 female students aged 15-25 years old who were the attendants of Postsecondary Vocational School in Lutsk on: Pharmacy, Medicine, Obstetrics, Nursing and Laboratory Diagnostics specialties.

A subjective questionnaire was used, which focused on: somatic, mental and social health profiles together with survival skills.

Results. The results indicated the intensification of individual profiles, with the highest value of social health. Somatic health identified HR as its highest index, for mental health it was tolerance and for social health- respecting basic values. When it comes to the survival skill health profile tolerating body imbalance obtained the highest index.

Conclusions. Most of the specialties showed a domination of different health profiles, which allowed to demonstrate forms of self-reported health models from the specialties of Nursing and Medicine.

Keywords: subjective health profiles, Ukrainian students, medical majors

Streszczenie

Wprowadzenie. Wiedza o różnych wymiarach zdrowia jest koniecznym warunkiem jego właściwego rozpoznania. Celem badań jest poznanie wiedzy o poczuciu zdrowia pozytywnego i zdolności przetrwania przez ukraińską młodzież ze Studium Medycznego w Łucku.

Materiał i metody. Badaniami objęto 467 uczennic w wieku 15-25 lat będących słuchaczkami Studium Policealnego w Łucku na kierunkach: farmacja, medycyna, położnictwo, pielęgniarstwo i diagnostyka laboratoryjna.

Zastosowano kwestionariusz subiektywnej oceny profili zdrowia: somatycznego, psychicznego, społecznego i zdolności przetrwania.

Wyniki. W wyniku badań wykazano wyraźne nasilenie określonych profili przy najwyższej wartości zdrowia społecznego. W zdrowiu somatycznym najwyższy wskaźnik cechuje HR, w zdrowiu psychicznym najwyższy wskaźnik uzyskała tolerancja, w zdrowiu społecznym najwyższa wartość przypada respektowaniu naczelnych wartości. W profilu zdrowia zdolności przetrwania najwyższy wskaźnik uzyskało tolerowanie zakłóceń równowagi.

Wnioski. Większość kierunków kształcenia wykazało dominację różnych profili zdrowia, co pozwoliło na przedstawienie swego rodzaju wzorów samooceny zdrowia z kierunków kształcenia młodzieży z pielęgniarstwa i medycyny.

Słowa kluczowe: subiektywne profile zdrowia, młodzież ukraińska, kierunki medyczne

Tables: 6

Figures: 0

References: 15

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Introduction

According to Eriksson and Lindstrom [1] human health is understood as a group of surfaces specified as: physical (also called somatic), mental, social, spiritual, environmental and sexual health. Physical health is best identified in the literature. It provides a foundation for other dimensions of health. A new element in these studies is the methodology of different dimensions of health initiated by Kalina [2]. According to Szymborski and Jakóbiak [3], Polish students' health is a highly neglected area of medicine and health policy. Because of that, a particular importance,

Address for correspondence / Adres korespondencyjny: Adam Szepeluk, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland, Sidorska 95/97, 21-500 Biała Podlaska, e-mail: a.szepeluk@pswbp.pl, phone: +48 83 344 99 00

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as defined in the definition of health by Eriksson and Lindstrom [1], is given to a health promoter, who enables to control individual surfaces of health. Kubińska [4] draws attention to the role of a coordinator of health education in the opinion of Physical Education teacher.

It is worth remembering that the most important measure in health education is movement and recently decreasing physical activity of societies is the cause of a large number of diseases.

The importance of physical activity on different stages of human development has been highlighted by many international authors over the last 20 years [5,6,7,8,9,10]. The research proves that being physically active at a younger age, increases the probability of intensive activity in the future [11,12,13].

Research Methodology

Objective

The purpose of this paper is to characterize the specificity of somatic, mental and social health profiles and the survival skill of the students on the following five specialties: Pharmacy, Medicine, Obstetrics, Nursing and Laboratory Diagnostics.

Material and research method

The study group comprised 467 women aged 15-25 years old, who were the attendants in Medical Vocational School in Lutsk, Ukraine. The method of diagnostic survey was applied on the basis of the original method of Kalina [2], which included four health indexes: somatic, mental, social and survival skill. All of the above indicate total health.

Results

Characteristics of respondents

The respondents comprise of female students of four learning cycles on five specialties: Medicine – 124 (26.6%), Nursing- 136 (29.1%), Pharmacy- 83 (17.8%), Obstetrics- 76 (16.3%) and Laboratory Diagnostics- 48 (10.3%). The majority of respondents had good educational achievements (58.7%), sufficient comprised of 22.9% and very good- 18.4% (Tab. 1).

Table 1. Characteristics of female student respondents

Variable	Amount (n)	(%)
Specialty		
Pharmacy	83	17.8
Medicine	124	26.6
Obstetrics	76	16.3
Nursing	136	29.1
Laboratory Diagnostics	48	10.3
Study Year		
First	98	21.0
Second	147	31.5
Third	140	29.0
Fourth	82	17.5
Educational achievements		
Sufficient	107	22.9
Good	274	58.7
Very goog	86	18.4

Positive health profiles

Social health obtained the highest total value among other health profiles (3.86 ± 0.64), with the highest index on Nursing (3.96 ± 0.67). This value, however, does not significantly differentiate other specialties (Tab.2).

Table 2. Health profiles levels for students of different specialties

Specialties		Health profiles				
		Somatic health	Mental health	Social health	Survival health	Total health
Total (n=467)	\bar{x}	2.88	2.87	3.86	2.57	2.90
	SD	0.38	0.60	0.64	0.73	0.36
Pharmacy (n=83)	\bar{x}	2.86	2.92	3.78	2.46^{Nu}	2.85
	SD	0.38	0.69	0.71	0.65	0.36
Medicine (n=124)	\bar{x}	2.90	2.86	3.88	2.52^{Nu}	2.89
	SD	0.39	0.58	0.63	0.70	0.34
Obstetrics (n=76)	\bar{x}	2.85	3.01^{Ob}	3.84	2.46^{Nu}	2.87
	SD	0.35	0.47	0.49	0.74	0.35
Nursing (n=136)	\bar{x}	2.87	2.78^{Nu}	3.96	2.79^{P,M,Ob}	2.97
	SD	0.40	0.60	0.67	0.74	0.39
Laboratory Diagnostics (n=48)	\bar{x}	2.98	2.86	3.76	2.48	2.89
	SD	0.37	0.62	0.68	0.80	0.34
Kruskal-Wallis Test	H	6.20	12.49	5.11	15.11	8.11
	p	0.1850	0.0140*	0.2758	0.0045*	0.0877

*-significant variation when $p < 0.05$

As regards somatic health, the highest index is assigned to HR (3.04 ± 0.67), and the highest value is obtained by Laboratory Diagnostics (3.27 ± 0.49). It is significantly higher than on the specialty of Pharmacy (2.86 ± 0.59) (Tab. 3).

Table 3. Somatic health levels for students of different specialties

Specialties		Somatic health							
		1	2	3	4	5	6	7	8
Total (n=467)	\bar{x}	3.00	3.04	2.86	2.80	2.76	2.81	2.93	2.87
	SD	0.62	0.61	0.69	0.73	1.06	1.09	0.81	1.06
Pharmacy (n=83)	\bar{x}	3.07	2.86^P	2.90	2.86	2.73	2.89	2.82	2.75
	SD	0.56	0.59	0.51	0.61	1.00	0.97	0.87	0.97
Medicine (n=124)	\bar{x}	3.07	3.06	2.94	2.86	2.81	2.83	2.82	2.79
	SD	0.56	0.64	0.61	0.62	0.99	1.11	0.77	1.01
Obstetrics (n=76)	\bar{x}	2.99	2.99	2.70	2.61	2.66	2.80	2.96	3.07
	SD	0.62	0.45	0.86	0.95	1.17	1.10	0.76	1.12

Nursing (n=136)	\bar{x}	2.88	3.07	2.83	2.78	2.73	2.80	3.01	2.88
	SD	0.72	0.67	0.73	0.74	1.14	1.13	0.79	1.08
Laboratory Diagnostics (n=48)	\bar{x}	3.10	3.27 ^P	2.92	2.90	2.90	2.63	3.15	2.96
	SD	0.52	0.49	0.77	0.75	0.88	1.12	0.87	1.20
Kruskal-Wallis Test	H	8.27	17.91	6.03	6.84	2.06	1.27	9.72	4.65
	p	0.0823	0.0013*	0.1970	0.1443	0.7243	0.8661	0.0455*	0.3257

1-BMI, 2-HR, 3-Systolic blood pressure, 4-Diastolic blood pressure, 5-Aerobic performance, 6-Anaerobic performance, 7-Muscle strength, 8-Flexibility

Class profile: P-Pharmacy, M-Medicine, Ob-Obstetrics, Nu-Nursing, N-Laboratory

Diagnostics

*-significant variation when $p < 0.05$

At the level of mental health, the highest index was reached by tolerance (-3.62 ± 0.88). The ability to overcome stress is significantly higher among nurses (3.26 ± 1.07) and the lowest on medical specialty (2.73 ± 1.03). In comparison to Nursing (2.25 ± 1.13), the anxiety index for the students of Pharmacy (2.87 ± 1.08) is much higher. Belligerence, however, reaches the highest value for Obstetrics students (2.72 ± 1.03), who obtained significantly higher indexes than the specialty of Nursing (2.01 ± 1.02) and Pharmacy (2.63 ± 1.21). In terms of tolerance, no significant relevancy was detected between the specialties (Tab. 4).

Table 4. Mental health levels for students of different specialties

Specialties		Mental health			
		Belligerence	Anxiety	Ability to overcome stress	Tolerance
Total (n=467)	\bar{x}	2.38	2.50	3.00	3.62
	SD	1.13	1.17	1.10	0.88
Pharmacy (n=83)	\bar{x}	2.63 ^{Nu}	2.81 ^{Nu}	2.87	3.40
	SD	1.21	1.08	1.13	0.92
Medicine (n=124)	\bar{x}	2.37	2.55	2.73 ^{Nu}	3.78
	SD	1.13	1.23	1.03	0.78
Obstetrics (n=76)	\bar{x}	2.72 ^{Nu}	2.51	3.13	3.68
	SD	1.03	1.05	1.18	0.70
Nursing (n=136)	\bar{x}	2.01 ^{P,Ob}	2.25 ^P	3.26 ^M	3.62
	SD	1.02	1.13	1.07	0.94
Laboratory Diagnostics (n=48)	\bar{x}	2.46	2.50	3.00	3.50
	SD	1.15	1.34	1.03	1.03
Kruskal-Wallis Test	\bar{x}	27.93	13.95	19.18	9.46
	SD	0.0001*	0.0075*	0.0007*	0.0505

*-significant variation when $p < 0.05$

Level of social health is characterized by huge diversification. The highest specific value falls on targets respecting basic values (4.21 ± 0.79), especially on Obstetrics (4.53 ± 0.64), which is characterized by significant differences in comparison to other specialties (Tab. 5). In terms of fair play value, the specialization of Pharmacy dominates (3.96 ± 0.93). It is characterized by considerably higher indexes than those reached on Obstetrics and Laboratory Diagnostics. Responsibility parameter, which has the average index of all the respondents (3.75 ± 0.90), has the highest value on Nursing (3.82 ± 0.94), which is significantly higher than one reached on Pharmacy (3.42 ± 0.94) (Tab. 5).

Table 5. Social health levels for students of different specialties

Specialties		Social health		
		Being fair play in everyday life	Respecting basic values	Responsibility
Total (n=467)	\bar{x}	3.64	4.21	3.75
	SD	1.03	0.79	0.90
Pharmacy (n=83)	\bar{x}	3.96^{Ob,L}	3.95^{Ob}	3.42^{Nu}
	SD	0.93	0.91	0.94
Medicine (n=124)	\bar{x}	3.56	4.27	3.81
	SD	1.07	0.71	0.82
Obstetrics (n=76)	\bar{x}	3.18^{P,Nu}	4.53^{P,Nu}	3.80
	SD	1.03	0.64	0.80
Nursing (n=136)	\bar{x}	3.88^{Ob,L}	4.17^{Ob}	3.82^P
	SD	0.89	0.78	0.94
Laboratory Diagnostics (n=48)	\bar{x}	3.31^{P,Nu}	4.13	3.85
	SD	1.15	0.87	0.95
Kruskal-Wallis Test	H	36.93	22.59	14.04
	p	0.0001*	0.0002*	0.0072*

*-istotne zróżnicowanie przy p<0.05

The level of survival skills significantly differs the eight analyzed components. It obtained the highest specific indexes in tolerating body imbalance (3.23 ± 1.07) and survival (3.21 ± 1.06), while the lowest in the ability of water rescue (1.47 ± 1.34) (Tab. 6).

Table 6. Survival skills levels for students of different specialties

Specialties		Survival skills							
		1	2	3	4	5	6	7	8
Total (n=467)	SD	3.23	2.73	2.21	2.61	2.33	1.47	2.81	3.21
		1.07	1.11	1.24	1.18	1.70	1.34	1.05	1.06
Pharmacy (n=83)	SD	3.31	2.36^{Nu}	1.96	2.67	2.41	1.27	2.67^{Nu}	3.02^{Nu}
		0.88	1.20	1.18	1.15	1.73	1.09	1.08	1.14
Medicine (n=124)	SD	3.36^{Ob}	2.69	2.07	2.42	2.50	1.48	2.48^{Nu}	3.15^{Nu}
		0.95	1.11	1.22	1.22	1.56	1.27	0.99	0.99
Obstetrics (n=76)	SD	2.75^{M,Nu}	2.70	2.13	2.47	2.22	1.70	2.75^{Nu}	2.93^{Nu}
		1.21	0.92	1.10	1.14	1.69	1.42	1.03	1.01
Nursing (n=136)	SD	3.43^{Ob}	2.96^P	2.42	2.82	2.28	1.47	3.30^{P,M,Ob,L}	3.64^{P,M,Ob,L}
		1.05	1.13	1.30	1.15	1.85	1.49	0.95	0.97
Laboratory Diagnostics (n=48)	SD	2.92	2.85	2.54	2.58	2.02	1.48	2.63^{Nu}	2.85^{Nu}
		1.18	1.07	1.30	1.25	1.64	1.35	1.00	1.03
Kruskal-Wallis Test	H	22.86	13.94	11.83	8.53	3.02	3.20	43.79	37.51
	p	0.0001*	0.0075*	0.0186*	0.0740	0.5540	0.5252	0.0001*	0.0001*

1-Tolerating body imbalance, 2-Precise performance, 3-The ability of falling securely, 4-The ability of self-defense, 5-The ability of swimming, 6-The ability of water rescue, 7-The ability of preclinical aid, 8-Survival

In the group of the highest values skills, which is survival (3.21 ± 1.06), the highest index was obtained on Nursing (3.64 ± 0.97), and the lowest on Laboratory Diagnostic (2.85 ± 1.03) with the significance in differences on every specialty. When it comes to tolerating body imbalance (3.23 ± 1.07), the highest values appeared on the specialties of Nursing (3.43 ± 1.05) and Medicine (3.36 ± 0.95), while the lowest on Obstetrics (2.75 ± 1.21) with the significance in differences on most of the specialties. The ability of water rescue, which obtained the lowest average value, did not show the significance of differences among specialties. The significance of differences was not also shown in self-defense and swimming abilities.

