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ANTIBACTERIAL THERAPY FOR PATIENTS WITH BURN INJURIES

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Background. *Treatment of burn wound infection is an urgent issue of contemporary medicine, including surgery, combustiology and microbiology. It is established that infectious complications are a challenge for burn patients. In the course of wound reparation, infectious complications may worsen. Along with surgical treatment, mechanical removal of pathogens from burn wounds is also important as well as antimicrobials for patients with severe burns.*

Objective. *The aim of the study was to define the most common pathogens of purulent-inflammatory complications of burn wounds and their susceptibility to antibiotics.*

Methods. *The study involved patients treated at the Center of Thermal Trauma and Plastic Surgery of Lviv I-Territorial Medical Association, the unit of St. Luke Hospital of Lviv. Collection of material from wound secretions of burn wounds was performed with sterile swab. The study was performed before prescription of antibiotics, at the end of the first and second weeks of the disease. The pathogens were isolated and identified. Antibiotic susceptibility was studied using standard research methods. The obtained results were analyzed by means of the software package of the microbiological monitoring system WHONET 5.2 (WHO Collaborating Centre for Surveillance of Antimicrobial Resistance) and the program Microsoft Office Excel 2007.*

Results. *The study of smears from burn wounds proved that 240 strains of gram-positive and gram-negative microorganisms that caused purulent-inflammatory processes were isolated. Among the selected causative agents of a burn wound complicated by a purulent-inflammatory process, gram-negative bacteria predominated (60.8% of all detected microorganisms). Gram-positive flora of S. epidermidis and S. aureus were more common in the wound surface during the first week of the disease. In most patients with severe burns, bacterial associations were isolated from the wound surface (66.3%) in two and three weeks, and in three weeks Candida spp. were isolated. Non-fermenting rods A. baumannii and P. aeruginosa dominated among the gram-negative flora isolated from the wound surface of burns. The analysis of susceptibility of microorganisms isolated from patients with burns to antibiotics showed that almost all of the cultures were polyresistant.*

Conclusions. *Gram-negative microorganisms, strains of non-fermenting bacteria predominated among the pathogens isolated from burn wounds complicated by purulent inflammation; Staphylococcus aureus prevailed among the gram-positive ones. The most significant clinical strains were highly polyresistant to antibiotics.*

KEYWORDS: smears from burn wounds; strains of microorganisms; antibiotics; resistance.

Introduction

According to the WHO, injuries, burns, poisonings, etc. are the third in the structure of human mortality. Every year about 840 million people suffer from burns and about 180 thousand people die in the world. In Ukraine, more than 100,000 cases of burns are registered annually, and 60-80% of those burned have superficial burns of the skin of II-III A degree, which do not require surgical intervention [1, 2, 3, 4].

Treatment of burn wound infection is an urgent issue of contemporary medicine, in particular, surgery and combustiology. According to literature [5, 6], despite the constant improvement of wound healing methods, the frequency of its infectious complications in surgery is 30%. Traditional remedies and treatments for infected burns are often ineffective. This necessitates further search for new and improvement of existing medications and treatment that stimulate reparative processes in infected wounds, as well as in-depth study of the mechanisms of action of antibiotics [7]. Today, there is a wide range of medications for conservative treatment of burns, but none of them is sufficiently effective.

It is established that infectious complications are a challenge for patients with burns. According to the literature, their frequency correlates with the depth and area of burns. Complications

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in patients with burns are caused by disturbance of barrier function of the skin, reduction of its protective properties due to the action of traumatic factors and suppression of the immune system of these patients [8, 9, 10].

The most common cause of patient mortality is infection, which accounts for about 76.3% of burn mortality. In cases of thermal damage, coagulation necrosis of the epidermis, of various layers of the dermis and adjacent tissues develops that creates favorable conditions for massive microbial invasion. Infectious complications worsen the course of reparative processes in the wound. In patients with severe burns antimicrobial therapy is important together with surgical treatment aimed at mechanical removal of pathogens from burn wounds [11, 12, 13].

