

тивная операция на экстракраниальных артериях, второй этап - спустя 4-6 суток после первого хирургического вмешательства – реваскуляризация аорто-подвздошно-бедренной артериальной зоны или обеих артериальных бассейнов одновременно.

#### რეზიუმე

ექსტრაკრანიალური არტერიების და აორტულ-თეძოსქვეშა-ბარდაყის სევემენტის შერწყმული ოკლუზიურ-სტენოზური დაზიანების ქირურგიული მკურნალობა რეპერფუზიულ-რეოქსიგენაციური გართულებების განვითარების მაღალი რისკის პირობებში

<sup>1</sup>ი.ვენგერი, <sup>2</sup>ა.კოლოტილო, <sup>1</sup>ს.კოსტივი, <sup>1</sup>ნ.გერასემიუკი, <sup>2</sup>ო.რუსაკი

<sup>1</sup>ტერნოპილის ი.გორბაჩევსკის სახელობის ეროვნული სამედიცინო უნივერსიტეტი, უკრაინა; <sup>2</sup>ბუკოვინის სახელმწიფო სამედიცინო უნივერსიტეტი, ჩერნოვიცი, უკრაინა

კვლევის მიზანს წარმოადგენდა ექსტრაკრანიალური არტერიების და აორტულ-თეძოსქვეშა-ბარდაყის სევემენტის შერწყმული ოკლუზიურ-სტენოზური დაზიანების ქირურგიული მკურნალობის შედეგების გაუმჯობესება რეპერფუზიულ-რეოქსიგენაციური გართულებების განვითარების მაღალი რისკის პირობებში.

გამოკვლეულია 58 პაციენტი ექსტრაკრანიალური არ-

ტერიების და აორტულ-თეძოსქვეშა-ბარდაყის სევემენტის შერწყმული ათეროსკლეროზული დაზიანებით. არტერიული ნაკადის დაზიანების ხასიათის და ჰემოდინამიკური დარღვევების თავისებურებების დიაგნოსტიკისათვის გამოყენებულია ულტრაბგერითი დოპლეროგრაფია, დუპლექსური სკანირება, რენტგენოკონტრასტული ციფრული ანგიოგრაფია. წინასაოპერციო მზადების სისტემაში რეპერფუზიულ-რეოქსიგენაციური გართულებების განვითარების პროფილაქტიკისათვის გამოყენებულია შეთავაზებულ ღონისძიებათა კომპლექსი.

ექსტრაკრანიალური არტერიების ოკლუზიურ-სტენოზური დაზიანებისა და კონტრალტერალური შიგნითა საძილე არტერიის სტენოზური პროცესის შერწყმის ხშირ გავრცელებასთან დაკავშირებით, თავის ტვინის სისხლის მიმოქცევის შედარებითი კომპენსაციის სტადიაზე 7 პაციენტს ოპერაცია ჩაუტარდა კისრის სისხლძარღვებზე. პირველი ქირურგიული ჩარევიდან 4-6 დღის შემდეგ ჩატარდა აორტულ-თეძოსქვეშა-ბარდაყის სევემენტის რევასკულარიზაცია.

51 პაციენტს ჩაუტარდა ერთმომენტიანი ქირურგიული ჩარევა ექსტრაკრანიალურ არტერიებსა და აორტულ-თეძოსქვეშა-ბარდაყის აუზზე.

ორივე არტერიული აუზის რევასკულარიზაცია ჩატარდა ეტაპობრივად: პირველი ეტაპი – რეკონსტრუქციული ოპერაცია ექსტრაკრანიალურ არტერიებზე, მეორე ეტაპი – პირველი ქირურგიული ჩარევიდან 4-6 დღის შემდეგ - აორტულ-თეძოსქვეშა-ბარდაყის არტერიული ზონის, ან ორივე არტერიული აუზის ერთმომენტიანი რევასკულარიზაცია.

## ANTIBACTERIAL THERAPY FOR PURULENT-SEPTIC COMPLICATIONS IN PATIENTS WITH COMBAT RELATED PENETRATING CRANIOCEREBRAL GUNSHOT WOUNDS

<sup>1</sup>Sirko A., <sup>1</sup>Yovenko I., <sup>1</sup>Zhyliuk V., <sup>2</sup>Mosentsev M., <sup>2</sup>Pilipenko G.

<sup>1</sup>State Establishment, Dnipropetrovsk Medical Academy, Ministry of Healthcare of Ukraine;

<sup>2</sup>Public Institution, Mechnikov Dnipropetrovsk Regional Clinical Hospital, Ukraine

Penetrating craniocerebral gunshot wounds (PCGW) are a threat to victims' lives and long-term health, primarily due to the injury and resulting destruction of brain tissue as well as bacterial penetration of detritus into the cranial cavity and subsequent risk of wound infection. Bacterial contamination is already known to occur in cases of soft tissue injuries of the head and increases considerably if a non-sterile injuring projectile penetrates the cranial cavity [6]. Following the injuring projectile, fragments of skull, skin, hair, cranial bones, hot air, powder gases, etc., pierce through the brain, significantly increasing the risk of intracranial purulent-septic complications (PSCs) [1,18].