Discussion

The result of the statistical analysis of five independent groups of specialties taking four changing health profiles into consideration: somatic, mental, social and survival skill, indicate a clear growth of specified indexes, similarly to the studies of Kalina [2], Jagiełło et al. [14] and Bergier [15].

Female students rate social health as the most important, at high similar values on every specialty (no significance of differences). Survival skill is the lowest evaluated, as confirmed by recent studies conducted among students from Medical majors [15], Physical Education [14] and Physiotherapy [2]. It should be noted that in studies conducted among students of Medical majors, survival skill was assessed much higher than other values.

It may be noted that the general health index is almost identical on every specialty, which can be the example of clearly defined choices of future professions and which corresponds to other conducted studies [15,14]. Statistically significant differentiation between specialties occurred in self-assessment of mental health, the highest index characterizes respondents from Obstetrics specialty, which shows its importance in this particular profession. Surprisingly, lower value was reached by Nursing students. As regards survival skills, in comparison to Pharmacy, Medicine and Obstetrics, higher values were reached by Nursing students. Possibly, this is the curriculum, which prepares for a better understanding of features connected with survival skills.

Among four health profiles, the lowest variety of indexes was observed in somatic health, as confirmed by studies carried out among Medical students [15].

The most significant differences (statistically relevant) were observed in the fields of mental and social health, which may be indicative of requiring these particular skills on before mentioned specialties.

As regards mental health, detailed index of the ability of stress overcoming was the highest on Nursing specialty. Anxiety was the highest on Pharmacy, while belligerence on Obstetrics specialty. It can be assumed with high probability that the values of the detailed indexes characterize a mental peculiarity of future professions.

As regards social health, detailed indexes are significantly higher on different specialties. Responsibility is rated the highest by Nursing students, while Obstetrics students consider respecting basic values as important, and Pharmacy students- being fair play in everyday life.

Survival skills differentiate studied groups in five out of eight analyzed detailed indexes, while the biggest differentiation between the specialties was shown in the abilities of pre-clinical aid and survival.

The highest self-esteem of pre-clinical aid characterizes Nursing students, as confirmed by the right choice of specialty. They have also obtained the highest rate of self-esteem for survival, which may be indicative of a comprehensive curriculum, which contains varied information essential for survival.

Conclusions

Taking into account a relatively large number of respondents on two specialties, which are: Nursing and Medicine (over 100 respondents on each specialty) we would like to depict forms of subjective models of health assessment for these specialties as well as in the perspective of future professions.

Medicine- domination of social and mental health profiles. Respecting basic values dominates among detailed indexes of social health profile. As regards mental health profile, the ability of stress overcoming dominates. When it comes to somatic health, a prevalence of BMI and HR indexes was observed.

Nursing- domination of social health profile, among detailed indexes respecting basic values. As regards somatic health, the highest value was reached by HR index. According to the authors, generalizations indicated in the conclusions may be used in further discussion concerning creating the curriculums on the before mentioned specialties.

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Part III. Other
Dział III. Różne

THE REVIEW OF RESULTS OF RESEARCH ON BREASTFEEDING
CONSIDERING MEDICINAL AND PROPHYLACTIC ASPECTS

PRZEGLĄD WYNIKÓW BADAŃ NA TEMAT KARMIENTA PIERSIĄ KOBIET
Z UWZGLĘDNIENIEM ASPEKTÓW LECZNICZYCH I PROFILAKTYCZNYCH

Anna Marszałek^{1(A,B,D,F)}, Robert Walaszek^{2(A,D,E,F)}

¹Public Elementary School of Friends of Catholic Schools Association in Hucisko-Pawelka

²Department of Recreation and Biological Regeneration of the University of Physical Education in Cracow

Authors' contribution

Wkład autorów:

A. Study design/planning

zaplanowanie badań

B. Data collection/entry

zebranie danych

C. Data analysis/statistics

dane – analiza i statystyki

D. Data interpretation

interpretacja danych

E. Preparation of manuscript

przygotowanie artykułu

F. Literature analysis/search

wyszukiwanie i analiza literatury

G. Funds collection

zebranie funduszy

Summary

Breastfeeding is an irreplaceable, in biological and emotional aspect, basis of mother and child's health. The aim of this paper was to present the review of research results on advantages of natural feeding and benefits of breastfeeding, presentation of breast massage technique as a way of supporting natural feeding, as well as contraindications to breastfeeding. In spite of the propagation, the number of mothers who feed their children in natural way is still considerably low. At present, the American Academy of Paediatrics recommends nursing for 6 months, and continuing it until first year of child's life (or longer, depending on mother or child's needs), introducing, at the same time, supplementary food. The issue of breastfeeding should be widely spread among women mainly by midwives, who should propagate nursing with commitment and provide proper information, emphasising its positive influence on the health of mother and child.

Keywords: breastfeeding, postnatal period, massage

Streszczenie

Karmienie piersią jest niezastąpioną biologicznie i emocjonalnie podstawą zdrowia matki i dziecka. Celem pracy było zaprezentowanie przeglądu wyników badań dotyczących zalet naturalnego karmienia i korzyści wynikających z karmienia piersią, przedstawienie metodyki masażu piersi jako środka wspomagającego naturalne karmienie oraz przeciwwskazań do karmienia piersią. Mimo propagowania karmienia piersią, odsetek matek karmiących naturalnie nadal jest niewysoki. Najnowsze rekomendacje Amerykańskiej Akademii Pediatrii zalecają wyłączne karmienie mlekiem matki przez 6 miesięcy życia i kontynuowanie go przy wprowadzaniu produktów uzupełniających do 1 roku życia dziecka lub dłużej, zgodnie z życzeniem matki lub dziecka. Problematyka karmienia piersią powinna być szeroko rozpowszechniana wśród kobiet, głównie przez położne, które z zaangażowaniem powinny propagować karmienie piersią i dostarczać odpowiednich informacji, podkreślając tym samym pozytywny wpływ tego sposobu karmienia na zdrowie matki i dziecka.

Słowa kluczowe: karmienie piersią, połóg, masaż

Tables: 1

Figures: 1

References: 40

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Introduction

Breastfeeding is an irreplaceable, in biological and emotional aspect, basis of mother and child's health [1]. It is confirmed by present recommendations of Polish, foreign, and international institutions and organisations that deal with the issues of child feeding. At present, the American Academy of Paediatrics [2] recommends nursing for 6 months, and continuing it until first year of child's life (or longer, depending on mother or child's needs), simultaneously introducing supplementary food. World Health Organisation [3] recommends breastfeeding for 2 years or more, emphasising that longer nursing, even for 3 years, does not have a bad influence on child's mental state (WHO). However, Polish Committee for Breastfeeding Promotion (Polski Komitet Upowszechniania Karmienia Piersią) recommends to breast-feed for 6 month and longer, at least until one year.

Address for correspondence / Adres korespondencyjny: Robert Walaszek, University of Physical Education, Department of Recreation and Biological Regeneration, 31-571 Kraków, Jana Pawła II Ave. 78, e-mail: robertwalaszek63@gmail.com, phone: +48 12 683 10 96

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In spite of the propagation of breastfeeding, the number of mothers who feed their children in natural way is still low. Research shows that relatively large number of mothers breast-feed infants, but few continues it, accordingly to recommendations, until 6 month of child's life [4]. In the group of examined 6 month old infants only 13.2% of them was fed only with breast milk [5]. Stolarczyk and Zagórecka [6] noticed frequent breastfeeding of children in similar age (68%), but only 9% of these infants were only breast-fed. Almost half of examined children in the first six months of life was breast-fed, but only 2.7% did not get any supplementary products [7].

In the subject literature among the most often indicated reasons for breastfeeding discontinuation there are agalactia and nipple problems [8]. According to the research on factors connected with keeping and continuation of natural feeding, the appearance of mentioned causes depends on duration of breastfeeding [9]. The insufficient amount of milk was the cause of breastfeeding discontinuation among mothers who were feeding their children this way at least for 2 months. The problems with breasts, however, were the most frequent reason to stop for mothers who did not maintain breastfeeding even for 2 months. Among other causes that limited nursing, one may list physical and mental exhaustion, but also the feeling of discomfort connected with appearance of breasts [10]. Nehring – Gugulska et al. [11] argue that if woman have doubts about her capability to feed a child only with breast milk, it will cause increased secretion of adrenaline which, being antagonist of oxytocin, will block the production and secretion of milk. Similar reasons of failing at breastfeeding are suggested by Cooke et al. [12].

In sum, it seems the most essential element that could mitigate described problem is proper prevention and change of lifestyle. Nevertheless, there is still no answer regarding applied therapeutic methods to prevent difficulties that lying-in women struggle with. Women having problems with nursing can choose from wide range of therapies, from medical procedures to physiotherapy and massage.

The aim of this paper was to present the review of research results on advantages of natural feeding and benefits from breastfeeding, presentation of breast massage as a way of supporting natural feeding and contraindications to breastfeeding. This paper is for information purposes only and it was written on the basis of the research on polish and foreign literature. It should be mentioned, that the literature on the subject rarely deals with the issue of breast massage application during postnatal period. Therefore, this paper is an attempt to synthesise the existing knowledge on this subject. .

The review of research results on benefits of breastfeeding

The assessment of women's knowledge of the advantages of natural feeding was repeatedly the subject of research, which is reflected in literature [7,13]. Numerous observations and research shows that the health care professionals have little contribution in the education of women about the benefits of breastfeeding. Therefore, this subject should be widely spread among women, especially by midwives who should propagate nursing with commitment and provide relevant information, emphasising positive influence of it on mother's health. The review of literature done by the authors of this paper, which regards the sources of the knowledge on the positive aspects of breastfeeding, proves that majority of Polish women draw information from popular science literature and books (above 70%), Internet, newspapers (ca. 55%), family and friends (respectively 48 and 45%). Marginal importance in this aspect have antenatal classes (24%) and informational leaflets (17%) (table 1).

Table 1. The review of research results on benefits of breastfeeding

Sources of knowledge on benefits of breastfeeding – results of survey research	
Paper	Sources of knowledge (%)
Grochans et al. [14]	71 – popular science literature
	63 - friends
	61 – specialist press
	24 – antenatal classes
	23 – instructional videos
Cierpka et al. [15]	73 - literature
	47 – family, friends
	29 - media
Gebuza et al. [16]	61 – books, magazines
	47 - friends
	17 – antenatal classes

Klejewski et al. [17]	64 – books, guidebooks
	50 – internet, press, television
	45 – family
	43 – friends
	13 – antenatal classes
Olejniczak et al. [18]	71 – internet
	60 – books
	45 – press
	38 – family
	26 – friends
	23 – television
Józefów et al. [19]	17 – information leaflets
	60 – family
	40 – internet
	40 – books
	40 – antenatal classes

Source: own elaboration

A mother gets benefits from breastfeeding already in early postnatal period. It results in decreasing postnatal blood loss and faster involution of uterus, which is connected with activity of oxytocin released during breastfeeding. Furthermore, oxytocin regulates the rhythm of sleep and wakefulness, reduces the feeling of anxiety and stimulates emphatic behaviours. It is secreted not only by irritating mechanoreceptors localised around nipples, but also by frequent contact defined in literature as „*skin to skin closeness*”, i.e. when mother’s body is close to child’s body, which is more frequent in the case of mothers who breastfeed [20]. Additionally, breastfeeding delays the occurrence of first menses after birth even to several months, whereas mothers who use formula have their first period 6 – 8 weeks after childbirth. It has, undoubtedly, considerably significant impact in the aspect of iron storage in woman’s body, which protects mothers from anaemia. Prolonged lactation and amenorrhea have also contraceptive effects, thanks to lowered gonadotropin release in hypothalamus (high level of prolactin and hypothalamic dopamine repress the release of follitropin and lutropin) [21].

The breastfeeding also limits the risk of postnatal depression which is a relatively frequent phenomena, involving from 10 to 20% of mothers in postnatal period. Women suffering from depression, more often resign from breastfeeding, which is connected with negative influence on child’s health, as well as mother’s. Postnatal depression risk factors include: stress, sleep deprivation, trauma and depressive and anxiety disorder episodes in medical history [22]. From research of Mezzacappa and Katlin [23] that compares the level of stress of mothers who breastfeed and those who use formula, and submits to comparative analysis both models of infants feeding in the same population of women, results that breastfeeding is connected with the improvement of wellbeing and acts protectively in relation to lowered mood, including depression. Heinrichs et al. [24] proved that nursing women are protected against harmful effects of stress on immune system thanks to reduced level of ACTH and cortisol – the hormones which are largely responsible for suppression of immune system during stress and fatigue. Breastfeeding is also conducive to better quality of sleep during maternity. Research comparing the quality of sleep of mothers who bottle-feed and those who breastfeed shows that the latter: sleep about 20 – 40 minutes longer, have definitely better quality of sleep, less often suffer of depression caused by deprivation of sleep [25]. However, Bylton et al. [26] state that the deep sleep stage of nursing women is three times longer in comparison to women who bottle-feed, and also the light sleep stage is shorter, resulting in lesser fatigue during a day.