The aim of the study was to define the most common pathogens of purulent-inflammatory complications of burn wounds and their susceptibility to antibiotics.

Methods

The study involved patients treated at the Center of Thermal Trauma and Plastic Surgery of Lviv I-Territorial Medical Association, the unit of St. Luke's Hospital of Lviv. Collection of material from the wound secretions of burn wounds was performed with sterile swab. burn wounds in all patients were studied before prescription of antibiotics, at the end of the first and second weeks of the disease, which included isolation of pathogens, their identification by morphological, cultural and biochemical properties.

Antibiotic susceptibility was studied using standard research methods according to the Order of the Ministry of Health of Ukraine No. 167 "On approval of guidelines for Determination of susceptibility of microorganisms to antibacterials", dated April 05, 2007 and the recommendations of the International Committee of Clinical Standards (NCCLS, 2002).

Statistical processing and analysis of the results was performed using the software package of the microbiological monitoring system WHONET 5.2 (WHO Collaborating Centre for Surveillance of Antimicrobial Resistance) and Microsoft Office Excel 2007 [14].

Results

The results of the studies showed that in patients with burn trauma during the first week of the disease gram-positive flora of *S. epidermidis* and *S. aureus* were more common according to microbiological examination of smears from wound surfaces. *Candida* spp. were isolated in patients with severe burns on the third week of the disease, which might have been associated with immunosuppression due to thermal trauma and development of antibacterial resistance [15]. Depending on this, susceptibility of the main pathogens to antibacterials was evidenced. The study found that *S. aureus* showed high resistance to ceftriaxone (78-80%) and carbapenems (70-73%), high susceptibility to fluoroquinolones, including ciprofloxacin (71.5%) and levofloxacin (67.5%). *P. aeruginosa* strains were susceptible to carbapenems, in particular to meropenem (80 %) and imipenem (95%).

On day 18-20 from the moment of the injury, *Pseudomonas aeruginosa* was isolated from the wound in 65-70% of patients. Strains of *Pseudomonas aeruginosa* were moderately resistant, retaining susceptibility to carbapenems.

As a result of microbiological examination of smears from burn wounds, etiologically significant pathogens of infectious complications in patients with dermal burns were isolated. A total of 240 strains of gram-positive and gram-negative microorganisms were isolated from burn wound surfaces, which led to development of purulent-inflammatory processes.

On the seventh day after burns in 62.3% of cases, microorganisms were isolated from patients in monoculture, and only 37.7% – in associations. In two and three weeks of the disease, most patients with severe burns had bacterial associations isolated from the wound surface (66.3%), and on the third week of the disease *Candida* spp. were isolated due to possible immunosuppression on the background of thermal trauma.

Acinetobacter baumannii (30.0%), *Pseudomonas aeruginosa* (20.4%) and *Staphylococcus aureus* (15%) are leading in the spectrum of isolated clinical strains (Fig. 1). Most often, they formed associations from the second week of the disease.

Among the isolated pathogens of purulent-inflammatory complications of burn wounds, gram-negative bacteria predominated (60.8 % of all isolated microorganisms) (Fig. 2).

Non-fermenting rods *A. baumannii* and *P. aeruginosa* (48.3% and 34.9%, respectively) dominated in the gram-negative flora isolated from the burn wound surface; they were most often isolated after the first week of the disease. In contrast, Enterobacteria accounted for only 17.1 % (Fig. 3); *Escherichia coli* (8.7 % of isolated