According to the U.S. military guidelines on the prevention of infections associated with combat-related injuries [8], cefazolin (2 g every 6-8 h) is prescribed as initial empiric antibiotic therapy

(ABT) for PCGWs, and if wound contamination is significant, metronidazole (500 mg every 8–12 h) is added. Clindamycin (1,800–2,700 mg/day) or ceftriaxone (2-4 g/day) and metronidazole (500 mg every 8-12 h) are considered to be therapeutic alternatives. In cases of penicillin allergy, vancomycin (2 g/day) and ciprofloxacin (400–800 mg/day) are recommended.

Intravenous antibiotics should be administered as soon as possible after the injury, preferably within 3 h. The antibiotic used should be sufficient to manage pathogenic microorganisms that can contaminate wounds during injury, including normal skin and intestinal flora, such as *Staphylococcus*, *Escherichia coli* and anaerobes of the gastrointestinal tract.

Initial antibacterial therapy should not target pathogens with multiple antibiotic resistance such as *Acinetobacter baumannii*,

*Pseudomonas aeruginosa* or *Klebsiella pneumoniae*. Because of decreased levels of methicillin-resistant *Staphylococcus aureus* infections and clinical evidence that adequate wound drainage, rather than antibiotics, is considered primary treatment in cases of abscesses, empiric therapy with vancomycin or linezolid may not be appropriate. Data have shown that empiric use of broad-spectrum antibiotics can lead to subsequent antibiotic-resistant infections [10].

The duration of ABT should be reduced to a minimum. Studies have reported that long-term therapy diminishes the outcome [15]. Wounds should be cleaned thoroughly at each bandage change with 4% chlorhexidine gluconate. Treatment of gunshot wounds often involves delayed initial closure of extremity wounds. However, facial and cerebral injuries require early primary closure of mucous membranes or dura mater to reduce the incidence of infections and aesthetic complications [4,18].

Study objective - to analyse pathogens and their susceptibility to antibiotic therapy in combat-related penetrating craniocerebral gunshot wounds patients and establish recommendations for the treatment of post-traumatic meningoencephalitis.

**Material and methods.** One hundred twenty-one patients who were admitted to the Public Institution, Mechnikov Dnipropetrovsk Regional Clinical Hospital, Dnipro, Ukraine, from 25 May 2014, to 31 December 2017, were successively enrolled in the study. The main inclusion criterion was a combat-related PCGW. All wounds were sustained during the combat operations in the eastern Ukraine.

Penetrating craniocerebral wounds (PCWs) are injuries that damage the integrity of the dura mater, which can lead to bacterial penetration into the skull. Clinical symptoms of PCWs include discharge of cerebrospinal fluid (CSF) and/or brain fragments from the wound. Symptoms of a penetrating craniocerebral wound on head and neck computed tomography include intradural or intracerebral foreign bodies and pneumocephalus [17].

ABT was administered according to the guidelines for the treatment of combat-related injuries [8]. Empirical ABT lasted for up to 5 days. Antibacterial therapy was adjusted according to results of bacteriological examination, and its efficacy was based on procalcitonin, a generally recognised marker for sepsis. Microbiological studies were performed in a clinicodiagnostic laboratory with a bacteriological analyser, VITEK 2 (bio-

Mérieux., Inc., France). We were able to identify the pathogen and prescribe targeted ABT (etiotropic treatment) in most cases of PSCs.

**Results and their discussion.** The study included 121 male patients aged 18 to 56 years (mean, 34.1±9.1). The Glasgow Coma Scale score ranged from 3 to 15 (mean, 10±4), and the Injury Severity Score ranged from 16 to 57 (mean, 27.7±7.6). Overall, 101 patients (83.5%) were diagnosed with shrapnel wounds and 20 (16.5%) with gunshot wounds.

The characteristics of microorganisms extracted during microbiological study of patients with PSCs are shown in Table 1.

Bacteriological examination of patients with PSCs due to penetrating CGSWs revealed that *Acinetobacter baumannii*, one of the most important representatives of so-called hospital flora, caused the highest incidence of infections, including post-traumatic meningitis. *A. baumannii* typically involves the skin and respiratory tract but can also cause other infections due to translocation, including those related to past medical procedures.

The most notable characteristic of this microorganism is its high pathogenicity in hospital patients who have been seriously ill for an extended period, including those with a weakened immune system. Patients with invasive medical devices, such as vascular and other catheters, surgical sutures or respiratory ventilators, and those who have received renal replacement therapy (haemodialysis) or antimicrobial therapy for the last 90 days are also at risk of developing *A. baumannii* infections.