According to observations, breastfeeding also helps in faster reduction of body mass and in avoiding metabolic complications connected with obesity, as well as reduces the risk of cardiovascular diseases [27]. The long-term research showed reduction in risk of type 2 diabetes in the case of nursing women during perimenopause, and women with type 1 diabetes who were breastfeeding needed smaller dose of insulin as a result of lowered blood sugar [28]. Prolonged lactation also results in the decrease of the level of total and LDL cholesterol and increase of the level of HDL cholesterol, and reduction of blood sugar and insulin in blood serum [29]. Therefore, breastfeeding is a factor decreasing the risk of diabetes or hyperlipidaemia that hasten the development of arteriosclerosis and ischaemic heart disease. Extensive prospective research evaluating the relations between the occurrence of heart attack in middle age and total duration of lactation during women’s reproductive period demonstrated that the risk of heart attack in women who were breastfeeding for 2 years or more, is 37% less in comparison to women who have never breastfed [30]. Schwarz et al. [31] got similar results. They examined a group of 60 years

old women while taking into account sociodemographic results, lifestyle, family history. The research showed positive correlation between the decrease in frequency of the occurrence of ischaemic heart disease risk factors (obesity, hyperlipidaemia, diabetes, hypertension, incident of coronary disease in history) and the duration of lactation period and breastfeeding during reproductive period of examined women. Besides, the multicentre study conducted by Cumming and Klineberg [32] demonstrates protective role of nursing in relation to the occurrence of osteoporosis during perimenopause. It was also proved that breastfeeding decreases the risk of endometrial, nipple or ovarian cancer [27]. The risk of endometrial cancer depends on the level of oestrogens, which increases during exogenous and endogenous stimulation and decreases during lactation and breastfeeding, as the result of the decrease of oestrogens level [27]. Other authors observed increased risk of this cancer as a result of using medications to suppress lactation [33]. Late start of menstruation, pregnancy and breastfeeding are mentioned among the main factors protecting against the occurrence of breast cancer [27]. The research conducted by Kotsopoulos et al. [34] reveals that there is connection between decreased risk of breast cancer in the case of carriers of mutated genes and prolonged lactation. It shows the reduction of the risk of breast cancer for women having BRCA 1 gene mutation is 32% with total duration of breastfeeding during reproductive period for about 12 months and draws out along with prolonged nursing for about 19%. This dependency was not observed in the case of women having BRCA 2 gene mutation. In turn, among the factors decreasing the risk of ovarian cancer are oral contraception and pregnancy. Both are connected with suppression of ovulation and diminishing of the level of gonadotrophins in woman's body. Similar effect may be observed during breastfeeding period [35].

The proposition of mammary gland massage technique for women in postnatal period

During the massage of mammary gland, one should create proper conditions and take care of woman's comfort. Preferably, it should take place in a room which temperature is 22°C. It is not recommended to hold a conversation with a massaged woman, as it may deconcentrate massager. The atmosphere should not give the feeling of nervousness and hastiness. The amount of time committed to interview, massage and rest should be planned before the treatment. Massager uses delicate technique of classical massage through caressing and rubbing. Each technique should be repeated for 4 – 6 times. All moves should be coordinated, calm, delicate and fluent.

Breast massage techniques

Longitudinal caressing is done with whole palm or pads of fingers II – V in the area from parasternal line to anterior axillary line in the direction from costal arch in nipple line to supraclavicular fossa, infracalvicular fossa and nearby shoulder joint (Fig.1a). **Longitudinal rubbing** is made with palmar side of fingers II – V in delicate, circular motions (Fig.1b). Direction of rubbing is the same as with caressing (Fig.1a). **Transverse longitudinal caressing** is done with whole palm or pads of fingers II – V in the area from parasternal line to midaxillary line in the direction from costal arch to midaxillary line, anterior axillary line, shoulder joint, supraclavicular fossa, infracalvicular fossa. Massage should end nearby nipple line (Fig.1c). **Transverse longitudinal rubbing** is made with palmar side of fingers II – V in delicate, circular motions (Fig.1d). Direction of rubbing is the same as with caressing (Fig.1c). **Circular caressing** is made with pads of fingers II – V in the direction from nipple to areola, supraclavicular fossa, infracalvicular fossa, shoulder joint, anterior axillary line (Fig.1e). **Circular rubbing** is made with palmar side of fingers II – V in delicate, circular motions (Fig.1f). Direction of rubbing is the same as with caressing (Fig.1e). **Transverse circular caressing** is done with pads of fingers II – V in the direction from costal arch in nipple line to nipple, areola. Massage should end nearby shoulder joint (Fig. 1g). **Transverse circular rubbing** is made with palmar side of fingers II – V in delicate, circular motions (Fig.1h). Direction of rubbing is the same as with caressing (Fig.1g).

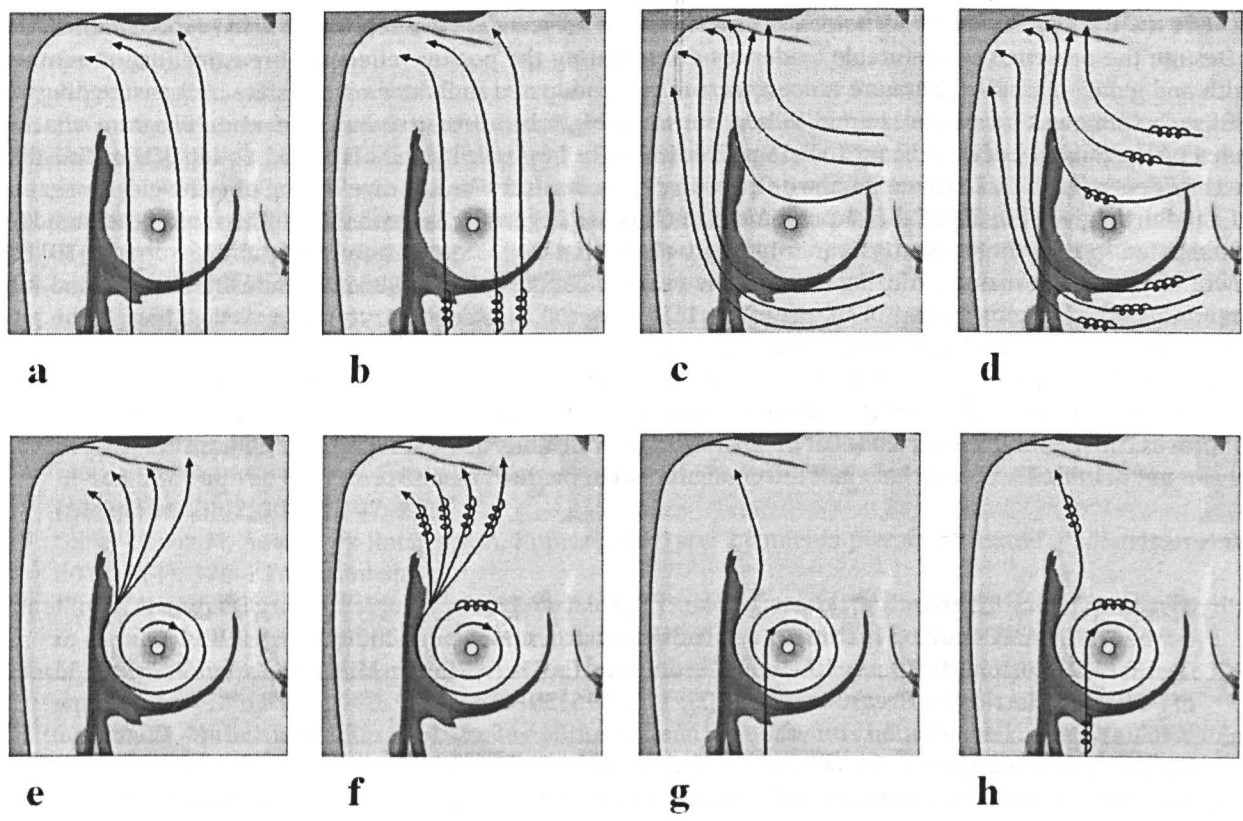


Figure 1. Mammary gland massage technique in postnatal period. *Source: own work on the basis of „Masaż kobiet w ciąży i niemowlęcia” [“The massage of pregnant women and infant”] by Lewandowski G. [36]*

Breastfeeding contraindications

Contraindications can be divided between those connected with mother and her treatment and those connected with child [37].

Contraindications connected with mother

- Medications used in chemotherapy,
- Taking radioactive substances,
- Mastitis during intensive antibiotherapy,
- Smoking,
- Drinking alcohol,
- Taking intoxicants,
- Active tuberculosis process,
- HIV infection,
- HTLV infection of type I and II,
- Inverted nipples.

Contraindications connected with child:

- galactosaemia,
- congenital lactose intolerance,
- weak sucking reflex,
- cleft lip and palate,
- underdeveloped mandible,
- severe hiperbilirubinaemia.

Conclusion

Despite the presence of irrefutable evidences documenting the positive effects of breastfeeding on mother's health and global initiative, there are no current analysis conducted in Poland on the state of breastfeeding. The latest such study was carried out in mid-90's in the scope of „Polish Breastfeeding Promotion Program” that was funded by the Ministry of Health and Social Services [38]. The implementation of the Regulation of the Minister of Health of September 23, 2010 on Standard Operating Procedures for health care during physiological pregnancy and childbirth, gives hopes for the improvement of situation regarding breastfeeding. The aim of the standards implemented in the whole country is to intensify actions that will effect in popularisation of nursing [39]. The growth of interest in massage during the last few years is connected with general tendency to more and more common usage of this treatment in therapeutics. It is essential that mammary gland massage have to be given by a professional in order to avoid undesirable side effects. Imprecisely established diagnosis and determination of wrong priorities during therapy, and consequently no effects, lead to disappointment and disincline lying-in women to continue breastfeeding. Previous observations show that it is effective and safe method. Bowles studies [40] proves considerable effectiveness of breast massage, which boosts milk secretion and improves caloric value and amount of milk. These conclusions need confirmation in further research.

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THE ROLE OF SCHOOL SEXUAL EDUCATION IN HEALTH PROMOTION

ROLA SZKOLNEJ EDUKACJI SEKSUALNEJ W PROMOCJI ZDROWIA

Joanna Skonieczna^{1(A,B,C,D,E,F)}, Dominik Olejniczak^{1(D,E)}

¹Department of Public Health, Medical University of Warsaw

Authors' contribution

Wkład autorów:

A. Study design/planning
zaplanowanie badań

B. Data collection/entry
zebranie danych

C. Data analysis/statistics
dane – analiza i statystyki

D. Data interpretation
interpretacja danych

E. Preparation of manuscript
przygotowanie artykułu

F. Literature analysis/search
wyszukiwanie i analiza literatury

G. Funds collection
zebranie funduszy

Summary

Sexuality is an integral part of personality of each human being. No earnestly conducted sex education is a common cause of engaging in risky sexual behaviours.

The aim of the study is to evaluate the role of sex education in health promotion and to present the results of the studies of the effects of school sex education on sexual behaviour of young people.

The period of adolescence is characterized by a more frequent risk-taking behaviour. Among adolescents it is observed that the average age of sexual initiation has decreased, the frequency of making sexual contact and a number of sexual partners has increased, as well as the insufficient dissemination of the use of condoms and other methods of contraception every time sexual intercourse takes place.

The task of health promotion is to influence determinants of health, among others, through sex education. Research confirms the positive impact of complex sex education, carried out in accordance with the recommendations of international organizations, on a lower frequency of engaging in risky sexual behaviour. It seems appropriate to take action to disseminate appropriate for the level of psychosexual development sex education in schools.

Keywords: sex education, health promotion, school

Streszczenie

Seksualność jest nieodłącznym elementem osobowości każdego człowieka. Brak rzetelnie prowadzonej edukacji seksualnej w tym zakresie jest częstą przyczyną podejmowania ryzykownych zachowań seksualnych.

Celem pracy jest ocena roli edukacji seksualnej w promocji zdrowia oraz zaprezentowanie wyników badań oceniających wpływ szkolnej edukacji seksualnej na zachowania seksualne młodzieży.

Okres adolescencji charakteryzuje się częstszym podejmowaniem ryzykownych zachowań. Wśród adolescentów obserwowany jest spadek średniego wieku inicjacji seksualnej, zwiększenie częstości podejmowania kontaktów seksualnych oraz liczby partnerów seksualnych, a także niedostatecznie rozpowszechnienie korzystania z prezerwatyw i innych metod antykoncepcji przy każdym stosunku seksualnym.

Zadaniem promocji zdrowia jest wpływanie na uwarunkowania zdrowia m.in. poprzez edukację seksualną. Badania potwierdzają pozytywny wpływ złożonej edukacji seksualnej, prowadzonej zgodnie z rekomendacjami organizacji międzynarodowych, na mniejszą częstotliwość podejmowania ryzykownych zachowań seksualnych. Właściwe wydaje się być podjęcie działań mających na celu rozpowszechnianie właściwej dla poziomu rozwoju psychoseksualnego edukacji seksualnej w szkołach.

Słowa kluczowe: edukacja seksualna, promocja zdrowia, szkoła

Tables: 1

Figures: 0

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Aim of the work

The aim of the study is to evaluate the role of sex education in health promotion and to present the results of studies of selected authors evaluating the relationship of school sex education on sexual behaviour of young people.

Brief description of the status of knowledge

Grounds for conducting sex education

Sexuality is an integral part of the personality of each human being. The World Health Organization (WHO – called. World Health Organization) provides the following definition of sexual health: “Sexual health is the well-being physically, emotionally and socially in relation to sexuality; it is not merely the absence of disease or infirmity

Address for correspondence / Adres korespondencyjny: Joanna Skonieczna, Department of Public Health, Medical University of Warsaw, Banacha 1a, 02-097 Warszawa, e-mail: jskonieczna90@gmail.com, phone: +48 22 599 21 08

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dysfunction (...). To achieve and maintain sexual health, sexual rights should be respected, protected and fulfilled" [1]. Thus, the definition of sexual health also refers to sexual rights. Sexual rights were formulated by the World Health Assembly in the Universal Declaration of Sexual Rights, whose most recent version was published in 2014 [2].