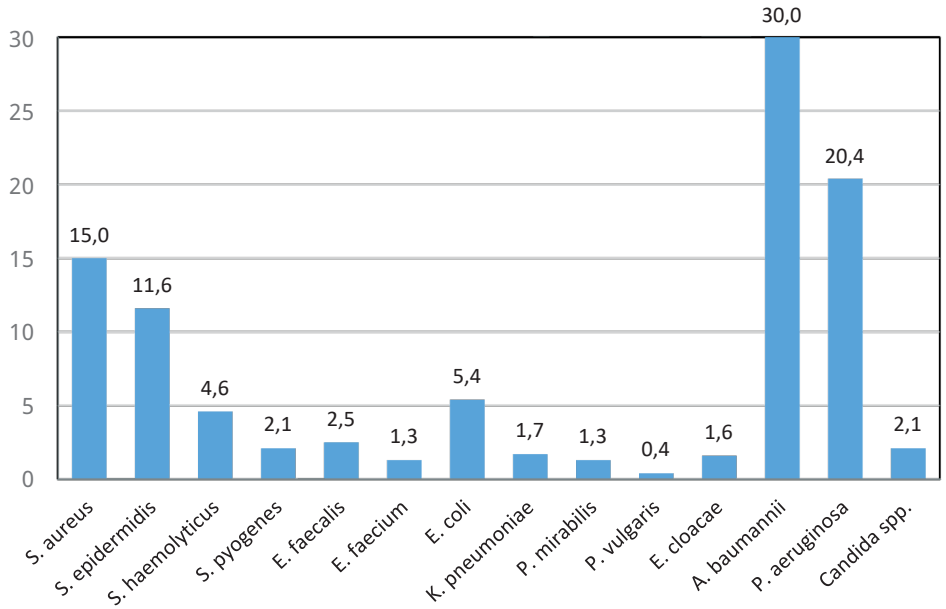

Fig. 1. The range of microorganisms isolated from burn surfaces,%.

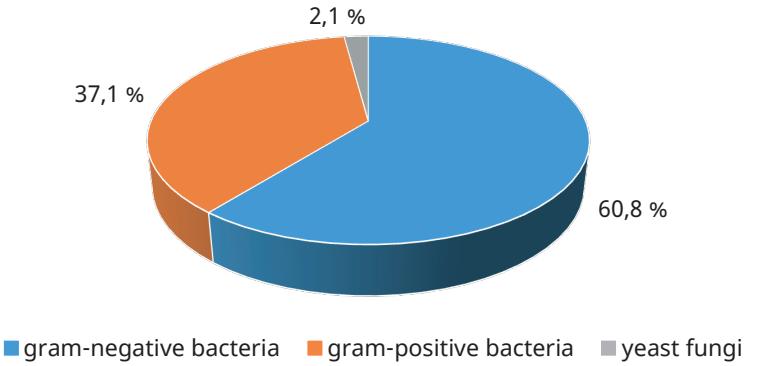

Fig. 2. The range of microorganisms isolated from purulent-inflammatory surfaces of burn wounds,%.

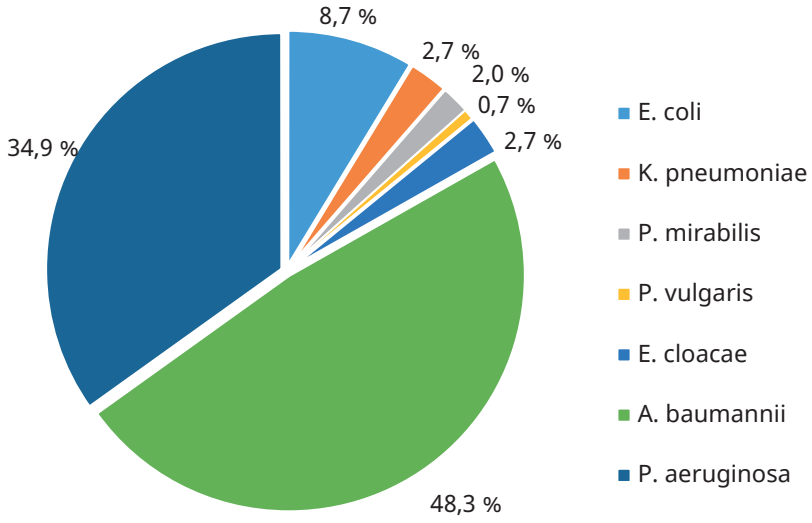

Fig. 3. Species of gram-negative bacteria isolated from burn surfaces,%

gram-negative rods), *Enterobacter cloacae* (2.7 %), *Klebsiella pneumoniae* (2.7 %), *Proteus mirabilis* (2.0%), *Proteus vulgaris* (0.7%) were isolated among them.