Data on the relationship between the high incidence of this pathogen in patients with combat-related gunshot wounds have been reported. *A. baumannii* became particularly well known during the U.S. Army's military operations in Iraq during Operation Iraqi Freedom, causing an increased incidence of bloodstream infections among U.S. military personnel, called Iraqibacter [9].

*A. baumannii* is more likely to affect moist tissues, such as mucous membranes or damaged skin areas, where it may cause necrotising infection. Areas of infection or colonisation may involve the respiratory tract, blood, pleural fluid, urinary tract, surgical wounds, central nervous system (CNS), skin and eyes. Pneumonia can pose a threat to patients requiring mechanical ventilation, as *A. baumannii* has the ability to produce biofilms on endotracheal tube surfaces. A study conducted in 2003 on board the U.S. Navy hospital ship *Comfort*, which provided

Table 1. Results of bacteriological examinations

Microorganism	Infection location				
	CSF	Wound infection	Respiratory tract infection	Urinary tract infection	TOTAL
<i>Acinetobacter baumannii</i>	5	1	5	0	11
<i>Klebsiella pneumoniae</i>	2	1	4	0	7
<i>Escherichia coli</i>	0	1	1	0	2
<i>Pseudomonas aeruginosa</i>	1	2	5	0	8
<i>Staphylococcus aureus</i>	0	0	1	0	1
<i>Staphylococcus epidermidis</i>	2	0	0	0	2
<i>Staphylococcus haemolyticus</i>	0	0	3	0	3
<i>Enterobacter agglomerans</i>	1	0	2	0	3
<i>Enterococcus faecalis</i>	1	1	0	0	2
<i>Enterococcus faecium</i>	0	0	1	0	1
<i>Candida</i>	0	0	0	1	1
TOTAL	12	6	22	1	41

emergency medical care to injured U.S. military personnel in the Persian Gulf, showed that 4.1% of all skin and soft tissue infections were associated with *A. baumannii* [5].

The incidence of *A. baumannii* infections is increasing, especially in the U.K. and the U.S., as coalition forces exposed to bacteria in field hospitals return home to recover and rehabilitate.

Together with the development of skin, soft tissue, respiratory tract and bloodstream infections due to *A. baumannii*, neurosurgical patients are reported to have worsening of nosocomial post-surgical meningitis, which is a serious problem in those undergoing intensive therapy [3,12].

The second most common pathogen in our patients was *Pseudomonas aeruginosa*, which is also characteristic of hospital-acquired postoperative wound, respiratory tract and bloodstream infections in patients with a weakened immune system and those requiring invasive medical devices.

The efficacy of infection control measures, particularly hand hygiene and disinfection of the surrounding area, plays a major role in the spread of *P. aeruginosa*. Antibiotic-resistant *Pseudomonas* can be fatal in critically ill patients. In total, 51,000 medically related *P. aeruginosa* infections are estimated to occur each year in the United States. More than 6,000 (13%) cases have multiple drug resistance, with approximately 400 deaths associated with these infections per year [2].

Meningitis and ventriculitis caused by *P. aeruginosa* are primarily nosocomial infections and are related to previous neurosurgical procedures. Statistics have shown that *P. aeruginosa* is responsible for 1%–18% of cases of nosocomial meningitis [14].

*K. pneumoniae* was the third most common pathogen with infectious complications in our patients. In cases of *K. pneumoniae*, meningitis is most often considered a hospital-acquired infection related to neurosurgery and is associated with high mortality, despite the wide availability of antimicrobial and adjunctive therapies, due to its abnormal characteristics and the difficulty in detecting it at an early stage. Clinical outcomes of *K. pneumoniae* meningitis are often unsatisfactory. Studies have reported higher rates of diabetes, alcoholism and chronic liver diseases in addition to pre-existing infections (such as pyogenic liver abscess, septic endophthalmitis, pneumonia, otitis media, urinary tract infection, lumbar discitis and perianal abscess) in patients with *K. pneumoniae* meningitis who had undergone neurosurgical procedures [11].

*Staphylococcus epidermidis* are typically in hospital infections associated with the use of intravenous catheters and permanent prostheses. Colonisation of *S. epidermidis* on the skin of patients and health care workers is considered the most common source of these infections. This pathogen's ability to stick and form biofilms on the surfaces of foreign bodies is considered to be its most important mechanism. *S. epidermidis* meningitis is typically associated with neurosurgical procedures and devices, such as ventriculoperitoneal shunts, as well as head injury [13].

Meningitis caused by *Enterobacter* species rarely occurs in adults, although it may develop in neurosurgery patients and those sustaining neurotrauma. Treatment is often complicated because of the resistance of many *Enterobacter* isolates to third-generation cephalosporins and poor penetration of other antibiotics into the CNS. The most common pathogens are *Enterobacter cloacae*, *Enterobacter aerogenes* and *Enterobacter agglomerans* (50%, 34% and 16% of cultures, respectively). Overall, 47% of patients had clinical recovery/improvement, whereas 21% died [7].