Declaration of Sexual Rights refers only to adults. Children's rights are contained in the Convention of the United Nations (UN) on the Rights of the Child, which was ratified by Poland in 1991 [1]. Committee on the Rights of the Child obliges State parties to ensure that minors have access to knowledge in the field of sexuality and reproduction covering such topics as: family planning methods and contraceptives, the risks associated with early pregnancy and prevention of sexually transmitted diseases, regardless of the consent of the parents / legal guardians or marital status of minors. This means that the school should be ensured at all levels of education, classes on sex education, which will be adjusted to the age of the students [3].

In Poland, the obligation of sex education in schools is set out in Article. 4 of the Act of 7 January 1993 on family planning, protection of the human fetus and conditions of permissible abortion notes "Knowledge on human sexual life, on principles of conscious and responsible are introduced to the school curriculum as well as on parenthood, family values, life in the prenatal stage and methods and means of conscious procreation (...)" [4].

The manner in which the subject of Education for family life is executed (WDZ) is defined in the Regulation of the Minister of National Education of 12 August 1999 on the way of school education and the scope of contents concerning the knowledge on human sexual life, on principles of conscious and responsible parenthood, family values, life in the prenatal stage and methods and means of conscious procreation contained in the core curriculum of general education [5].

Classes on sex education are implemented on the basis of binding since the school year 2009 // 2010 new core curriculum regulated by the Regulation of the Minister of National Education of 23 December 2008. on core curricula for pre-school education and general education in particular types of schools (Dz. U. of 2009. No. 4, pos. 17) replaced the Regulation of the Minister of National Education of 27 August 2012. on core curricula for pre-school education and general education in the different types of schools (OJ 2012 No. 0 pos. 977).

These documents show the importance of sexual health care for every human being and free access to information on sexuality. The state has the obligation to provide adequate sexual education and not discriminate against anyone in this regard.

According to the standards, sexual education is defined as "the science of cognitive, emotional, social, interactive and physical aspects of sexuality. Sex education begins in early childhood and is carried further into adolescence and adulthood. In the case of children and young people in order to support and protect the sexual development" [1]. International Guidelines on Sexual Education were developed by the Organization of the United Nations. Educational, Scientific and Cultural Organization defines sexual education as "adjusted to the age and cultural way of teaching about sex and relationships, providing accurate, realistic, non-judgemental information. Sex education provides the opportunity to "research" one's own values and attitudes that enables us to acquire decision-making skills, communication and risk reduction with respect to many aspects of sexuality" [6].

Sex education is conducted in a just way and transmitting the current knowledge in scientific manner it enables children and adolescents to broaden the knowledge, skills acquisition, as well as acquiring positive values. In the future, it greatly increases the chance of correct understanding of one's own sexuality, creating fulfilled and secure relationships and a sense of responsibility for one's own sexual health.

In accordance with the Standards of sexual education in Europe the following types of sex education are distinguished:

Type 1 - "abstinence only", which is based on promoting abstinence. The following behaviours are condemned: having sex before and outside of marriage, contraceptive methods (except the so-called Natural methods), abortion, masturbation, oral and anal sex, orientations other than heterosexual. The administration of Republican states in the USA strongly promoted and supported this type of program [1, 7, 8].

Type 2. - general sex education, the aim of which is to provide the full knowledge of contraception and abortion, which are not condemned. Sexual abstinence is presented as an option. There is acceptance for the intercourse before and outside of marriage (except when it's illegal), various activities of sexual taken for the free and informed consent of all individuals participating in them, as well as masturbation and other sexual orientations [1, 7, 8].

Type. 3. - "holistic sex education" in the English literature referred to as Sex and Relationship Education (SRE). It is characterized by the fact that the above aspects are presented depending on the sexual development of recipients. Sexual intercourse is an important value in human life, but inseparable from one other. It combines sexual awareness with shaping positive attitudes. The feeling of love, maturity and responsibility are developed conditions for recognition before and extramarital relations. The institution of marriage is important but forms of creating relationships are not limited. The following are accepted: masturbation and contraceptives as a method of preventing unwanted pregnancies and STD. Sexual orientation other than heterosexuality are treated as equivalent

to a heterosexual one. Abortion is a negative phenomenon, but there are circumstances in which access to abortion seems to be expedient, for example, in the absence of a properly conducted sex education. Sex education type 3 is conducted, among others in Canada [1, 7, 8, 9].

The role of sex education in promoting sexual health

Sexual activity of young people is one of the areas of interest of public health. It is associated with phenomena such as sexual initiation, pregnancy, sexually transmitted disease (STD) and sexual violence [10]. A common cause of making risky sexual behaviour is the lack of sex education conducted fairly. In Poland, neither family nor school fulfil its role in the field of sex education in a satisfactory manner. There is a phenomenon of shifting this obligation by institutions to one another. Parents, even those declaring desire to educate their children, have problems with speaking with them about issues of sexuality. This may be due to a lack of sufficient knowledge and skills in this area. Teenagers are ashamed or afraid of talking about sex with their parents [11]. In addition, the influence of the Church and youth organizations (eg. Scouts) which were potentially developing young people's positive behaviour and values nowadays has weakened. The fact that young people themselves do not attach significance to sexual and reproductive health may be problematic. An increasingly important role in transferring knowledge and creating behaviours is played by mass media [10].

According to the WHO - defined directions, activities in the field of health promotion in sexual health should: create positive attitudes towards sexuality; take into account the complex conditions and factors that determine sexual behaviour, relationships and satisfaction; to prevent any form of segregation, isolation and discrimination based on sexual orientation, gender, disability and general health; prevent sexual violence; seek to establish legal norms that would guarantee free access to counselling and therapy, and to broaden this access; strive for broad access to modern methods of contraception; include the prevention of STDs; promote safer sex and take into account the cultural traditions of a society [12].

Sexual activity of adolescents and young adults may present a risk of gynaecological complications, sexually transmitted diseases, emotional disorders (eg. Fear of sexual contact), disorders in the creation / development interactions, sexual behaviour, as well as unplanned pregnancy and its consequences [12].

Honestly led sex education is aimed at preventing the negative consequences of sexual activity of teens and young adults, developing assertiveness and responsible decision-making [13]. The following is a role of sex education in the prevention of some negative consequences of sexual activity of young people.

Age of sexual initiation, number of sexual partners and frequency of sexual activity taking

Sexual initiation is defined as "the first sexual intercourse" [10]. According to the Polish legal norms premature sexual activity is determined at the age of 15 (Law of 6 June 1997. Criminal Code) [14]. The first sexual intercourse is one of the most important events in one's life, and marks the transition to the next phase of psychosexual development. Participating in sexual intercourse should include full biological, psychological and social maturity. The fulfilment of these conditions allows young people to develop a sense of responsibility for their sexual activity and its consequences, and to build respect for sexual partner [15].

Social and biological change that have taken place over the last century caused a lowering of the age of sexual initiation and changed the understanding of this concept [10, 16]. In Western Europe there was a decrease in the average age of initiation by nearly 2 - 3 years since 1960. The same changes occurred in eastern Europe, but about 20 - 30 years later. In the years 1998 - 2002, among 15-year-olds in the area of 29 European countries, the percentage declaring sexual initiation was varied and ranged among girls from 3.6% (in Macedonia) to 40.4% (in England) among boys from 18% (Spain) to 47.2% (in Ukraine) [17, 18].

Most Canadians' first sexual intercourse takes place during the teenage years. Percentage of 18/19 year olds who have ever had sexual intercourse decreased from 70% in 1996/1997 to 65% in 2005 [19].

A study in 2000 indicated that among Poles the average age of initiation was then 19 years (for women - 19.4, men - 18.6) [16]. A study conducted in 2005 among respondents aged 15 - 49 years of age showed a decrease to 18.08 for men and 18.82 for women. According to another study 47.3% of girls and 49.9% of boys in the age of eighteen have already had sexual initiation, of which 13.9% of girls and 19.4% boys have experienced this before they have completed fifteen years of age. The average age of initiation was 16.8 years for girls and 16.5 years in boys [10]. Research by Institute of Educational Research among young adults showed that 51% of the respondents (48% women and 53% men) have already had sexual intercourse. In this group of people, sexual intercourse took place for the first time at the age of 15 or less - for almost 10% of respondents, aged 16 - 18%, 17 years - 26%, 18 years or more - 24% [20]. In summary, men experience sexual initiation earlier than women, it is also observed that the age of initiation has lowered for both sexes.

Review by Kirby showed that sex education can be a factor protecting from or inducing early sexual initiation. This may be due to the way in which it is conducted [21].

The analysis of studies on sexual education programs in the United States, carried out by SIECUS (*The Sexuality Information and Education Council of the United States*), has indicated that complex sexual education is one of the most effective methods of delaying sexual initiation among the youth. This type of sexual education does not encourage teenagers to have sexual intercourse or to increase the frequency of sexual relations and does not influence the growth of the number of sexual partners. The program increases the average age of sexual initiation and the popularity of condoms and other contraception methods as well as reduces the sexual intercourse frequency and the number of partners [22].

Meta-analysis of 83 studies conducted in many countries has shown that a significant proportion of sexual education programs delayed the moment of sexual initiation, while only one of them accelerated it. Among 52 studies, that have measured the impact on the start of sexual intercourse, 22 (42%) programs have delayed sexual initiation by at least 6 months, in 29 (55%) there was no significant association and only in one case (in the US) the program was related to earlier sexual initiation. Among developing countries, six from 14 programs contributed to delaying the start of sexual intercourse, while among developed countries—16 from 38 programs [23, 24].

Adolescence is characterized by the intensity of the frequency of undertaking risky situations and the change of sexual partners is more frequent than among people over 25 years of age. The studies conducted by Woynarowska in 2005 indicated that 52, 1% of young people who have already started sexual intercourse had only one partner, while every fourth person tested (13,1% girls and 36,1% boys) has had at least three partners [25].

Kirby's meta-analysis has shown that sexual education programs do not encourage the increase in frequency of sexual relations while some of them might even reduce it. Among 31 of studies, in nine (29%) the decrease of frequency has been observed, 19 (1%) have not resulted in significant changes and three of them (all in developed countries) have influenced the increase in frequency of sexual intercourse.

Regarding the number of sexual partners, the educational programs have not increased it and only some of them have caused its reduction. All over the world, 12 from 34 programs (35%) have contributed to the decrease of the number of sexual partners, while 21 (62%) programs have not have a significant impact on it. The percentage of programs that have had positive effect in developing and developed countries was practically the same. Only one program (in the US) might have contributed to the increase of the number of sexual partners. The programs were somewhat more effective among younger respondents [23, 24].

Sexually transmitted diseases, with particular emphasis on HIV/AIDS

The frequency of sexual intercourse and the number of sexual partners is reflected in the occurrence of the STD and the probability of pregnancy. There is a positive correlation between the age of sexual initiation and the incidence of STD. According to estimates, nearly 25% of all STD infections are reported among adolescence. Only long-term, reliably planned and executed preventive measures can succeed in this field [12].

Youth is the group most exposed to the occurrence of new HIV infections. The European Council decided to incorporate HIV/AIDS awareness campaigns targeted to this age group (www.aids.gov.pl). Education and prevention are currently the only tools to fight HIV/AIDS [25].

According to SIECUS, neither restrictive education programs, nor complex sexual education indicated important relation between reduction of the risk of STD and lack of sexual education [22].

However, some studies show that health education including information about STD (also HIV/AIDS) might decrease the frequency of STD prevalence which might be also related to the lack of premature sexual initiation.

Haberland has reviewed evaluation studies of educational programs on sexuality and HIV, conducted in developed and developing countries in years 1990-2012. Out of 22 programs that met the inclusion criteria, 10 took into account the area of *gender* and *power* in a sexual relationship. Those programs were five times more effective and about 80% of them were associated with a significantly reduced rate of STD or unwanted pregnancy, while among programs that did not take into account gender and power relations, only 17% had such effect [26].

Ten studies evaluating the connection between carried out programs and changes in incidence rates for STD have been analyzed. Two of them have indicated positive influence, six of them have shown no significant impact, while another two have demonstrated adverse effects. To conclude, the studies indicate that health promotion programs can affect the frequency of the incidence of STD [24].

Uganda can serve as a good example of the fight against HIV/AIDS at the national level. Implemented ABC strategy has brought positive results - the percentage of people infected with HIV fell from almost 18.2% to 7% in the period 1992-2014 [27]. ABC strategy is based on:

A – *abstinence* – the promotion of sexual abstinence, reducing the number of sexual partners, delaying sexual initiation – especially among young women who make sexual relations with older men which significantly increases their risk of HIV infection,

B – *being faithful*– recommending mutual fidelity in stable relationships

C – *condom use* – encouraging general and proper use of condoms [28].

ABC program causes much controversy and debate about its effectiveness, in recent years, a renewed increase in the percentage of people living with HIV (from 4.1% in 2003 to 7% in 2014) has been observed [29].

The use of condoms and other contraception methods

UNAIDS (*The Joint United Nations Programme on HIV and AIDS*) recognized the male latex condom as the only and the most effective, currently available method for reducing the transmission of HIV and other sexually transmitted diseases [30, 31]. Consistent and correct use of condoms during sexual intercourse protects against many STDs and unwanted pregnancy [32].

Laboratory in vitro studies indicate that latex condoms provide an effective physical barrier to pathogens STD [30].

The effectiveness of condoms is confirmed by the growing number of clinical trials. The strongest evidence comes from the cohort study, conducted on heterosexual couples in which one partner is infected with HIV. The study showed that consistent use of condoms reduces the risk of HIV infection by nearly 80% [33].

Wojnarowska's study from 2005 showed that during the last sexual intercourse 11.1% of respondents did not applied any method of contraception, while methods of low efficiency (method of "natural" or rejected sexual intercourse) has been adopted by a total of 41.1% of respondents. Condom was the most widely used method of contraception [25].

HBSC (*Health Behaviour in School-aged Children*) study from 2010 confirms that the most common method of contraception among adolescents is a condom (86.6% among middle school students and 89.0% among secondary school students). Subsequently, teenagers declared the use of rejected sexual intercourse (respectively 31.8% and 50.5%), a pill (17.1% and 26.9%) and natural methods (16.1% and 19.4%). Among the young people who underwent sexual initiation up to 15.1% of middle school students and 14.9% of secondary school students did not apply any method of contraception during their last intercourse. A condom was applied during last intercourse by 79.2% of middle school students and 69.9% of secondary school pupils [34].