Gram-positive cocci were isolated 1.6 times less (37.1%) (Fig. 4). Staphylococci were predominant among them. They accounted for 75 % of isolated strains of cocci, and cultures of *S. aureus* (40.4% of all identified strains of cocci) were most often isolated among them. Coagulase-negative cocci were represented by cultures of *S. epidermidis* and *S. haemolyticus* (31.5 % and 12.4%, respectively). Enterococci were represented by strains of *Enterococcus faecalis* and *Enterococcus faecium*, which accounted for 10.1 % of the coccal flora, respectively. *Streptococcus pyogenes* was isolated only in 5.6%. Enterococci were more often isolated in the first week of the disease, staphylococci in the following weeks.

Candida spp. accounted for only 2.1 % of all isolated microorganisms.

The analysis of the susceptibility of microorganisms isolated from patients with burn disease to antibiotics showed that these clinical strains had high resistance to antibacterials, especially those that most often infect the wound surfaces. Almost all isolated strains were polyresistant.

The identified strains of *P. aeruginosa* were low susceptible to cephalosporins, in particular: cefepime (92.3%), ceftriaxone (86.5%), ceftazidime (80.8%), cefotaxime (69.2%). Almost half of the isolated cultures of *Pseudomonas aeruginosa* were resistant to aminoglycosides: to gentamicin – in 46.2% cases, to amikacin – 42.3 %. Meropenem and imipenem showed also low effectiveness, although they were reserve antibiotics. Clinical strains of *P. aeruginosa* showed resistance in 51.9 % and 82.7 % cases, respectively. The most effective antimicrobial against *Pseudomonas aeruginosa* was doxycycline. Resistance to it was only 19.2 %.

Like *P. aeruginosa* strains, isolated cultures of *A. baumannii* had a high level of antibiotic resistance. Cephalosporin antibiotics, in particular ceftazidime (97.2 %), ceftriaxone (95.8 %), cefepime (91.7 %), cefotaxime (86.1 %), were ineffective against acinetobacteria. Strains of *A. baumannii* to gentamicin and amikacin (73.6 % and 79.2 %, respectively) were highly resistant. They were also low susceptible to fluoroquinolones, i.e.: levofloxacin (76.4 %), ciprofloxacin (68.1%), gatifloxacin (63.9%). Meropenem and imipenem were more effective than other groups of antibacterials against acinetobacteria, only in 31.9% and 40.2% of resistant cultures of *A. baumannii.*

Isolated cultures of *S. aureus* were resistant to oxacillin (63.9%) that indicated methicillin resistance of these strains, as well as cephalosporin antibiotics, in particular: cefepime, ceftazidime, ceftriaxone (from 19.4 % to 33.3 %, respectively). *Staphylococcus aureus* was highly resistant to azithromycin (66.7 %) and lincosamides such as clindamycin (72.2 %) and doxycycline (52.8 %). Fluoroquinolones were also low effective, i.e.: ciprofloxacin (58.3 %) and