*Enterococcus faecalis* caused by meningitis is an uncommon disease accounting for <1% of all cases of adult meningitis. This infection typically affects patients with immune disorders or CNS injuries, primarily in the form of hospital-acquired infections. It is also associated with neurosurgical procedures and shunting. The overall mortality rate was 21% in the present study. Adverse outcomes largely correspond with old age, presence of serious underlying disease, associated enterococcal infection, bacteraemia, septic shock and absence of fever on admission [16].

Thus, our careful analysis of infectious complications of pathogens in patients with PCWs revealed that most cases are nosocomial infections. The most effective prevention strategy includes a modern infection control system focusing on barrier measures to prevent the spread of infection. Targeted ABT toward the pathogen's sensitivity to antibiotics and antiseptics is the preferred treatment strategy.

We performed a detailed analysis of the sensitivity of microorganisms extracted from biological tissues to antibacterial agents (Table 2).

Sensitivity analysis of microorganisms detected in our patients to antibiotics revealed that, in most cases, the efficacy of the first-line ABT (ACCESS) was low and it was often necessary to prescribe broad-spectrum antibacterial drugs, including those related to second-line antibiotics (WATCH) and reserve drugs (RESERVE), according to the World Health Organisation classification [20].

Data in the literature confirm the results of our bacteriological studies.

Modern *A. baumannii* infections are characterised by multi-drug resistance to antimicrobials and antiseptics. The MYSTIC study, performed in 48 European hospitals between 2002 and 2004, reported that only 73.1% of *A. baumannii* isolates were susceptible to meropenem and 69.8% to imipenem. Susceptibility to other antibiotics was also extremely low: 32.4%, 34.0% and 47.6% were sensitive to ceftazidime, ciprofloxacin and gentamicin, respectively. Despite extensive administration of broad-spectrum ABT, the mortality rate in such infections can reach 70% [19].

The high resistance of *P. aeruginosa* infections requires treatment with intravenous antibiotics such as ceftazidime, carbapenems (meropenem and imipenem), aminoglycosides (gentamicin, amikacin or tobramycin) and ciprofloxacin, often in combination with intrathecal agents such as aminoglycosides or colistin. The recommended duration of therapy is from 14 to 28 days. In spite of this, treatment failures and relapses occur, with mortality reaching 80% [14].

For the treatment of *K. pneumoniae* infections in patients with CNS injury undergoing neurosurgical procedures, the primary component of survival, recovery and a favourable neurological outcome is early intravenous administration of first-line antibiotics before decline in neurological status (GCS≤7). Extended-spectrum cephalosporins are typically the drugs of choice, but aztreonam, carbapenems, aminoglycosides and ciprofloxacin are also used with varying degrees of effectiveness. Expected therapy duration ranges from 14 to 21 days [11].

In the present study, intracranial PSCs were detected in 14 (11.6%) patients. In addition, isolated meningoencephalitis occurred in eight patients, meningoencephalitis combined with ventriculitis in three and meningoencephalitis combined with ventriculitis and subdural empyema in two. Recurrent meningoencephalitis was complicated by multiple brain abscesses in one patient.

Table 2. Detected microorganism sensitivity to antibiotics

Microorganism	Sensitivity to antibiotics			
	CSF	Wound infection	Respiratory tract infection	Urinary tract infection
<i>Acinetobacter baumannii</i>	Cefoperazone/sulbactam, Meropenem, Tigecycline, Tobramycin	Tobramycin	Colistin, Tigecycline, Cefoperazone/sulbactam	-
<i>Klebsiella pneumoniae</i>	Amikacin, Piperacillin/tazobactam, Tigecycline, meropenem	Tobramycin	Amikacin, Cefoperazone/sulbactam, Meropenem, Gentamicin, Tobramycin, Trimethoprim/sulfamethoxazole, Ciprofloxacin	-
<i>Escherichia coli</i>	-	Gentamicin, Amikacin, Meropenem, Tobramycin, Ciprofloxacin	Meropenem, cefoperazone/sulbactam, Ceftriaxone	-
<i>Pseudomonas aeruginosa</i>	-	Cefoperazone/sulbactam, Gentamicin, Amikacin, Meropenem, Ciprofloxacin, Colistin, Ceftazidime	Cefoperazone, cefoperazone/sulbactam, Tigecycline, Tobramycin, Colistin, Levomycetin	-
<i>Staphylococcus aureus</i>	-	-	Vancomycin, Tigecycline, Gentamicin	-
<i>Staphylococcus epidermidis</i>	Levofloxacin, Tigecycline, Trimethoprim	-	-	-
<i>Staphylococcus haemolyticus</i>	-	-	Levofloxacin, Tigecycline, Cefoperazone/sulbactam, Clindamycin	-
<i>Enterobacter agglomerans</i>	Amikacin, Meropenem	-	Tigecycline, Meropenem	-
<i>Enterococcus faecalis</i>	Linezolid, Vancomycin	-	Imipenem, Colistin, Cefoperazone/sulbactam, Tobramycin	-
<i>Enterococcus faecium</i>	-	-	Amphotericin B, Caspofungin	-
<i>Candida</i>	-	-	-	Fluconazole, Voriconazole

