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The effect of microflora resistance to antibiotics on the outcomes of the treatment of patients with severe craniocerebral injury

Analiza wyników leczenia pacjentów z ciężkim uszkodzeniem czaszkowo-mózgowym w zależności od oporności mikroflory na antybiotyki

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Keywords

severe craniocerebral injury, resistance of microflora to antibiotics

Słowa kluczowe

ciężkie uszkodzenie czaszkowo-mózgowe, antybiotykooporność

Summary

Introduction. Resistance of patients' microflora to antibiotics is the factor, gravely aggravating the course of many surgical diseases. Many authors regard the problem of microflora resistance to antibiotics as a priority of the today's medicine.

Aim. To study therapeutic outcomes in the patients with severe craniocerebral injury depending on the microflora resistance to antibiotics.

Material and methods. Objects of the study are 188 microorganism isolates, taken from 149 patients with severe craniocerebral injury – the in-patients of anaesthesiology and intensive care units at the Ternopil University Hospital (Ukraine) and the hospital in Biala Podlaska (Poland). The expertise of biological material and interpretation of the results were performed according to standard principles. The Berey classification was used. Following primary isolation of the pathogen, the Kdisc-diffusion technique (Kirby-Bauer) was implied to identify its antibiotic susceptibility.

Results. The mortality rate from severe craniocerebral injuries at the Ternopil University Hospital was 35.8%, whereas at the Biala Podlaska hospital – 17.5%. This was despite the fact that the number of patients with concomitant polytrauma at the hospital of Biala Podlaska was twice as the number at the Ternopil University Hospital that aggravated the course of disease and its prognosis considerably. Microbiological characteristics of microflora strains at the two hospitals were different enough. In Biala Podlaska, Gram-positive microorganisms accounted for 38.4% of cases in the general structure of microflora, whereas in Ukraine – for 16.6%. In comparison with the hospital in Biala Podlaska, the indices of microbial resistance to antibiotics at the Ternopil University Hospital were worse.

At the Ternopil University Hospital, 53.3% of *Pseudomonas aeruginosa* and 62.5% of *Acinetobacter baumannii* isolates were resistant to 5 basic groups of antibiotics, whereas at the hospital of Biala Podlaska the indices were 10.0 and 8.3%, respectively.

Conclusions. Presumably, the treatment outcomes of patients with severe craniocerebral injury directly depend on the resistance of patients' microflora to antibiotics. The use of the obtained results in the treatment of patients with severe neurotrauma will improve the results of so kind patients treatment.

Conflict of interest
Konflikt interesów

None
Brak konfliktu interesów

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Streszczenie

Wstęp. Oporność mikroflory pacjentów na antybiotyki jest czynnikiem poważnie zaostrzającym przebieg wielu chorób chirurgicznych. Duża część autorów uważa problem oporności mikroflory na antybiotyki za priorytet dzisiejszej medycyny.

Cel pracy. Analiza wyników leczenia pacjentów z ciężkim uszkodzeniem czaszkowo-mózgowym w zależności od oporności mikroflory na antybiotyki.

Materiał i metody. Przedmiotem badań było 188 izolatów drobnoustrojów pobranych od 149 pacjentów z ciężkim uszkodzeniem czaszkowo-mózgowym, przebywających na Oddziale Anestezjologii i Intensywnej Terapii Szpitala Uniwersyteckiego w Tarnopolu (Ukraina) oraz szpitala w Białej Podlaskiej (Polska). Ekspertyza materiału biologicznego oraz interpretacja wyników badań zostały przeprowadzone w oparciu o standardy.

W badaniu zastosowano klasyfikację Bereya. Po pierwszej izolacji patogenu zastosowano Kdisc – technikę dyfuzyjną (Kirby-Bauer), aby zidentyfikować oporność na antybiotyki.