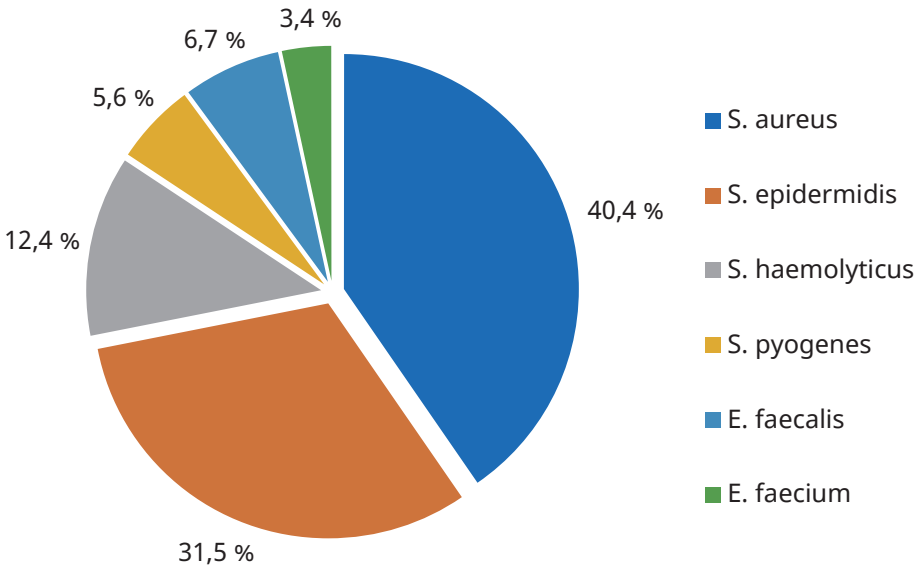

Fig. 4. Species of gram-positive bacteria isolated from burn surfaces,%

levofloxacin (25.0-44.4 %), as well as aminoglycosamides: gentamicin (30.6 %) and amikacin (38.9 %). In contrast to non-fermenting bacteria, clinical strains of *S. aureus* were the most susceptible to carbapenems: meropenem and imipenem resistant cultures of *Staphylococcus aureus* were only 8.3% and 5.6% of strains.

Discussion

Burns destroy the first barrier of human innate immunity that protect tissue from the colonised external world, and microorganisms can easily spread and infiltrate necrotic tissue [15, 16]. Our data confirmed many published studies, which have reported gram-negative bacteria as the commonest microorganisms that colonize burn wounds [17]. Initial burn wounds are sterile. However, within a few days, Gram-positive strains, such as *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, and *Streptococcus spp.*, start to colonize the wounds from deeper structures (hair follicles and glands). In the second phase, a Gram-negative shift takes place, where *P. aeruginosa, E. coli*, and *Proteus* are the predominant isolates [18, 19, 20]. If left untreated, this colonization can lead to infection [20, 21]. Our data confirmed the steps of infectious process developing on burn wounds. The study had established that *S. aureus* among gram-positive microbes and *P. aeruginosa* among gram-negative microbes were the most frequent microbial isolates in our patients(40.4% and 34.9% respectively). Similar observation was seen in the study by Tsolakidis S. et. al. [18].

In our study, we found a variable percentage of antibiotic resistance among the cultured bacteria. The analysis of the studied isolates susceptibility to antibiotics showed that most often infecting the wound surfaces clinical strains had high resistance to antibacterials. Almost all isolated bacteria were multiresistant. 63.9% of identified *S. aureus* belong to MRSA staphylococci. This had less incidence with other studies on MRSA in burn patients by Mandal [21]. Isolates of *S. aureus* (more than 70 % of all of them) were found as highly resistant to cephalosporins, including cefepime, ceftazidime, ceftriaxone, to lincosamides, such as clindamycin (72.2 %) and doxycycline (52.8 %). *S. aureus* was highly resistant to fluoroquinolones, i.e.: ciprofloxacin (58.3 %) and levofloxacin (25.0-44.4 %), as well as aminoglycosamides: gentamicin (30.6 %) and amikacin (38.9 %). However, isolates of *S. aureus were* susceptible to fluoroquinolones, including ciprofloxacin (71.5 %) and levofloxacin (67.5%). In contrast to non-fermenting bacteria, clinical strains of *S. aureus* were the most susceptible to carbapenems: meropenem and imipenem; only 8.3 % and 5.6 % of strains of *S. aureus* were resistant to these antibiotics.

P. aeruginosa strains as well as *S. aureus* were resistant to cephalosporins, in particular: cefepime (92.3 %), ceftriaxone (86.5 %), ceftazidime (80.8 %), cefotaxime (69.2 %); to aminoglycosides: gentamicin (46.2 %), amikacin (42.3 %); to meropenem and imipenem (almost half of the isolated cultures of *P. aeruginosa).* and moderate resistant to carbapenems, in particular: to meropenem (80 %) and imipenem (95 %). The most resistant antibiotics found in most of studies were cephalosporins and quinolones [7, 8, 23, 24, 25]. In contrast, some authors reported no isolated bacteria found resistant to gentamicin [24], or susceptible to aminoglycosides [25].