Public Opinion Research Center in 2008 published a study which shows that the use of contraceptive methods is relatively common, but not sufficiently widespread and regular. The majority of respondents declares that they used contraception during their first sexual contact (61.1%), most often a condom (85.2%). 8,9% of the respondents used a contraceptive pill [25].

The research of the Institute for Educational Research also shows that the most common method of contraception for young people is a condom. During the last sexual intercourse a condom was used by almost 65% of respondents, hormonal agents - 17%, coitus interruptus - 12%, counting the days since the last menstrual period - 8%. As many as 11% of respondents did not use any method of contraception [20].

The percentage of sexually active Canadian teenagers who have declared using a condom during their last intercourse has been increasing in recent years. Among the participants of the B.C. Adolescent Health Survey questionnaire, the use of a condom increased from 64.6% in 1992 to 74.9% in 2003. Among adolescents aged 15-19 years participating in the Canadian Community Health Survey the use of a condom during the last intercourse increased from 72% in 2003 to 75% in 2005. Although the proportion of condom use among the sexually active Canadian youth is clearly increasing, a downward trend in the use of condoms with age is also noticeable. Among 15-19 year-olds surveyed in the Canadian Community Health Survey, 81% of sexually active 15-17 year olds and only 70% of teens aged 18-19 reported using a condom during their last intercourse. Therefore, it can be concluded that many young people, not only in Canada, disregards the risk of STD infection [19].

Worldwide, 54 studies evaluated the impact of sexual education programs on the use of condoms. Almost half of the programs (48%) resulted in an increase in the frequency of condom use, none of them had the effect of causing a reduction in the use of condoms. The percentage of successful programs in developing countries (seven of 12) was similar to the percentage in developed countries. The programs were equally effective regardless of the gender and age of the recipients.

Among 15 studies measuring the impact of sexual education programs on the frequency of the use of contraception in total, six have shown increased use of contraception, eight had no effect, and one (in the US) showed a reduction in the rate of contraceptive use [23, 24].

Unwanted, teenage pregnancies and abortions

The main public health problem in Poland and abroad are unwanted pregnancies, inextricably linked with many negative phenomena such as:

- teenage pregnancy (women who became pregnant and/or gave birth before turning 18),

- increase of the likelihood of complications among adolescent pregnant mothers whose reproductive system is at an early stage of development,
- abortions (legal and illegal), abandonment of newborns and infanticide,
- increased risk of alcohol and smoking by the mother during pregnancy,
- increased risk of depression among women,
- reduction of the scope of prenatal care and the likelihood of breastfeeding by the mother after birth [35].

Sexual abstinence is the only way to completely protect teenagers against unplanned pregnancy and STD and which does not have any negative side effects. But it is not possible for all young people to choose to live in sexual abstinence and therefore programs on sex education should be carried out in order to prevent unwanted pregnancies and their negative effects such as abortion.

Studies show that pregnancy of women aged up to 15 years is associated with higher maternal mortality by nearly 60% compared to mature women. Child mortality also increased 2.5-fold when the mother is under 20 [37]. Comparing with other age groups, there has been a 2 to 5-fold more gynaecological problems, pregnancy pathology and abortion on demand among adolescents. In countries that have legalized abortion on demand, you can measure the extent of unwanted pregnancies on the basis of data on abortion on demand among minors. In France in 2003 the abortion rate for women aged 15-17 was 9.6 per 1,000 [12].

Underage pregnancy may involve the risk of the following complications: premature placenta abruption, oligohydramnios, pregnancy-induced hypertension, renal neck-isthmus, premature birth and postpartum complications. The postpartum period is a significant emotional burden for a teenage mother and can lead to psychosocial problems. Minor pregnant women more likely than adults decide to put a child up for adoption [37].

According to the Central Statistical Office data, in Poland in 1998 the number of teen births (up to 19 years of age) was 20/1000 live births. In 2008 the number was 21 305, including 411 mothers who were under 15. In the period 2006 - 2008 unchanged increase in the number of births among young women up to 19 years of age was observed and the number of births by 15 year-olds and younger girls increased by 10%. The younger the age group the greater was the increase in fertility - fertility of 15-year-old increased by 63% between 2002-2010, of 16-year-old by 48%, of 17-year-old by 16%, of 18-year-old has not changed, and of the 19-year-old decreased by 12%. Since 2010 a slight decrease in teen pregnancy has been observed [38]. Królikowska's study demonstrated that teenage pregnancy was the result of gaps in sexual education, and not for example of desire to escape from a dysfunctional home [39].

California Department of Public Health announced that the pregnancy rate of minors has dropped to 28 births per 1,000 teens aged 15-19. It is the lowest result since 1991 when it reached the highest value of 70.9/1000. The decrease in the number of births among teens occurred in all ethnic groups. California has several programs and strategies aimed at preventing teenage pregnancies. Some of the key elements include:

- state law which requires that school and other state-funded activities including sexual education were comprehensive, accurate from a medical point of view and adapted to the age and culture,
- local education programs for young people and their parents that provide information about sexual health, skills development, supportive environments and opportunities for young people,
- support for pregnant teenagers and teenage parents in order to strengthen the situation of young families.

Activities in California are holistic and fit in with the 3rd type of sexual education. The positive effects of the activities of the above-mentioned programs support the role of sexual education in promoting sexual health.

In Canada, where sexual education of the 3rd type is generally conducted, the pregnancy rate (including live births, abortions and miscarriages) for both younger (15 - 17 years) and older (18 - 19 years) teenage women significantly decreased over the past few decades. The pregnancy rate among 15-19 year-old women fell from 47.6 per 1,000 in 1995 to 29.2 per 1,000 in 2005. The most visible is the decrease in the number of pregnancies of 15-17 year old girls, for whom the rate fell from 28.5 1000 in 1995 to 15.8 per 1,000 in 2005 [19].

SIECUS reports that complex sexual education programs resulted in a 50% decrease in the risk of teen pregnancy. By contrast, programs focused on abstinence had no effect on the number of teenage pregnancies [22].

Kirby's meta-analysis showed that in thirteen studies the impact of programs on the pregnancy rate was examined. Out of these 13 studies, in three of them positive effects were concluded, nine had a negligible impact, and one (in the US) suffered a significantly adverse effect [23, 24].

Table 1. Summary of numerical test results showing the impact of programs on sexual behavior

Results	N*	Studies in developing countries N=18			Studies in developed countries N=65			Total N=83		
		-	0	+	-	0	+	-	0	+
Delay of the moment of sexual initiation	52	0	8	6	1	21	16	1	29	22
Reduction in the frequency of sexual relations	31	0	3	2	3	16	7	3	19	9
Decrease in the amount of sexual partners	34	0	5	3	1	16	9	1	21	12
Increase in the frequency of the use of a condom	54	0	5	7	0	23	19	0	28	26
Increase in the frequency of the use of contraception	15	0	2	0	1	6	6	1	8	6
Sexual risk reduction	28	0	2	0	0	12	14	0	14	14
Reduction of the number of pregnancies	13	0	1	1	1	8	2	1	9	3
Reduction of the number of STDs infections	10	1	2	0	1	4	2	2	6	2

*N - number of studies, which reported a profit; "+" - a positive (desirable) effect on factor; "0" - a statistically insignificant impact; "-" -a negative (undesirable) impact factor.
Source: [24].

The above summary of the studies clearly shows that the programs have a much more positive relation with the decrease in the frequency of engaging in risky sexual behaviours among the audience, than cause negative effects. Out of all 83 studies, nearly two-thirds (65%) had significantly positive impact on at least one of the studied sexual behaviour or indicators, and only 7% significantly negative [24].

Studies comparing the results of the programs of type 1 and 2 conducted in the United States showed that education promoting only sexual abstinence does not produce favourable implications in terms of sexual behaviour of young people and the risks of teenage pregnancies compared to the model of comprehensive sexual education [1].

The phenomenon of unwanted pregnancies is permanently associated with the phenomenon of abortion. In 2012, as much as 1021 new-born babies were left after birth in hospital for reasons other than health, which may prove directly that the woman had an unwanted pregnancy. The number of abandoned new-borns increased by 263 compared to 2011. There are no data how many new-borns were abandoned by their mothers out of the hospital and the parents who are not Polish citizens. In 2012 a total of 752 abortions were carried out in accordance with the law, including 23 among women under 20 years of age [40].

Conclusions

Adolescence is characterized by frequent risk-taking behaviour. The task of health promotion is to influence health determinants, among others through sexual education. Studies confirm the positive impact of complex sexual education conducted according to the recommendations of international organizations on a lower frequency of engaging in risky sexual behaviour. It seems appropriate to take action in order to disseminate sexual education appropriate for the level of psychosexual development in schools.

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INTERACTION OF THREE-DRUG COMBINATION OF LACOSAMIDE, CARBAMAZEPINE AND PHENOBARBITAL IN THE MOUSE MAXIMAL ELECTROSHOCK-INDUCED SEIZURE MODEL – AN ISOBOLOGRAPHIC ANALYSIS

INTERAKCJA TRÓJLEKOWEJ KOMBINACJI LAKOZAMIDU, KARBAMAZEPINY I FENOBARBITALU W TEŚCIE MAKSYMALNEGO WSTRZĄSU ELEKTRYCZNEGO U MYSZY – ANALIZA IZOBOLOGRAFICZNA

Maria W. Kondrat-Wróbel^{1(A,B,E,F)}, Jarogniew J. Łuszczki^{1(A,B,C,D,E,F,G)}

¹Department of Pathophysiology, Medical University of Lublin, Poland

Authors' contribution

Wkład autorów:

- A. Study design/planning
zaplanowanie badań
- B. Data collection/entry
zebranie danych
- C. Data analysis/statistics
dane – analiza i statystyki
- D. Data interpretation
interpretacja danych
- E. Preparation of manuscript
przygotowanie artykułu
- F. Literature analysis/search
wyszukiwanie i analiza literatury
- G. Funds collection
zebranie funduszy

Summary

Background. Epilepsy is one of the serious neurological diseases characterized by seizures that affect about 1% of people worldwide (65 million), and therefore, epilepsy can be considered as a disease of civilization. Although seizures are controllable with antiepileptic drugs (AEDs) in about 70% of cases, it remains still about 30% of epilepsy patients inadequately medicated with these AEDs, who need a full control of their seizure attacks. One of the treatment options in these patients is application of two or three AEDs in combination. The aim of this study was to characterize the anticonvulsant effects of a combination of three AEDs (i.e., carbamazepine [CBZ], lacosamide [LCM] and phenobarbital [PB]) at the fixed-ratio of 1:1:1 in the mouse maximal electroshock (MES)-induced seizure model.

Materials and methods. Tonic hind limb extension (seizure activity) was evoked in adult male albino Swiss mice by a current (sine-wave, 25 mA, 500 V, 50 Hz, 0.2 s stimulus duration) delivered via auricular electrodes. Type I isobolographic analysis was used to analyze the three-drug combination.

Results. Type I isobolographic analysis revealed that the combination of CBZ, LCM and PB (at the fixed-ratio of 1:1:1) exerted additive interaction with a slight tendency towards antagonism in the mouse MES-induced seizure model.

Conclusions. A special caution is advised to patients taking LCM in combination with CBZ and PB because this three-drug combination offered additive interaction with a slight tendency towards antagonism in the mouse MES model.

Keywords: antiepileptic drugs, isobolographic analysis, maximal electroshock, three-drug combination

Streszczenie

Wprowadzenie. Padaczka jest jedną z poważnych chorób neurologicznych charakteryzującą się występowaniem drgawek, które dotyczą około 1% ludzi na świecie (65 milionów) i dlatego też padaczka może być uważana za chorobę cywilizacyjną. Chociaż drgawki padaczkowe kontrolowane są lekami przeciwpadaczkowymi w około 70% przypadków, wciąż pozostaje około 30% pacjentów z padaczką niewłaściwie leczonych tymi lekami, którzy wymagają pełnej kontroli napadów. Jedną z opcji leczniczych u tych pacjentów jest zastosowanie dwóch lub trzech leków przeciwpadaczkowych w kombinacji. Celem badania była ocena działania przeciwdrgawkowego kombinacji trzech leków przeciwpadaczkowych (tj.: karbamazepiny [CBZ], lakoamidu [LCM] i fenobarbitalu [PB]) w stałej proporcji dawek 1:1:1 w teście maksymalnego wstrząsu elektrycznego u myszy.

Materiały i metody. Toniczny wyprost kończyn tylnych (aktywność drgawkowa) wywoływano u dorosłych myszy szczepu albino Swiss prądem (25 mA, 500 V, 50 Hz, 0,2 s czas stymulacji) dostarczanym przez elektrody uszne. Zastosowano typ I analizy izobolograficznej do oceny trójkątowej kombinacji.

Wyniki. Typ I analizy izobolograficznej wykazał, że kombinacja CBZ, LCM i PB (w stałej proporcji dawek 1:1:1) wykazuje interakcje addytywną z niewielką tendencją do antagonizmu w teście maksymalnego wstrząsu elektrycznego u myszy.

Wnioski. Zaleca się szczególną ostrożność pacjentom przyjmującym LCM do kombinacji CBZ i PB ponieważ ta trójkątowa kombinacja oferuje addycję z niewielką tendencją do antagonizmu w teście maksymalnego wstrząsu elektrycznego u myszy.

Słowa kluczowe: leki przeciwpadaczkowe, analiza izobolograficzna, maksymalny wstrząs elektryczny, trójkątowe kombinacje

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Address for correspondence / Adres korespondencyjny: JJ. Łuszczki, Department of Pathophysiology, Medical University, Jaczewskiego 8b, PL 20-090 Lublin, Poland, e-mail: jarogniew.łuszczki@umlub.pl, phone: +48 81 4486500

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Background

In spite of advanced knowledge on pathophysiological processes underlying epileptogenesis and a wide range of antiepileptic drugs (AEDs), currently available for the treatment of patients with epilepsy, there is still about 30% of epilepsy patients inadequately medicated with these AEDs in monotherapy [1-3]. For these patients, some new therapeutic options are required to stop their seizures so as not to decrease their quality of lives [2-4]. Of these options, combinations of various AEDs in duo- and triple therapy and/or application of some novel AEDs in monotherapy seem to be the most adequate [5, 6]. At present, several two-drug and three-drug combinations are recommended for patients, who are resistant to monotherapeutic use of the first-line AEDs [2, 3]. From a clinical point of view, there exists a general rule for combining AEDs to provide the most advantageous combinations. This rule is based on co-administration of AEDs with diverse molecular mechanisms of anticonvulsant action in order to complementary enhance their antiseizure effects in the mixture [6, 7]. Simultaneously, the ideal AED combination should reduce side effects of the AEDs in mixture [7, 8].