Wyniki. Odsetek śmiertelności pacjentów z ciężkim uszkodzeniem czaszkowo-mózgowym przebywających w Szpitalu Uniwersyteckim w Tarnopolu wyniósł 35,8%, z kolei w szpitalu w Białej Podlaskiej – 17,5%. Pomimo faktu, iż liczba pacjentów ze współistniejącym urazem wielonarządowym w szpitalu w Białej Podlaskiej była dwukrotnie wyższa niż w Szpitalu Uniwersyteckim w Tarnopolu, miało to wpływ na pogorszenie przebiegu choroby oraz jej rokowanie. Charakterystyka mikrobiologiczna szczepów mikroflory w dwóch szpitalach wystarczająco się od siebie różni. W Białej Podlaskiej mikroorganizmy Gram-dodatnie stanowiły 38,4% przypadków w stosunku do ogólnej struktury mikroflory, z kolei na Ukrainie – tylko 16,6%. W porównaniu ze szpitalem w Białej Podlaskiej, w Szpitalu Uniwersyteckim w Tarnopolu wskaźniki oporności drobnoustrojów na antybiotyki były gorsze. W Szpitalu Uniwersyteckim w Tarnopolu 53,3% pałeczek ropy błękitnej (*Pseudomonas aeruginosa*) oraz 62,5% izolatów *Acinetobacter baumannii* było opornych na 5 podstawowych grup antybiotyków, podczas gdy w szpitalu w Białej Podlaskiej wskaźniki te wynosiły odpowiednio 10,0 i 8,3%.

Wnioski. Prawdopodobnie wyniki leczenia pacjentów z ciężkim uszkodzeniem czaszkowo-mózgowym zależą bezpośrednio od oporności mikroflory pacjentów na antybiotyki.

INTRODUCTION

Resistance of patients' microflora to antibiotics is the factor, gravely aggravating the course of many surgical diseases (1). The study of this issue is referred to as fundamental. Many authors regard the problem of microflora resistance to antibiotics as a priority of the today's medicine (2).

AIM

Numerous works evidence high dependence of treatment outcomes of various surgical pathologies on the patients' microflora sensitivity to antibiotics. We have failed to find the like works concerning the patients with craniocerebral injury. The prevalence and high mortality rate of the pathology taken into consideration, the purpose of this work was to assess the relationship between the results of treatment of patients with severe craniocerebral trauma and the resistance of the microflora isolated from the patients to antibiotics.

MATERIAL AND METHODS

Treatment results of 92 patients who had been treated for sepsis-complicated severe craniocerebral injury at the anaesthesiology and intensive care unit of Ternopil University Hospital in 2017, and 57 similar patients of the Province Hospital in Biala Podlaska (Poland), were analysed. Both facilities followed the guidelines of the American Association of Neurological Surgeons (3), which include securing adequate brain perfusion, observation of the principles of adequate patients' ventilation, hyperventilation being prevented, adequate analgosedation, control of hypo- and hyper osmolarity, hypo- and hypercapnia, and hyperthermia. The infusion therapy was performed to the extent, sufficient for the correction of hypovolemia and electrolyte disorders. Early stimulation of the gastrointestinal tract with enteral feeding and adequate antibiotic therapy were practised. Microflora sensitivity to antibiotics was the major factor of differentiating treatment conditions in both intensive care units.

The expertise of biological material and interpretation of the results were performed according to standard principles (4, 5). The Berey classification was used. Following primary isolation of the pathogen, the Kdisc-diffusion technique (Kirby-Bauer) was implied to identify its sensitivity to antibiotics. The conducted studies did not require the existence of special ethical permits for their conduct and publication.

RESULTS AND DISCUSSION

Craniocerebral injury is a major cause of mortality and disability throughout the world, remaining among the leading causes of death in the first four decades of life (6). In Great Britain, craniocerebral injury occurs in 1500 cases per 100 thousand people. 9 individuals of 100 thousand die because of craniocerebral injury (7). World-wide, the morbidity due to severe craniocerebral injury is as high as 80% (8). Thus, the values 35.8 and 17.54% in the hospitals of Ukraine and Poland are moderate enough. However, the morbidity in Ukraine is twice as the one in Poland. This is despite the fact that the number of patients with concomitant polytrauma in Poland is about twice as many as in Ukraine. Had the number of patients with concomitant polytrauma in Ukraine been larger, the mortality rate would have been higher correspondingly.

Microbiological characteristics of microflora strains for the two hospitals were different enough (tab. 1). In Biala Podlaska, Gram-positive microorganisms accounted for 38.4% of cases in the general structure of microflora, whereas in Ukraine – for 16.6%. Dominating in Biala Podlaska was *Staphylococcus aureus*, whereas at the hospital of Ternopil Medical University – *Klebsiella*. The lethality of surgical patients with Gram-negative flora is known to be higher as compared to those with Gram-positive flora (1). The indices of microflora resistance to antibiotics at the hospital of Ternopil Medical University were by far worse against those at the hos-