Post-traumatic meningoencephalitis caused by *S. epidermidis* is characteristically associated with neurosurgical procedures and devices, such as ventriculoperitoneal shunts, as well as head injury. Glycopeptides (vancomycin and teicoplanin) are usually effective for intensive therapy, and oxazolidinones (linezolid) are effective in treating methicillin-resistant strains [13].

Treatment of meningoencephalitis caused by *Enterobacter* family microorganisms is characterised by low resistance to third-generation cephalosporins. Successful therapy involves intravenous and intrathecal administration of aminoglycosides, trimethoprim-sulfamethoxazole, piperacillin and ciprofloxacin [7].

Treatment of meningoencephalitis associated with *Enterococcus faecalis* usually includes ampicillin, penicillin, vancomycin and linezolid, with or without aminoglycosides, for an average period of 18 days. Other effective agents are intrathecal gentamicin and intravenous dexamethasone [16].

On the basis of the present study, we have formulated recommendations for antibiotic treatment of post-traumatic meningoencephalitis in combat-related CGSWs (Table 3).

Thus, because of the high risk of multi-drug-resistant hospital flora translocation, with clinical laboratory data indicating development of post-traumatic meningoencephalitis, we started de-escalation of empiric ABT with the broadest-spectrum drugs as monotherapy, and combination therapy was primarily used in cases of expected gram-positive and gram-negative aerobic and anaerobic pathogenic bacteria. Modification of empiric ABT was performed on the basis of clinical data regarding development of the infection process over time, SIRS markers, sepsis and multisystem failure. After receiving results of microbiological studies, targeted medication of ABT was initiated immediately, with a preference for etiotropic therapy and aggressive microbiological control.

**Conclusions.** Modern combat-related GSWs are serious injuries with numerous entry points for infection. Factors leading to immunosuppression in patients and promoting generalised infection of gunshot wounds include the presence of multiple primary wound infections, blood loss, anaemia, shock, malnutrition and chronic stress.

Table 3. Post-traumatic meningoencephalitis ABT for craniocerebral gunshot wounds

ABT					Microorganism
Empiric in escalation mode De-escalation	Empiric de-escalation modified (when there is no culture growth)	Targeted, initial (according to inoculation results) Etiotropic-1	Targeted, modified for the 1 <sup>st</sup> time (according to inoculation results) Etiotropic-2	Targeted, modified for the 2 <sup>nd</sup> time (according to inoculation results) Etiotropic-2	
Meropenem+metronidazole (3) Meropenem-vancomycin (6) Meropenem-colimycine (1) Meropenem-ornidazole (1) Meropenem-cefosulbin Cefoperazone/sulbactam-ertapenem, Tienam-ornizol	Cefoperazone/sulbactam, Vancomycin-meropenem, Tienam-vancomycin, Vancomycin-tigecycline, Tigecycline-piperacillin/tazobactam-linezolid, Tigecycline-linezolid-colomycin, Linezolid-colomycin Tigecycline, Levofloxacin-vancomycin	Ceftriaxone/sulbactam, Colomycin, Piperacillin/tazobactam, Cefoperazone/sulbactam, Tigecycline, Biseptol,	Tigecycline	+Tigecycline, etc.	<i>Acinetobacter baumannii</i>
		Tigecycline		Gentamicin	<i>Klebsiella pneumoniae</i>
		Meropenem (2)			<i>Escherichia coli</i>
			Tigecycline	Chloramphenicol	<i>Pseudomonas aeruginosa</i>
		Vancomycin			<i>Staphylococcus aureus</i>
		Biseptol, vancomycin	Tigecycline		<i>S. epidermidis</i>
			Tigecycline (2)		<i>S. haemolyticus</i>
					<i>Enterobacter agglomerans</i>
			Vancomycin		Linezolid
				<i>Escherichia faecium</i>	
	Fluconazole			<i>Candida</i>	

ABT for severe PSCs of PCGWs is effective when thoroughly and continuously controlled (daily or every 2–3 days) by bacteriological monitoring, a so-called monitoring-based antibiotic therapy.

Initial elimination of pathogens is often accompanied by superinfection development with ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* species), and use of procalcitonin-guided ABT is recommended. Procalcitonin level <0.5 ng/mL is a sign to stop ABT.

It is reasonable to use combined ABT, combining drugs with different mechanisms of action, and it is acceptable to monitor the mode of dose- and time-dependent antibiotics administration.