Because the assessment and characterization of types of interactions among AEDs in clinical trials is very difficult and performed empirically, pre-clinical studies on animals may help to provide evident information on the exact nature of interaction occurring among drugs. In such cases, pre-clinical *in vivo* experiments can confirm whether or not the theoretically selected AED combinations are favorable [8].

Lacosamide (LCM) is a novel third-generation AED that has recently been licensed as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult patients with epilepsy [9-11]. Similarly, carbamazepine (CBZ) and phenobarbital (PB) – two AEDs are widely used in patients with tonic-clonic seizures and partial convulsions [12]. From a clinical viewpoint, the combined application of LCM with CBZ or PB should result in a favorable combination because it should offer suppression of tonic-clonic seizures in patients with epilepsy refractory to the separate use of these AEDs in monotherapy [13]. Additionally, the selection of this three-drug combination (LCM, CBZ and PB) in our study fulfils theoretical criteria of an ideal AED combination providing maximal therapeutic effects along with minimal or no toxic effects [7]. However, this hypothesis needs experimental verification and confirmation in the mouse MES model. Of note, the maximal electroshock-induced seizures (MES) are thought to be an experimental model of tonic-clonic seizures and, to a certain extent, of partial onset seizures with or without secondary generalization in humans [14]. This is the reason to conduct experiments using LCM, CBZ and PB in this seizure model.

The aim of this study was to experimentally assess and characterize the type of interactions among three AEDs (LCM, CBZ and PB) in the mouse MES model. The characteristics of interaction among LCM, CBZ and PB was evaluated with type I isobolographic analysis, which is considered to be the method of choice for examining interaction in pre-clinical studies [15].

Materials and methods

All experiments were carried out on adult male albino Swiss mice (weighing 22-26 g) purchased from a licensed breeder (Dr. J. Kolacz, Warszawa, Poland). The experimental protocols and procedures described hereupon were approved by the Second Local Ethics Committee at the University of Life Sciences in Lublin (License no.: 45/2014).

The following AEDs were used in this study: CBZ (Polfa, Starogard Gdanski, Poland), LCM (Vimpat®, UCB Pharma, Brussels, Belgium), and PB (Polfa, Kraków, Poland). All drugs were suspended in a 1% solution of Tween 80 (Sigma-Aldrich, Poznań, Poland) in distilled water and were administered i.p. in a volume of 5 ml/kg body weight as follows: LCM and CBZ at 30 min, PB at 60 min, prior to maximal electroconvulsions.

Maximal electroconvulsions (seizure activity) were produced by a current (25 mA, 500 V, 50 Hz, 0.2 s stimulus duration) delivered *via* standard auricular electrodes by a Hugo Sachs generator (Rodent Shocker, Type 221, Freiburg, Germany). The criterion for the occurrence of seizure activity was the tonic hind limb extension. The animals were administered with different drug doses so as to obtain a variable percentage of protection against MES-induced seizures, allowing for the construction of a dose-response effect line (DREL) for the studied AEDs administered alone, according to Litchfield and Wilcoxon [16]. The protective activities of CBZ, LCM and PB administered separately and their combinations were evaluated and expressed as their median effective doses (ED_{50} in mg/kg), protecting 50% of mice against MES-induced seizures. The anticonvulsant activity of the mixture of LCM, CBZ and PB at the fixed-ratio of 1:1:1 was evaluated and expressed as the experimental median effective dose ($ED_{50\text{ exp}}$ value) against MES-induced seizures.

To assess the nature of interactions among three drugs in combination in preclinical studies on animals, an isobolographic analysis of interaction was applied according to the method described earlier [15, 17]. The percentage of animals protected against MES-induced seizures per dose of an AED administered singly and the

dose-response effect line (DREL) for each investigated AED in the mouse MES model were fitted using log-probit linear regression analysis according to Litchfield and Wilcoxon [16]. The median effective doses (ED_{50} values) of AEDs administered alone were calculated from the respective linear equations. The test for parallelism of DRELs for LCM, PB and CBZ based on the log-probit analysis was used. Subsequently, the median additive doses of the three-drug mixture of LCM, PB and CBZ ($ED_{50\text{ add}}$ – i.e., a dose of the three-drug mixture, which theoretically should protect 50% of the animals tested against MES-induced seizures) for the fixed-ratio combination of 1:1:1 was calculated from the equation of additivity, as follows: $x/ED_{50\text{ LCM}} + y/ED_{50\text{ PB}} + z/ED_{50\text{ CBZ}} = 1$; where x – is the dose of LCM, y – is the dose of PB, and z – is the dose of CBZ, co-administered as a mixture that exerts the desired effect (50% effect for ED_{50}), respectively. The calculation of the $ED_{50\text{ add}}$ value for the three-drug mixture at the fixed-ratio combination of 1:1:1 is always associated with determination of fractions of three drugs in mixture, as follows: $ED_{50\text{ add}} = (f_{\text{LCM}} \times ED_{50\text{ LCM}}) + (f_{\text{PB}} \times ED_{50\text{ PB}}) + (f_{\text{CBZ}} \times ED_{50\text{ CBZ}})$; where: f_{LCM} , f_{PB} and f_{CBZ} – are the fractions of LCM, PB and CBZ in a total amount of the mixture, respectively. Thus, for the three-drug mixture the above expression is true when: $f_{\text{LCM}} + f_{\text{PB}} + f_{\text{CBZ}} = 1$. To simplify the notation and nomenclature of interactions in isobolography, the drug doses were administered at the fixed-ratio combination (e.g. 1:1:1). The fixed-ratio combination of 1:1:1 refers to ratios that were based on the ED_{50} values of the constituent drugs. In this study, the mixture at the fixed-ratio of 1:1:1 comprised $1/3$ of the ED_{50} of LCM, $1/3$ of the ED_{50} of PB and $1/3$ of the ED_{50} of CBZ. Thus, the isobolographic notation of the fixed-ratio combination comprises numerators of fractions of ED_{50} values for AEDs used in the mixture (1:1:1). Afterwards, proportions of the AEDs in the mixture were calculated and the respective mixtures of LCM, PB and CBZ were administered to animals. The anticonvulsant effects offered by the studied AEDs in combination at the fixed-ratio of 1:1:1 in the mouse MES model were evaluated and expressed as the experimentally-derived $ED_{50\text{ exp}}$ value, corresponding to a dose of three-drug mixture, sufficient for the 50% protective effect against MES-induced seizures in mice. Finally, to determine the separate doses of LCM, PB and CBZ in the mixture, the $ED_{50\text{ exp}}$ and $ED_{50\text{ add}}$ values were multiplied by the respective proportions of AEDs.

The experimentally-derived $ED_{50\text{ exp}}$ value for the mixture of LCM, PB and CBZ at the fixed-ratio of 1:1:1 was statistically compared with its respective theoretical additive $ED_{50\text{ add}}$ value by using the unpaired Student's t -test. All statistical tests were performed using GraphPad Prism version 5.0 for Windows (GraphPad Software, San Diego, CA, USA).

Results

LCM, PB and CBZ administered alone produced a clear-cut anticonvulsant effect against MES-induced seizures. The equations of DRELs for LCM ($y = 7.6636x - 1.6044$; Figure 1), PB ($y = 12.428x - 13.572$; Figure 1), and CBZ ($y = 14.671x - 11.93$; Figure 1), allowed the determination of the ED_{50} values for LCM, PB and CBZ, which were 7.27 ± 0.77 mg/kg, 31.21 ± 2.04 mg/kg and 14.25 ± 0.79 mg/kg, respectively (Table 1).

Table 1. Anticonvulsant effects of carbamazepine (CBZ), lacosamide (LCM), and phenobarbital (PB) administered singly against maximal electroshock (MES)-induced seizures in mice

Drug	ED_{50}	n	Drug combination	S. R.	f ratio S.R.	Test for parallelism
CBZ	14.25 ± 0.79	16	LCM vs. CBZ	1.154	1.126	non-parallel
LCM	7.27 ± 0.77	16	LCM vs. PB	1.122	1.134	parallel
PB	31.21 ± 2.04	16	CBZ vs. PB	1.029	1.107	parallel

Results are presented as median effective doses (ED_{50} values in mg/kg \pm S.E.M.) of CBZ, LCM and PB administered singly against MES-induced seizures in mice. The drugs were administered systemically (i.p.), as follows: CBZ and LCM – 30 min, PB – 60 min before the MES-induced seizures. n – total number of animals used at doses whose expected anticonvulsant effects ranged between 4th and 6th probit (16% and 84%); S.R. – slope function ratio for the respective two-drug combinations (i.e., $S_{\text{LCM}}/S_{\text{PB}}$, $S_{\text{LCM}}/S_{\text{CBZ}}$ and $S_{\text{PB}}/S_{\text{CBZ}}$); f ratio S.R. – factor for slope function ratio for the respective two-drug combinations. *Test for parallelism: if the S.R. value determined for two dose-response effect lines (DRELs) is lower than the f ratio S.R. value (S.R. < f ratio S.R.), the examined two DRELs are parallel to one another [16].

Source: own elaboration.

The test for parallelism of DRELs between LCM and PB, CBZ and PB revealed that the drugs had their DRELs parallel to each other (Table 1). In contrast, DRELs between LCM and CBZ are non-parallel to one another (Table 1). The three-drug combination of LCM, PB and CBZ at the fixed-ratio of 1:1:1 exerted the anticonvulsant activity in the MES test and the experimentally derived $ED_{50\text{ exp}}$ value for the mixture of three AEDs ($y = 5.7745x - 2.6105$; Figure 1) was 20.79 ± 2.39 mg/kg (Table 2; Figure 2).

Table 2. Type I isobolographic analysis of interaction among carbamazepine (CBZ), lacosamide (LCM) and phenobarbital (PB) at the fixed-ratio of 1:1:1 in the mouse maximal electroshock (MES)-induced seizure model

ED ₅₀ exp	n _{exp}	LCM _{exp}	PB _{exp}	CBZ _{exp}	ED ₅₀ add	n _{add}	LCM _{add}	PB _{add}	CBZ _{add}
20.79 ± 2.39	24	2.87	12.31	5.62	17.58 ± 0.70	50	2.42	10.40	4.75

Data are presented as median effective doses (ED₅₀ values in mg/kg ± S.E.M.) protecting 50% of animals tested against MES-induced seizures. The ED₅₀ values were either experimentally determined from the mixture of three drugs (ED₅₀ exp) or theoretically calculated as additive for the three-drug mixture (ED₅₀ add). The actual doses of LCM, PB and CBZ that comprised the mixtures at the fixed-ratio combination of 1:1:1 for both ED₅₀ exp and ED₅₀ add values are presented in separate columns. Statistical evaluation of data was performed by using unpaired Student's *t*-test. *n* – total number of animals used at those doses whose expected anticonvulsant effects were ranged between 4th and 6th probit, denoted for the experimental mixture of drugs (*n*_{exp}) and theoretically calculated (*n*_{add} = *n*_{LCM} + *n*_{PB} + *n*_{CBZ} – 6).
Source: own elaboration.

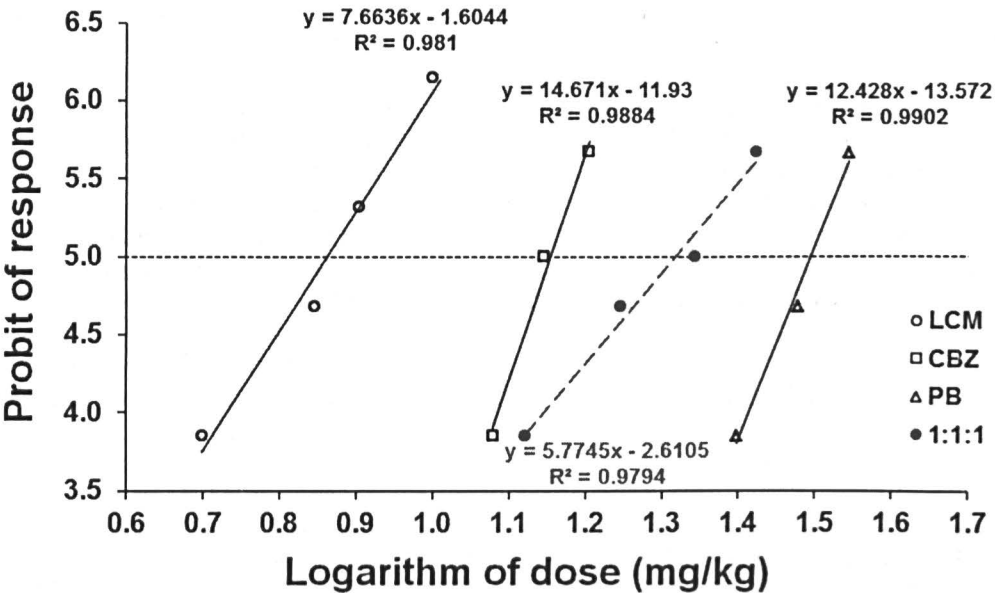


Figure 1. Log-probit dose-response effect lines (DREs) of carbamazepine (CBZ), lacosamide (LCM) and phenobarbital (PB) administered alone and in combination at the fixed-ratio of 1:1:1 against maximal electroshock (MES)-induced seizures in mice

Doses of CBZ, LCM and PB administered alone and in combination at the fixed-ratio of 1:1:1 were transformed to logarithms, whereas the protective (anticonvulsant) effects offered by the AEDs against MES-induced seizures were transformed to probits according to Litchfield and Wilcoxon [16]. Linear regression equations of dose-response effects for CBZ, LCM and PB administered alone and in combination are presented on the graph; where *y* – is the probit of response; *x* – is the logarithm (to the base 10) of an AED dose or a dose of the mixture of the studied AEDs; and *R*² – coefficient of determination.