pital in Biala Podlaska. It would be appropriate to use the index of microflora poly-resistance for the comparison of microorganisms' resistance to antibiotics. The microorganisms, resistant to 5 and more antibiotics are regarded as poly-resistant. Poly-resistant strains *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were found in Ternopil and Biala Podlaska. However, at the hospital of Ternopil Medical University the number *Pseudomonas aeruginosa* isolates was 53.3% against 10.0% at the hospital in Biala Podlaska. For resistant *Acinetobacter baumannii* the indices were 62.5 and 8.3%, respectively. The situation with resistance to three antibiotics was alike. At the hospital of Ternopil Medical University, all *Pseudomonas aeruginosa* isolates were resistant to 3 antibiotics, whereas in Poland the figure was 10% only. The *Acinetobacter baumannii* index for Ternopil and in Biala Podlaska was 93.8 and 16.7%, respectively. Obviously, the situation with resistance to microorganisms at the Ternopil University Hospital was by far worse than that at Biala Podlaska province hospital (tab. 2).

Comparing conditions, treatment tactics, and patient contingent at the Ternopil University Hospital and Biala Podlaska province hospital, one can argue that in 2017 they were very much alike. The only significant difference was in the index of microflora resistance to antibiotics. At the Ternopil University Hospital, the situation with microflora resistance was several times worse than at the Polish hospital. Along with this, mortality rate at the Ukrainian hospital was twice the rate at the Polish one. This could be due to the increased microflora resistance to antibiotics.

As compared to the average values in Europe, microflora resistance to antibiotics at the hospital in Biala Podlaska is worse. Particularly, the WHO report of April 30, 2014 (1) contains description of resistance to antibiotics in 114 countries, according to CDC committee data. In this, resistant to meropenem *E. coli* was found in France and England less than in 0.03 per cent of cases, in Bulgaria – 0.66%, in Greece – 0.72%. Carbapenem-resistant *Klebsiella pneumoniae* were found: 0% in Austria, Denmark, Germany, Latvia, Lithuania, Sweden; 0.17% in Spain, France; 0.72% in Poland. Resistance of *E. coli* to meropenem in Poland amounts on average to 1.0%, whereas *Klebsiella* resistance does not exceed 2.0% (2).

Comparison of Ternopil University Hospital data and those from the other Ukrainian medical institutions

Tab. 1. Description of patients who were treated for severe craniocerebral injury at the anaesthesiology and intensive care units (AICU) of Ternopil University Hospital and Province Hospital in Biala Podlaska (Poland) in 2017

Description of patients with severe craniocerebral injury	Absolute values		Relative values	
	Hospital in Biala Podlaska, Poland	Ternopil University Hospital, Ukraine	Hospital in Biala Podlaska, Poland	Ternopil University Hospital, Ukraine
Number of patients with severe craniocerebral injury who were treated at AICU	57	92	100	100
Number of patients with severe craniocerebral injury who died	10	33	17.5	35.8
Number of patients with concomitant polytrauma	28	24	49	26.1

Tab. 2. Resistance of microorganisms to antibiotics at the intensive care units of Biala Podlaska province hospital (Poland) and Ternopil University Hospital (Ukraine)

Strains of microorganisms, dominating at AICU		Amount of microorganisms isolates, resistant to antibiotics	
Hospital in Biala Podlaska (73 isolates)	Ternopil University Hospital (115 isolates)	Hospital in Biala Podlaska (73 isolates)	Ternopil University Hospital (115 isolates)
Staphylococcus aureus 20.5% *Acinetobacter baumannii* 16.4% *Pseudomonas aeruginosa* 13.7% *Enterococcus faecalis* 11.0% *Escherichia coli* 8.2% *Klebsiella pneumonia* 6.8% *Enterobacter cloacae* 6.8%	*Klebsiella pneumonia* 42.6% *Acinetobacter baumannii* 13.9% *Pseudomonas aeruginosa* 13.0% *Staphylococcus aureus* 9.6% *Staphylococcus epidermidis* 7.0% *Escherichia coli* 6.1% *Enterobacter cloacae* 4.3%	*Pseudomonas aeruginosa* resistant to carbapenems 30.0% *Pseudomonas aeruginosa* resistant to 3rd generation cephalosporins, fluoroquinolones and carbapenems 10.0% *Acinetobacter baumannii* resistant to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides 16.7% *Acinetobacter baumannii* resistant to penicillins, 3rd generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems 8.3%	*Acinetobacter baumannii* resistant to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides 93.8% *Pseudomonas aeruginosa* resistant to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides 100% *Acinetobacter baumannii* resistant to penicillins, 3rd generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems 62.5% *Pseudomonas aeruginosa* resistant to penicillins, 3rd generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems 53.3%