In order to achieve minimum inhibitory (suppressive) concentration of an antibacterial drug in cases of increased clearance, the maximum permitted dose of the drug should be used. Increased drug clearance may be due to increased renal blood flow, hypervolaemia, overhydration or hyperdynamic circulation.

### Conclusions.

Regarding PSC pathogens: Our results showed that, in most cases, such infections are considered nosocomial and are related to invasive medical procedures and devices. The most effective strategy in their prevention is implementing a modern infection control system with an emphasis on barrier measures against the spread of infection. Targeted ABT with early identification of the pathogen and its sensitivity to antibiotics and antiseptics is the preferred treatment strategy.

Regarding AB sensitivity of PSC pathogens: Our results showed that the efficacy of first-line antibiotics (ACCESS) was typically low and it was often necessary to prescribe broad-spectrum antibiotics, including those related to second-line antibiotics (WATCH) and reserve drugs (RESERVE), according to the WHO classification.

Regarding ABT of PSC: The use of initial de-escalation of empiric ABT using the broadest-spectrum drugs, mainly as a part of combination therapy for expected gram-positive and gram-negative aerobic and anaerobic infection pathogens, is recommended. Modification of empiric ABT is made on the basis of clinical

data regarding development of the infectious process over time, SIRS markers, sepsis and multiple organ dysfunction. Targeted modification of ABT is performed immediately upon determining the results of microbiological studies, with a preference for etiotropic therapy and aggressive microbiological control.

## REFERENCES

1. Alvis-Miranda HR, Adie Villafañe R, Rojas A, Alcalá-Cerra G, Moscote-Salazar LR. Management of Craniocerebral Gunshot Injuries: A Review. *Korean Journal of Neurotrauma*. 2015; 11(2): 35.
2. Antibiotic resistance threats in the United States, 2013. United States Department of Health and Human Services. Centers for Disease Control and Prevention (CDC)
3. Briggs S, Ellis-Pegler R, Raymond N, Thomas M, Wilkinson L. Gram-negative bacillary meningitis after cranial surgery or trauma in adults. *Scand J Infect Dis*. 2004; 36(3): 165-173.
4. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, Harris OA, Kisson N, Rubiano AM, Shutter L, Tasker RC, Vavilala MS, Wilberger J, Wright DW, Ghajar J. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery*. 2017 Jan 1;80(1):6-15.
5. Centers for Disease Control and Prevention (CDC). Acinetobacter baumannii infections among patients at military medical facilities treating injured U.S. service members, 2002-2004. *MMWR Morb Mortal Wkly Rep*. 2004 Nov 19; 53(45): 1063-1066
6. Fathalla H, Ashry A, El-Fiki A. Managing military penetrating brain injuries in the war zone: lessons learned. *Neurosurg Focus*. 2018; 45 (6):E6.
7. Foster DR, Rhoney DH. Enterobacter meningitis: organism susceptibilities, antimicrobial therapy and related outcomes. *Surg Neurol*. 2005; 63(6): 533-537
8. Hospenthal DR, Murray CK, Andersen RC et al. Guidelines for the prevention of infection after combat-related injuries. *J Trauma*. 2008 Mar; 64(3 Suppl): S211-S220
9. Howard A, O'Donoghue M, Feeney A, Sleator RD. Acinetobacter baumannii. An emerging opportunistic pathogen. *Virulence*. 2012 May 1; 3(3): 243-250
10. Khilnani GC, Zirpe K, Hadda V, Mehta Y, Madan K, Kulkarni A, Mohan A, Dixit S, Guleria R, Bhattacharya P. Guidelines for antibiotic prescription in intensive care unit. *Indian Journal of Critical Care Medicine*. 2019; 23(Suppl 1): S1-S63.
11. Lee B, Yeroushalmi K, Me HM, Sojitra P, Jilani U, Iqbal S, Ahmed S, Verley J, Akella J. Community acquired Klebsiella pneumoniae meningitis: a case report. *Germs*. 2018 Jun; 8(2): 92-95
12. Metan G, Alp E, Aygen B, Sumerkan B. Acinetobacter baumannii meningitis in post-neurosurgical patients: clinical outcome and impact of carbapenem resistance. *J Antimicrob Chemother*. 2007; 60(1): 197-199
13. Noguchi T, Nagao M, Yamamoto M, Matsumura Y, Kitano T, Takaori-Kondo A, Ichiyama S. Staphylococcus epidermidis meningitis in the absence of a neurosurgical device secondary to catheter-related bloodstream infection: a case report and review of the literature. *J Med Case Rep*. 2018 Dec; 12(1): 106
14. Pai S, Bedford L, Ruramayi R, Aliyu SH, Sule J, Maslin D, Enoch DA. Pseudomonas aeruginosa meningitis/ventriculitis in a UK tertiary referral hospital. *QJM* 2016 Feb; 109(2): 85-89
15. Petersen K, Waterman P. Prophylaxis and treatment of infections associated with penetrating traumatic injury. *Expert Review of Anti-Infective Therapy*. 2011; 9(1): 81-96.
16. Pintado V, Cabellos C, Moreno S, Meseguer MA, Ayats J, Viladrich PF. Enterococcal meningitis: a clinical study of 39 cases and review of the literature. *Medicine (Baltimore)*. 2003; 82(5): 346-364.
17. Rosenfeld JV, Bell RS, Armonda R. Current Concepts in Penetrating and Blast Injury to the Central Nervous System. *World Journal of Surgery*. 2014; 39(6): 1352-1362.
18. Smith JE, Kehoe A, Harrison SE, Russell R, Midwinter M. Outcome of penetrating intracranial injuries in a military setting. *Injury*. 2014; 45(5): 874-878.
19. Unal S, Garcia-Rodriguez JA. Activity of meropenem and comparators against Pseudomonas aeruginosa and Acinetobacter spp. isolated in the MYSTIC Program, 2002-2004. *Diagn Microbiol Infect Dis*. 2005 Dec; 53(4): 265-671.
- 20 WHO Model List of Essential Medicines. <http://www.who.int/medicines/publications/essentialmedicines>