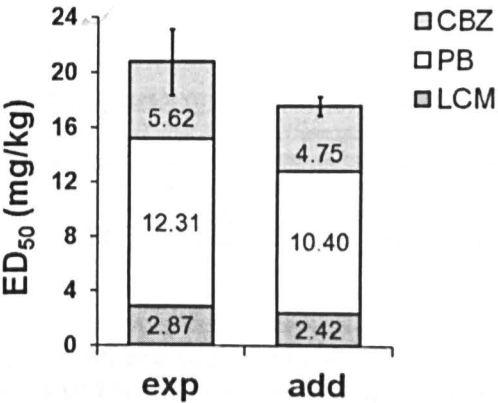


Figure 2. Doses of carbamazepine (CBZ), lacosamide (LCM) and phenobarbital (PB) in the three-drug mixture at the fixed-ratio combination of 1:1:1 against maximal electroshock (MES)-induced seizures in mice

Columns represent median effective doses (ED₅₀ in mg/kg ± S.E.M.) of the mixture of three drugs at the fixed-ratio of 1:1:1 that were experimentally determined in the MES-induced seizure test in mice (exp), and theoretically calculated as additive (add). Doses of CBZ, PB and LCM in combination at the fixed-ratio of 1:1:1 are presented as stacked bars. Statistical comparison of data was performed by using unpaired Student's *t*-test.

The isobolographic analysis of interaction revealed that the three-drug mixture at the fixed-ratio of 1:1:1 exerted additive interaction with a slight tendency towards antagonism in the MES test in mice (Figure 3A-3C).

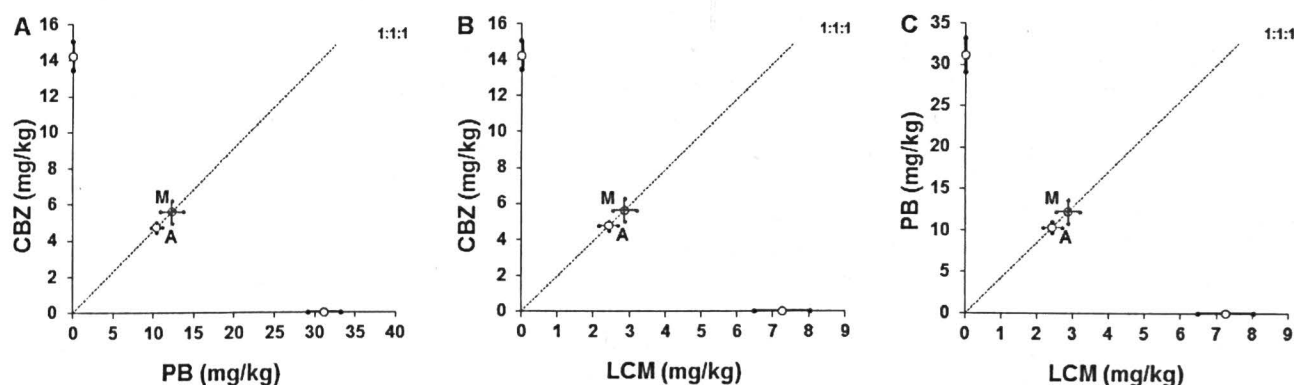


Figure 3A-3C. Isobolograms showing additive interactions among carbamazepine (CBZ), lacosamide (LCM) and phenobarbital (PB) against maximal electroshock (MES)-induced seizures in mice

The median effective doses (ED₅₀ values) for CBZ, LCM and PB are plotted graphically on X-axis and Y-axis (Figure 3A-3C). The solid lines on the X and Y axes represent the S.E.M. for the AEDs administered alone. The open circles (o) depict the experimentally-derived ED₅₀ values (\pm S.E.M.) and theoretically calculated ED₅₀ values (\pm S.E.M.) for total doses expressed as the proportions of AEDs that produced a 50% protection of animals against MES-induced seizures. The S.E.M. values are presented as horizontal and vertical error bars for the ED₅₀ values and ED₅₀ values. Points M and A on each graph reflect the ED₅₀ values and ED₅₀ values, respectively. The line starting from the point (0, 0) and crossing through the points M and A corresponds to the fixed-ratio of 1:1:1 for the combination of CBZ, LCM and PB. The experimental ED₅₀ value of the three-drug mixture for the fixed-ratio of 1:1:1 is placed close to the theoretically calculated ED₅₀ value, indicating the additive interaction.

(A) Interaction between CBZ and PB. The X- and Y-coordinates for all points presented on the isobologram are as follows: M (12.31; 5.62) and A (10.40; 4.75).

(B) Interaction between LCM and CBZ. The X- and Y-coordinates for all points presented on the isobologram are as follows: M (2.87; 5.62) and A (2.42; 4.75).

(C) Interaction between LCM and PB. The X- and Y-coordinates for all points presented on the isobologram are as follows: M (2.87; 12.31) and A (2.42; 10.40).

The experimentally-derived ED₅₀ value for this fixed-ratio combination (20.79 ± 2.39 mg/kg) did not differ significantly from the corresponding additively calculated ED₅₀ value (17.58 ± 0.70 mg/kg) (Table 2; Figure 2).

Discussion

Results presented herein indicate clearly that the three-drug combination of LCM, PB and CBZ at the fixed-ratio of 1:1:1 exerted additive interaction with a slight tendency towards antagonism in the mouse MES model. The observed anticonvulsant effect of the three-drug combination (LCM+PB+CBZ) can be compared with the results obtained for three two-drug combinations (i.e., LCM+PB, LCM+CBZ and PB+CBZ) in the mouse MES model. The available experimental data indicated that the interaction between PB and CBZ in the mouse MES model was additive in nature [18]. At present, there is no information on the interaction between LCM and PB or CBZ in the mouse MES model. However, it was documented that the combination of LCM with CBZ produced supra-additive (synergistic) interaction in the mouse psychomotor seizure (6 Hz) model [19]. In light of the above-mentioned facts, the combination of three drugs (i.e., LCM, PB and CBZ) in the mouse MES model has no advantage over the combination of CBZ with PB, as determined in this seizure model. On the other hand, evaluation of acute adverse effects for the AEDs in combination revealed that the tested three-drug mixture was devoid of any side effects with respect to motor coordination, long-term memory or skeletal muscular strength in mice (results not shown). Lack of any acute side effects in animals receiving the combination of LCM, PB and CBZ, in doses corresponding to the ED₅₀ value, indirectly indicated that the combination was safe enough to be used in further clinical trials.

It should be stressed that in this study we described, for the first time, a modified method of type I isobolographic analysis dedicated to assess the nature of pharmacodynamic interaction among three AEDs. As suggested in the Introduction, the combination of three AEDs (LCM, CBZ and PB) with various molecular mechanisms of anticonvulsant action should exerted beneficial interaction in the mouse MES model. It is important to note that the selection of AEDs to this three-drug combination (i.e., LCM, PB and CBZ) was based on theoretical presumptions

related with diverse complementary molecular mechanisms of anticonvulsant action ascribed to these AEDs. More specifically, CBZ reduces the frequency of sustained repetitive firing of action potentials in neurons and blocks voltage-dependent sodium channels [20]. PB enhances γ -aminobutyric acid (GABA)_A receptor-mediated currents through the binding to an allosteric regulatory site on the GABA_A-benzodiazepine receptor-chloride ionophore complex [21, 22]. Additionally, PB blocks excitatory responses induced by glutamate thereby the α -amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptors [23]. In the case of LCM, the drug through the selective enhancement of slow inactivation of voltage-gated sodium channels, stabilizes hyperexcitable neuronal membranes [24, 25]. The drug displays also affinity for the glycine strychnine-insensitive recognition site of the NMDA receptor complex, and allosterically blocks NMDA receptors with a specific action on receptors containing the NR2B subunit [24, 25].

Thus, considering the above-mentioned various molecular mechanisms of anticonvulsant action of the tested AEDs, the combination of LCM, CBZ and PB is expected to synergistically or additively suppress tonic-clonic seizures in experimental animals subjected to the MES test due to their complementary mechanisms of action.

Another fact needs special attention when explaining the results obtained in this isobolographic study. We used the combination of 3 drugs in doses that were 3-times lower than their corresponding ED₅₀ values, as determined separately in the mouse MES model. This reduction of drug doses was dependent on an isobolographic equation of additivity, suggesting that every n -drug mixture must comprise n -times reduced ED₅₀ values of the tested drugs alone; where n – is the number of drugs used in combination. In any isobolographic case, the equation of additivity is equal to unity and we have results corresponding to monotherapy with one effective drug, in terms of suppression of MES-induced seizures in mice. It is worthy of noting that the reduction of drug doses is advantageous because of limitation of side effects of singly used drugs that would appear in experimental animals.

Conclusions

1. The three-drug combination of LCM, CBZ and PB exerted additive interaction with a slight tendency towards antagonism in the mouse MES model.
2. This three-drug combination should be avoided in clinical trials in patients with drug resistant epilepsy because it did not provide any additional advantages over the use of the combination of CBZ with PB.
3. LCM added to the combination of PB and CBZ did not change significantly the nature of additive interaction.

Disclosures and acknowledgements

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NOTES ON THE AUTHORS

Ács Pongrác	PhD, University of Pécs, Hungary
Bergier Józef	Professor, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Bergier Barbara	PhD, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Bulikowski Włodzimierz	Professor, Department of Rehabilitation, Physiotherapy and Balneotherapy of Medical University in Lublin, Poland
Ilżecka Joanna	Professor, Department of Rehabilitation, Physiotherapy and Balneotherapy, Independent Laboratory of Neurological Rehabilitation of Medical University in Lublin, Poland
Junger Ján	Professor, University of Presov in Presov, The Slovak Republic
Kondrat-Wróbel Maria	MD, Department of Pathophysiology, Medical University of Lublin, Poland
Krasiy Nataliya	Ternopil University Hospital, Ukraine
Marszałek Anna	MSc, Public Elementary School of Friends of Catholic Schools Association in Hucisko-Pawelka, Poland
Łuszczki Jarogniew	Professor, Department of Pathophysiology, Medical University of Lublin, Poland
Niżnikowska Ewelina	PhD, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Olejniczak Dominik	PhD, Department of Public Health, Medical University of Warsaw
Oliynyk Oleksandr	Professor, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland; I.Ya. Horbachevskyi Ternopil State Medical University of Ministry of Public Health, Ukraine
Paszkiewicz Justyna	MSc, Institute of Health Sciences, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Pereviznyk Bohdana	I.Ya. Horbachevskyi Ternopil State Medical University of Ministry of Public Health, Ukraine
Piskorz Jolanta	PhD, MD, Department of Anesthesiology and Intensive Care, Zofia Tarnowska from the Zamoyskis Provincial Hospital in Tarnobrzeg, Poland
Plewik Dorota	MSc, Pope John Paul II State School of Higher Education in Biała Podlaska, Innovation Research Centre, Poland
Salonna Ferdinand	PhD, Palacký University of Olomouc, The Czech Republic
Skonieczna Joanna	MSc, Department of Public Health, Medical University of Warsaw
Szepeluk Adam	MSc, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Ślifirczyk Anna	PhD, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Tokarska-Rodak Małgorzata	Associate professor, Institute of Health Sciences, Pope John Paul II State School of Higher Education in Biała Podlaska, Poland
Tsos Anatolii	Professor, Lesya Ukrainka Eastern European National University, Lutsk, Ukraine
Walaszek Robert	PhD, Department of Recreation and Biological Regeneration, the University of Physical Education in Cracow, Poland
Wójcik Gustaw	PhD, MD, Department of Rehabilitation, Physiotherapy and Balneotherapy of Medical University in Lublin, Poland; Department of Imaging Diagnosis, Zofia Tarnowska from the Zamoyskis Provincial Hospital in Tarnobrzeg, Poland
Yemiashev Oleh	Ternopil University Hospital, Ukraine
Zabihailo Yulia	I.Ya. Horbachevskyi Ternopil State Medical University of Ministry of Public Health, Ukraine

GUIDELINES FOR THE AUTHORS / RULES OF PUBLISHING

- Journal *Health Problems of Civilization*

Aims and scope

„Health Problems of Civilization” is a scientific journal which is the continuation of the journal “Human and Health” (ISSN 2082-7288). The journal is issued exclusively in English and concerns various groups of subjects such as: biomedical aspects of health, modern diseases, physical activity, obesity, health-related behaviors and some of the authors of particular articles are the acknowledged specialists in the scope of medical sciences and physical culture sciences.

The mission of our journal is to popularize knowledge in the scope of various health problems of men in the face of dynamic changes of modern life caused by civilization growth, industrialization, urbanization and environmental changes. Papers should be submitted to the Editorial Office on-line via: <http://www.editorialsystem.com/hpc/login/>

Ethical requirements

When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000 (concerning the ethical principles for the medical community and forbidding releasing the name of the patient, initials or the hospital evidence number) and with the ethical standards of the responsible committee on human experimentation (institutional and national). The authors presenting case studies are obligated not to disclose patients’ personal data. Regarding photographs, in case of any doubt that the picture inadequately protects the patient’s anonymity his consent is required for publication.

Conflict of interest

Authors are expected to describe sources of the research funding, a role of the potential sponsor in planning, executing and analysis of the study, and the influence (bias) the funding organization had on the content of the article. Other relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony) providing potential sources of conflict of interest in relation to the submitted article should also be revealed.

Ghostwriting, guest authorship and plagiarism policy

„Health Problems of Civilization” has procedures in place to prevent ghostwriting, guest authorship, and plagiarism.

Preparation of manuscripts

The paper should be written in English and be communicative, clear and concise, while maintaining the classic layout.

Work layout

The texts of the submitted articles should not exceed:

- In original papers and in review papers, 4400 words including tables and references – about 20 sheets, typewritten, double-spaced, 11 point font, 30 items of literature;
- In case studies, 1000 words including tables and references – about 7 sheets, typewritten, double-spaced, 11 point font, 10 items of literature;

- In editorial, 1500 words excluding references – about 10 sheets, double-spaced, 11 point font, 15 items of literature, without summary and key words, tables and figures can be included, sections can be included;
- In book reviews, 750 words, without sections, summary and key words.