revealed no significant differences, Gram-negative flora currently prevailing in the Ukrainian anaesthesiology and intensive care units (9). Data on the sensitivity to various groups of antibiotics are numerous, so in the discussion we give the results of microflora sensitivity to carbapenems only. Here are the data on the analysis of 4974 clinical strains of *Pseudomonas aeruginosa*, isolated from the pus of pathological foci and drainage discharge in the patients who had been admitted to the surgical units of 97 multidisciplinary in-patient hospitals of 25 Ukrainian regions, Kyiv and Sevastopol throughout 2009 (10). The highest resistance levels of the studied strains to carbapenems were found at the hospitals of Kharkiv (38.6%), Vinnytsya (32%), and Volyn (30.9%) regions, whereas the lowest – in Ivano-Frankivsk (6.1%) and Khmelnytsk (11.5%) regions.

According to the most extensive Ukrainian research, conducted in 2008-2010 (11), resistance of *E. coli* clinical strains to carbapenems was: in Chernihiv region – 69.8 ± 7.0%, Cherkasy region – 23.1 ± 4.06%, Sumy region – 23.2 ± 5.64%, Kherson region – 22.3 ± 3.53% (13).

According to statistical information of the Ukrainian Centre for Disease Control and Monitoring, Ministry of Public Health (12), regarding analysis of poly-resistant strains, which are not susceptible to 5 or more basic antibiotics including carbapenem, in 2011 their list was as follows: poly-resistant *Acinetobacter baumannii* were found in 29.1% of the cases, *Pseudomonas aeruginosa* – 26.1%, *Klebsiella pneumoniae* – 12.7%, *Staphylococcus haemolyticus* – 12.7%, *Enterobacter cloacae* – 7.9%, *Escherichia coli* – 7.4%, *Staphylococcus aureus* – 1.8%, others – 2.3%.

According to professor Nestrenko, Donetsk Medical University (13), in 2012 the efficacy of meropenem against *Pseudomonas aeruginosa* at the largest hospital amalgamation of Donetsk amounted to 46.8%.

In 2016, Kreniov (14) studied the trends in microflora among the patients of the anaesthesiology and intensive care unit (AICU) at the Khmeknytskyi regional hospital. In 2015, 64 isolates were taken from the patients of AICU, 42 of them being poly-resistant (63%). The percentage of poly-resistant isolates was: *Acinetobacter baumannii* – 31.3%, *Pseudomonas aeruginosa* – 24.7%; *Klebsiella pneumoniae* – 9.2%; *Staphylococcus epidermidis* – 6.3%; *Enterococcus faecalis* – 3.2%; *Staphylococcus aureus* – 1.6%; Gram-negative microorganisms – 82%.

The same study showed that in 2014 and 2015 *Acinetobacter baumannii* resistance to meropenem was 52 and 79%, *Pseudomonas aeruginosa* – 31 and 71%, *Klebsiella pneumoniae* – 50.0 and 72%, *Escherichia coli* – 3.0 and 52.2%, respectively.

Similar findings were obtained in the two other studies (9, 15), the first one analysing information on antibiotic resistance at 14 large hospitals of Ukraine. According to this research, in 2015 *Klebsiella pneumoniae* were meropenem-susceptible in 58.3% of cases, *Enterococcus faecium* – in 7.5% of cases only, *Acinetobacter baumannii* – 19.0%, and *Pseudomonas aeruginosa* – 37.3%.

The primary cause of the catastrophic situation with microflora resistance is that over-the-counter drugs are easily available. Very often, the patients resort to self-treatment without adequate examination and physician's advice. It is not uncommon that reserve antibiotics are administered for prophylactic purposes. Extensive and uncontrolled use of antibiotics as feed additives in stock-raising is the factor, contributing to the growth of antibiotic resistance in Ukraine.

CONCLUSIONS

Growing microflora resistance to antibiotics entails significant increase in the death rate of the patients. The use of the obtained results in the treatment of patients with severe neurotrauma will improve the results of so kind patients treatment. The implementation of sanitary, hygienic and medical measures aimed in reducing of the resistance of microflora of patients with neurotrauma to antibiotics will lead to the reduction of the treatment duration, to the reduction in mortality, number of complications and cost of treatment. The obtained results could be evidence of the need for further similar studies.

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