## SUMMARY

### ANTIBACTERIAL THERAPY FOR PURULENT-SEPTIC COMPLICATIONS IN PATIENTS WITH COMBAT RELATED PENETRATING CRANIOCEREBRAL GUNSHOT WOUNDS

<sup>1</sup>Sirko A., <sup>1</sup>Yovenko I., <sup>1</sup>Zhyliuk V.,  
<sup>2</sup>Mosentsev M., <sup>2</sup>Pilipenko G.

<sup>1</sup>State Establishment, Dnipropetrovsk Medical Academy, Ministry of Healthcare of Ukraine; <sup>2</sup>Public Institution, Mechnikov Dnipropetrovsk Regional Clinical Hospital, Ukraine

Aim - to evaluate pathogens and their susceptibility to antibi-  
otic therapy (ABT) in combat-related penetrating craniocerebral  
gunshot wound (PCGW) patients and develop recommendations  
for treatment of post-traumatic meningoencephalitis.

We conducted a prospective analysis of examination and  
treatment results of 121 patients who were admitted to the Pub-  
lic Institution, Mechnikov Dnipropetrovsk Regional Clinical  
Hospital, Dnipro, Ukraine, from 25 May 2014, to 31 December  
2017, and were successively enrolled in the study. Intracranial  
purulent-septic complications were diagnosed in 14 (11.6%)  
patients including eight cases of isolated meningoencephalitis,  
three cases of meningoencephalitis combined with ventriculitis,  
two cases of meningoencephalitis combined with ventriculitis  
and subdural empyema and one case of multiple brain abscesses.

In most cases of combat-related craniocerebral wounds, infec-  
tions are considered nosocomial and typically related to medi-  
cal procedures and devices. In most cases, the effectiveness of  
first-line antibiotics was low, and it was often necessary to pre-  
scribe broad-spectrum ABT, including those related to second-  
line antibiotics and reserve drugs, according to the World Health  
Organisation classification. The use of initial de-escalation of  
empiric ABT with the broadest-spectrum drugs, mainly as a part  
of combination therapy for expected gram-positive and gram-  
negative aerobic and anaerobic infection pathogens, is recom-  
mended.

**Keywords:** purulent-septic complications, pathogens, sus-  
ceptibility of pathogens, antibacterial therapy, penetrating cra-  
niocerebral wounds, combat-related gunshot wounds.

РЕЗЮМЕ

**АНТИБАКТЕРИАЛЬНАЯ ТЕРАПИЯ ГНОЙНО-СЕПТИЧЕСКИХ ОСЛОЖНЕНИЙ У ПАЦИЕНТОВ С БОЕВЫМИ ОГНЕСТРЕЛЬНЫМИ ПРОНИКАЮЩИМИ ЧЕРЕПНО-МОЗГОВЫМИ РАНЕНИЯМИ**

**<sup>1</sup>Сирко А.Г., <sup>1</sup>Йовенко И.А., <sup>1</sup>Жилюк В.И., <sup>2</sup>Мосенцев Н.Ф., <sup>2</sup>Пилипенко Г.С.**

*<sup>1</sup>Государственное учреждение «Днепропетровская медицинская академия МОЗ Украины»; <sup>2</sup>Коммунальное учреждение «Днепропетровская областная клиническая больница им. И.И. Мечникова», Украина*

Цель исследования - анализ возбудителей инфекций и их чувствительности к антибактериальной терапии у пациентов с боевыми огнестрельными проникающими черепно-мозговыми ранениями; разработка рекомендаций по лечению посттравматического менингоэнцефалита.