Papers exceeding the required length or the number of items of literature will be individually considered by the Editor-in-Chief.

Original papers should be organized in a standard form with separate:

- Title Key words (from the Medical Subject Headings [MeSH] catalogue of the Index Medicus)
- Summary (150-250 words, structured)
- Background
- Material and methods
- Results
- Discussion
- Conclusions
- Disclosures and acknowledgements
- References.

Case studies should be divided to the following sections:

- Title
- Key words (from the Medical Subject Headings [MeSH] catalogue of the Index Medicus)
- Summary (150-200 words, structured)
- Introduction
- Case description
- Conclusions
- References.

Review papers should be divided to the following sections:

- Title
- Key words (from the Medical Subject Headings [MeSH] catalogue of the Index Medicus)
- Summary (150-250 words)
- Introduction
- Aim of the work
- Brief description of the status of knowledge
- Conclusions
- References.

Tables

Tables should be numbered according to their sequence in the text. The text should include references to all tables. Each table should be provided in a separate file.

Illustrations

Each figure should be provided in a separate file, not included in the text.

Figures should preferably be provided in the TIF or EPS format. JPG is also acceptable.

All figures, whether photographs, graphs or diagrams, should be numbered consecutively throughout.

Citation and references

References should be quoted in square brackets in order of citation.

The reference list should be arranged in the order in which the citations appear in the text. If the number of authors exceed 6, after the sixth name “et al.” should be written.

Journal citation:

Tomao P, Ciceroni L, D'Ovidio MC, De Rosa M, Vonesch N, Iavicoli S, et al. Prevalence and incidence of antibodies to *Borrelia burgdorferi* and to tick-borne encephalitis virus in agricultural and forestry workers from Tuscany, Italy. *Eur J Clin Microbiol Infect Dis*. 2005; 24(7): 457–463.

Journal with a supplement number:

Zajkowska J. Lyme borreliosis – guidelines of treatment and expectations of patients. *Przegl Epidemiol*. 2008; 62(Suppl.1): 142–151 (in Polish).

Journal volume with part number:

Abend SM, Kulish N. The psychoanalytic method from an epistemological viewpoint. *Int J Psychoanal*. 2002;83(Pt 2):491-5.

Journal issue with part number:

Ahrar K, Madoff DC, Gupta S, Wallace MJ, Price RE, Wright KC. Development of a large animal model for lung tumors. *J Vasc Interv Radiol*. 2002;13(9 Pt 1):923-8.

Online journal citation:

Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. *BMJ*. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752.

Electronic Publish Ahead of Print:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. *Blood*. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Book:

Biernat E. Aktywność fizyczna mieszkańców Warszawy. Na przykładzie wybranych grup zawodowych. Warszawa: Oficyna Wydawnicza SGH; 2011 (in Polish).

Chapter from a book:

Piątkowska M. Uczestnictwo Polaków w aktywności fizycznej w porównaniu do innych krajów Unii Europejskiej. In: Buśko K, Charzewska J, Kaczanowski K., editors. *Współczesne metody badań aktywności, sprawności i wydolności fizycznej człowieka*. Warszawa: Akademia Wychowania Fizycznego w Warszawie; 2010. p. 38-57.

Forthcoming/In press:

Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in *Arabidopsis*. *Proc Natl Acad Sci U S A*. Forthcoming 2002.

Materials published online without DOI number:

Aboud S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12]; 102(6): [about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

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Review Process

The registered manuscripts are sent to 2-3 independent experts for scientific evaluation. Submitted papers are accepted for publication after a positive opinion of the independent reviewers. „Health Problems of Civilization” uses a double-blind review process in which authors do not know the identity of their reviewers, nor do the reviewers know the identities of the authors. The evaluation process usually takes 2-4 months.

Correspondence address:

Pope John Paul II State School In Higher Education in Biała Podlaska, Sidorska 95/97, room 334, 21-500 Biała Podlaska, e-mail: p.rynkiewicz@pswbp.pl

WSKAZÓWKI DLA AUTORÓW/REGULAMIN PUBLIKOWANIA - Journal Health Problems of Civilization

Cele i zakres

"Health Problems of Civilization" to czasopismo naukowe, które jest kontynuacją czasopisma "Human and Health" (ISSN 2082-7288). Czasopismo to wydawane jest wyłącznie w języku angielskim i dotyczy różnych grup tematycznych, takich jak: biomedyczne aspekty zdrowia, współczesne choroby, aktywność fizyczna, otyłość, zachowania prozdrowotne. Wśród autorów poszczególnych artykułów znajdują się uznani specjaliści w zakresie nauk medycznych oraz nauk o kulturze fizycznej.

Misją naszego czasopisma jest promowanie wiedzy w zakresie różnych problemów zdrowotnych człowieka w świetle szybko postępujących zmian życia współczesnego, spowodowanego rozwojem cywilizacyjnym, industrializacją, urbanizacją oraz zmianami środowiska naturalnego. Artykuły należy przysyłać do Redakcji czasopisma za pomocą <http://www.editorialsystem.com/hpc/login/>.

W przypadku przesłania do Redakcji artykułu w j. polskim, Redakcja nie ponosi kosztów tłumaczenia artykułu na język angielski. Opłata za tłumaczenie wynosi 20 zł brutto za stronę obliczeniową, tj. 1800 znaków ze spacjami. Tłumaczenie będzie wykonywane przez aktualnie współpracujące z Redakcją biuro tłumaczeń, artykuł zostanie przekazany do tłumaczenia za pośrednictwem Redakcji po pozytywnej recenzji i ostatecznym zaakceptowaniu artykułu do publikacji. Po otrzymaniu od Redakcji informacji o zaakceptowaniu artykułu i ostatecznej kwocie tłumaczenia, Autor zobowiązany jest do przelania podanej kwoty na konto Państwowej Szkoły Wyższej: Bank Zachodni WBK S.A., 45 1500 1331 1213 3001 7949 0000. Obowiązkiem Autora jest również dostarczenie do Redakcji potwierdzenia dokonania wpłaty (np. w formie elektronicznej na adres mailowy).

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W przypadku opisywania eksperymentów przeprowadzanych na człowieku autorzy wskazują, czy zastosowane procedury były zgodne z Deklaracją Helsińską z roku 1975, uaktualnioną w 2000 (dotyczącą zasad etyki dla społeczności medycznej oraz zakazu ujawniania nazwiska pacjenta, inicjałów lub numeru ewidencyjnego szpitala) oraz ze standardami etycznymi komisji ds. eksperymentów na ludziach (instytucjonalnej i państwowej). Autorzy prezentujący studia przypadków są zobowiązani do tego, by nie ujawniać danych osobowych pacjentów. Odnosnie do zdjęć, w przypadku wątpliwości, czy dane zdjęcie odpowiednio zabezpiecza anonimowość pacjenta, wymagana jest zgoda pacjenta na publikację danego zdjęcia.

Konflikt interesów

Oczekujemy od autorów opisanie źródeł finansowania badań, roli potencjalnego sponsora w planowaniu, wykonywaniu i analizie badań oraz wpływu, jaki organizacja finansująca mogła mieć na zawartość artykułu. Pozostałe relacje (takie jak zatrudnienie, konsultacje, posiadanie akcji, honorarium, płatne zaświadczenia eksperckie), które mogą być potencjalnie źródłami konfliktu interesów w związku z dostarczonym artykułem, należy ujawnić.

Ghostwriting, guest authorship i zasady dotyczące plagiatu

"Health Problems of Civilization" stosuje procedury, które zapobiegają wystąpieniu zjawisk „ghostwriting”, „guest authorship” oraz plagiatu.

Przygotowanie manuskryptów

Artykuł powinien być napisany w j. angielskim, powinien być komunikatywny, przejrzysty i spójny, a także utrzymywać klasyczny wygląd edycyjny.

Wygląd pracy

Teksty przesłanych artykułów nie powinny przekraczać:

- W oryginalnych artykułach naukowych i artykułach przeglądowych, 4400 słów, łącznie z tabelami i bibliografią – ok. 20 stron, napisanych komputerowo, z podwójnym odstępem, z czcionką 11 pkt i 30 pozycjami literatury;
- W studiach przypadków, 1000 słów, łącznie z tabelami i bibliografią – ok. 7 stron, napisanych komputerowo, z podwójnym odstępem, z czcionką 11 pkt i z 10 pozycjami literatury;
- W artykułach od redakcji, 1500 słów wyłączając spis literatury – ok. 10 stron, z podwójnym odstępem, z czcionką 11 punktów, 15 pozycjami literatury, bez streszczenia i słów kluczowych; tabele i ryciny mogą być dołączone, artykuł może zawierać podział na sekcje;
- W recenzjach książek – 750 słów, bez podziału na sekcje, bez słów kluczowych i streszczenia.

Artykuły przekraczające wymaganą długość lub liczbę pozycji literatury będą rozstrzygane w drodze indywidualnej decyzji Redaktora Naczelnego.

Oryginalne artykuły naukowe powinny zawierać następujące elementy:

- Tytuł (w j. polskim i j. angielskim)
- Słowa kluczowe (z Medical Subject Headings [MeSH], katalog Index Medicus; w j. polskim i j. angielskim)
- Streszczenie (150-250 słów, w j. polskim i j. angielskim, podzielone na części)
- Wprowadzenie
- Materiał i metody
- Wyniki
- Dyskusja
- Wnioski
- Ujawnienia i uznania
- Bibliografia

Studia przypadków powinny zawierać następujące elementy:

- Tytuł (w j. polskim i j. angielskim)
- Słowa kluczowe (z Medical Subject Headings [MeSH], katalog Index Medicus; w j. polskim i j. angielskim)
- Streszczenie (150-200 słów, w j. polskim i w j. angielskim, podzielone na części)
- Wstęp
- Opis przypadku
- Wnioski
- Bibliografia

Artykuły przeglądowe powinny zawierać następujące elementy:

- Tytuł (w j. polskim i j. angielskim)
- Słowa kluczowe (z Medical Subject Headings [MeSH], katalog Index Medicus; w j. polskim i j. angielskim)
- Streszczenie (150-250 słów, w j. polskim i j. angielskim)
- Wstęp
- Cel pracy
- Krótki opis stanu wiedzy
- Wnioski
- Bibliografia

Tabele

Tabele powinny być ponumerowane zgodnie z ich kolejnością w tekście. Tekst powinien zawierać odniesienia do tabel.

Każda tabela powinna być przesłana w osobnym pliku.

Ilustracje

Każdy rysunek powinien być wysłany w osobnym pliku, nie zawartym w tekście.

Obrazki najlepiej przesłać w formacie TIF lub EPS. Format JPG jest także dozwolony.

Wszystkie obrazki, zarówno fotografie, wykresy, jak i diagramy, powinny być ponumerowane kolejno, zgodnie z pojawieniem się w tekście.

Cytaty i bibliografia

Pozycje literatury powinny być cytowane w nawiasach kwadratowych w kolejności cytowania.

Bibliografia powinna być ułożona w kolejności cytowania w tekście. Jeżeli liczba autorów przekracza 6, po 6 nazwisku należy dopisać „et al.”.

Cytowanie czasopisma:

Tomao P, Ciceroni L, D'Ovidio MC, De Rosa M, Vonesch N, Iavicoli S, et al. Prevalence and incidence of antibodies to *Borrelia burgdorferi* and to tick-borne encephalitis virus in agricultural and forestry workers from Tuscany, Italy. *Eur J Clin Microbiol Infect Dis*. 2005; 24(7): 457–463.

Czasopismo – suplement:

Zajkowska J. Lyme borreliosis – guidelines of treatment and expectations of patients. *Przegl Epidemiol*. 2008; 62(Suppl.1): 142–151 (po polsku).

Tom czasopisma z numerem części:

Abend SM, Kulish N. The psychoanalytic method from an epistemological viewpoint. *Int J Psychoanal*. 2002;83(Pt 2):491-5.

Wydanie czasopisma z numerem części:

Ahrar K, Madoff DC, Gupta S, Wallace MJ, Price RE, Wright KC. Development of a large animal model for lung tumors. *J Vasc Interv Radiol*. 2002;13(9 Pt 1):923-8.

Cytat z czasopisma online:

Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. *BMJ*. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752.

Publikacja elektroniczna przed drukowaną:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. *Blood*. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Książka:

Biernat E. Aktywność fizyczna mieszkańców Warszawy. Na przykładzie wybranych grup zawodowych. Warszawa: Oficyna Wydawnicza SGH; 2011 (in Polish).

Rozdział z książki:

Piątkowska M. Uczestnictwo Polaków w aktywności fizycznej w porównaniu do innych krajów Unii Europejskiej. In: Buśko K, Charzewska J, Kaczanowski K, editors. Współczesne metody badań aktywności, sprawności i wydolności fizycznej człowieka. Warszawa: Akademia Wychowania Fizycznego w Warszawie; 2010. p. 38-57.

Zapowiedzi/w druku:

Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in *Arabidopsis*. *Proc Natl Acad Sci U S A*. Forthcoming 2002.

Materiały opublikowane online nieposiadające numeru DOI:

Aboud S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12]; 102(6): [about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

Wydawca otrzymuje wszelkie prawa autorskie na zasadach wyłączności w odniesieniu do manuskryptów publikowanych, a także prawo do publikacji w formie drukowanej, z wykorzystaniem nośników elektronicznych lub innych oraz publikacji online. Streszczenia mogą być publikowane bez zezwolenia Wydawcy.

Proces recenzji

Zarejestrowane manuskrypty są przysyłane do 2-3 niezależnych ekspertów do oceny naukowej. Przesłane artykuły są akceptowane do publikacji po otrzymaniu pozytywnej opinii niezależnych recenzentów. „Health Problems of Civilization” prowadzi proces recenzji „double-blind”, w którym autorzy nie znają tożsamości recenzentów, a recenzenci – tożsamości autorów. Proces oceny zajmuje zazwyczaj 2-4 miesiące.

Adres do korespondencji

Państwowa Szkoła Wyższa im. Papieża Jana Pawła II w Białej Podlaskiej, Sidorska 95/97, room 334, 21-500 Biała Podlaska, e-mail: p.rynkiewicz@pswbp.pl