Conclusions

It was established that among the pathogens isolated from complicated purulent-inflammatory burn wounds, gram-negative microorganisms of non-fermenting bacteria predominated and *Staphylococcus aureus* among gram-positive ones. The most significant clinical strains were highly multiresistant to antibiotics.

Funding

This research received no external funding.

Conflict of interest

The authors declare no conflict of interests in this study.

Author's Contributions

Stepan Zaporozhan **–** conceptualization, writing – original draft; *Dmytro Fira* – formal analysis, writing – original draft, writing – reviewing and editing; *Olena Pokryshko* – data curation, writing – reviewing and editing.

АНТИБАКТЕРІАЛЬНА ТЕРАПІЯ У ХВОРИХ ІЗ ОПІКОВОЮ ТРАВМОЮ

С. Й. Запорожан, Д. Б. Фіра, О. В. Покришко
ТЕРНОПІЛЬСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ ІМЕНІ І. Я. ГОРБАЧЕВСЬКОГО, ТЕРНОПІЛЬ, УКРАЇНА

Вступ. *Лікування опікової ранової інфекції є актуальною проблемою сучасної медицини, зокрема хірургії, комбустіології й мікробіології. Відомо, що у хворих з опіками інфекційні ускладнення становлять серйозну проблему. Інфекційні ускладнення погіршують перебіг репаративних процесів у рані. Водночас із хірургічними методами лікування, спрямованими на механічне видалення збудників з опікових ран, важливе значення має застосування антимікробних лікарських засобів у хворих із тяжкими опіками.*

Мета. *Визначити найбільш поширені збудники гнійно-запальних ускладнень опікових ран у хворих та їх чутливість до антибіотиків.*

Методи. *Дослідження проводилось у пацієнтів, що перебували на стаціонарному лікуванні у центрі термічної травми і пластичної хірургії КНП «І-е територіальне медичне об'єднання м. Львова» відокремленого підрозділу «Лікарня святого Луки» м. Львів. Забір матеріалу із ранових виділень опікових ран здійснювали за допомогою стерильного тампону. Дослідження проводили у хворих до початку застосування антибіотиків, наприкінці першого і другого тижня захворювання. Виділяли збудники, ідентифікували їх. Чутливість до антибіотиків вивчали за допомогою стандартних методів дослідження. Отримані результати піддавали аналізу, який включав пакет програм системи мікробіологічного моніторингу "WHONET 5.2" (WHO Collaborating Centre for Surveillance of Antimicrobial Resistance) та програму «Microsoft Office Exel 2007».*

Результати. *У результаті проведеного дослідження мазків з опікових ран виділено 240 штамів грампозитивних та грамнегативних мікроорганізмів, які спричиняли гнійно-запальні процеси. Серед виділених збудників гнійно-запальних ускладнень опікових ран переважали грамнегативні бактерії (60,8% усіх виділених мікроорганізмів). Впродовж першого тижня захворювання у рановій поверхні частіше зустрічалися грампозитивна флора S. epidermidis та S. aureus. Після двох і трьох тижнів захворювання у більшості пацієнтів із важкою опіковою травмою з ранової поверхні висівали асоціації бактерій (66,3%) та на третьому тижні захворювання виділяли ще й гриби роду Candida spp. У грамнегативній флорі, висіяній із ранової поверхні опіків, домінували неферментуючі палички A. baumannii та P. aeruginosa. Результати аналізу чутливості мікроорганізмів, виділених від хворих із опіковою хворобою, до антибіотиків показали, що практично всі висіяні культури були полірезистентними.*

Висновки*. Серед виділених збудників гнійно-запальних ускладнень опікових ран переважали грамнегативні мікрорганізми, штами неферментуючих бактерій, серед грампозитивних – золотисті стафілококи. Найбільш значущі клінічні штами були високо полірезистентними до антибіотиків.*

КЛЮЧОВІ СЛОВА: мазки з опікових ран; штами мікроорганізмів; антибіотики; резистентність.

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