Проведен проспективный анализ результатов обследования и лечения 121 пациента с боевыми проникающими черепно-мозговыми ранениями. Пострадавшие поступили в Днепропетровскую областную клиническую больницу им. И.И. Мечникова в период с 25 мая 2014 г. по 31 декабря 2017 г. Внутрочерепные гнойно-септические осложнения выявлены у 14 (11,6%) раненных: изолированный менингоэнцефалит - 8 случаев, менингоэнцефалит в сочетании с вентрикулитом - 3 случая, менингоэнцефалит в сочетании с вентрикулитом и субдуральной эмпиемой - 2 случая, множественное абсцедирование

вещества головного мозга - 1 случай. Инфекции у пациентов с боевыми черепно-мозговыми ранениями в большинстве случаев следует рассматривать как нозокомиальные, связанных с медицинскими процедурами и устройствами. Терапия антибиотиками первого выбора (ACCESS) в большинстве случаев оказалась неэффективной, часто возникала необходимость назначения антибактериальных препаратов широкого спектра действия, в том числе антибиотиков второго выбора (WATCH) и препаратов резерва (RESERVE) по классификации ВОЗ. В результате проведенного исследования доказано преимущество использования стартовой эмпирической дескалационной антибактериальной терапии препаратами максимально широкого спектра действия в режиме комбинированной терапии грам-положительных и грам-отрицательных аэробных и анаэробных возбудителей инфекций.

რეზიუმე

ჩირქოვან-სეპტიკური გართულებების ანტიბაქტერიული თერაპია პაციენტებში საბრძოლო ცეცხლნასროლი გამჭოლი ქალა-ტვინის ჭრილობებით

<sup>1</sup>ა.სირკო, <sup>1</sup>ი.იოვენკო, <sup>1</sup>ვ.ჟილიუკი, <sup>2</sup>ნ.მოსენცევი, <sup>2</sup>გ.პილიპენკო

<sup>1</sup>სახელმწიფო დაწესებულება „უკრაინის ჯანდაცვის სამინისტროს დნეპროპეტროვსკის სამედიცინო აკადემია“; <sup>2</sup>ი. მენჩიკოვის სახ. დნეპროპეტროვსკის საოლქო კლინიკური საავადმყოფო, უკრაინა

კვლევის მიზანს წარმოადგენდა ინფექციების გამომწვევების და მათი ანტიბაქტერიული თერაპიის მიმართ მგრძობელობის ანალიზი დაზარალებულებში ცეცხლნასროლი გამჭოლი ქალა-ტვინის ჭრილობებით, რეკომენდაციების შემუშავება ტრავმის შემდგომი მენინგოენცეფალიტის მკურნალობის თაობაზე.

გაანალიზებულია 121 საბრძოლო ცეცხლნასროლი გამჭოლი ქალა-ტვინის ჭრილობებით დაზარალებულის მკურნალობა ი. მენჩიკოვის სახელობის დნეპროპეტროვსკის საოლქო კლინიკური საავადმყოფოში, 2014 წლის 25 მაისიდან 2017 წლის 31 დეკემბრამდე. შიდაქალის ჩირქოვან-სეპტიკური გართულებები გამოუვლინდა 14 (11,6%) დაჭრილს: იზოლირებული მენინგოენცეფალიტი - 8 შემთხვევა, მენინგოენცეფალიტი ვენტრიკულიტთან ერთად - 3 შემთხვევა, მენინგოენცეფალიტი ვენტრიკულიტთან და სუბდურალურ ემპიემასთან ერთად - 2 შემთხვევა, თავის ტვინის ნივთიერების მრავლობითი აბსცედირება - 1 შემთხვევა.

ინფექციები დაზარალებულებში საბრძოლო ცეცხლნასროლი ქალა-ტვინის ჭრილობებით უმეტეს შემთხვევაში უნდა განვიხილოთ, როგორც ნოზოკომიალური, რომლებიც დაკავშირებულია სამედიცინო პროცედურებსა და მოწყობილობებთან. თერაპია პირველადი შერჩევის ანტიბიოტიკებით (ACCESS) უმეტეს შემთხვევაში არ იყო ეფექტური, ხშირად აუცილებელი ხდებოდა მოქმედების ფართო სპექტრის მქონე ანტიბაქტერიული პრეპარატების დანიშვნა, მათ შორის, რომლებიც განეკუთვნება მეორე შერჩევის ანტიბიოტიკებს (WATCH) და რეზერვის პრეპარატებს (RESERVE), მსოფლიო ჯანდაცვის ორგანიზაციის კლასიფიკაციის თანახმად. ჩვენებაშია სასტარტო ემპირიული დეესკალაციური ანტიბაქტერიული თერაპიის გამოყენება მოქმედების მაქსიმალურად ფართო სპექტრის პრეპარატებით, უპირატესად, კომბინირებული თერაპიის რეჟიმში სავარაუდო გრამ-დადებითი და გრამ-უარყოფითი აერობული და ანაერობული ინფექციების გამომწვევების მიმართულებით.