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Antimicrobial activity of antiseptics in the prevention of postoperative infectious complications

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Recently, among hospital strains of microorganisms, an increase in the number of antiseptic-resistant strains of opportunistic pathogens has been registered, which significantly affects the effectiveness of these drugs. It is important to study their antimicrobial efficacy to justify rational use. The aim is to conduct a comparative study of the antimicrobial efficacy of antiseptics of decamethoxine, chlorhexidine, polyhexanide. During study we examined the antimicrobial activity against 186 clinical strains of microorganisms (*Acinetobacter baumannii*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus* spp., *Enterobacter* spp.) isolated from patients with infectious complications in the postoperative period. The minimum inhibitory (MIC) and bactericidal concentrations (MBC) of 0.02 % and 0.1 % decamethoxine, 0.05 % chlorhexidine bigluconate, 0.1 % polyhexanide were determined; antimicrobial efficacy of drugs was evaluated by the index of antiseptic activity by conventional methods. The study found high antimicrobial properties of decamethoxine, chlorhexidine, which had a high bactericidal effect on clinical strains of *S. aureus*, *Enterococcus* spp., *Enterobacter* spp. Proved the benefits of antimicrobial activity of the drug based on decamethoxine ($p < 0.001$). The polyhexanide has pronounced antimicrobial properties against *A. baumannii*, bacteria of the family Enterobacteriaceae, *P. aeruginosa*. Thus, the leading gram-positive (*Staphylococcus aureus*, enterococci) and gram-negative pathogens (enterobacteria, acinetobacteria, pseudomonads) are sensitive to polyhexanide, chlorhexidine and the domestic drug decamethoxin, with a probable advantage of the antimicrobial properties of the latter over all gram-positive and most gram-negative microorganisms.

Keywords: antiseptics, decamethoxin, chlorhexidine, polyhexanide.

Introduction

Prevention of postoperative infectious complications has been and remains one of the most pressing problems of surgery, both in our country and abroad [20]. In modern conditions, infectious complications in the postoperative patient in most cases occur due to opportunistic pathogens that have become resistant to a wide range of antimicrobials [20]. The ability to develop resistance to antimicrobials is one of the leading properties of infectious complications. The high adaptability of pathogens to survival in the context of widespread use of antibiotics has led to a decrease in the effectiveness of antibiotic therapy, which significantly narrowed the possibilities in the fight against resistant isolates of microorganisms [2, 7, 10, 11]. The selective action of antiseptic drugs also leads to the elimination of sensitive cells of the microbial population and the spread of antiseptic-resistant strains [13, 18].

In such conditions, the use of antiseptics with a wide range of antimicrobial action is considered a priority. Among the known list of antiseptic drugs registered in Ukraine, 0.02 % decamethoxine and 0.05 % chlorhexidine bigluconate are actively used in the prevention and treatment of infectious complications of the respiratory system [3]. For the purpose of perioperative prophylaxis, antiseptic treatment of means for respiratory and oxygen support of severe surgical patients is performed. Polyhexanide is known among the arsenal of modern antiseptics [12].

Nowadays, despite the proven high antimicrobial efficacy of antiseptics, there are more and more reports of a decrease in their effectiveness as a result of the formation of resistance to opportunistic pathogens. In view of the above, the study of antimicrobial activity of antiseptics

against the leading pathogens remains relevant, which can be a scientific justification for the choice of rational antiseptic prophylaxis and antiseptic therapy in clinical practice [4, 21].

The aim is to conduct a comparative study of the antimicrobial efficacy of antiseptic drugs decamethoxine, chlorhexidine, polyhexanide.

Materials and methods

On clinical strains of opportunistic pathogens isolated from patients with infectious complications in the postoperative period, who were treated in burns for severe burns, were studied antimicrobial efficacy of antiseptics based on polyhexanide, decamethoxine, chlorhexidine. Identification of microorganisms was performed in accordance with conventional methods for morphological, tinctorial, cultural, biochemical properties. A total of 186 clinical strains of opportunistic pathogens were used in the study. The structure of the studied pathogens of infectious complications was represented by isolates of *S. aureus* (n=56), *P. aeruginosa* (n=44), *A. baumannii* (n=43), *Enterobacter* spp. (n=23), *Enterococcus* spp. (n=22).

The antimicrobial properties of antiseptics based on 0.02 % and 0.1 % decamethoxine, 0.05 % chlorhexidine bigluconate, 0.1 % polyhexanide were investigated. The study evaluated the antimicrobial action of antiseptics, determining their minimum inhibitory (bacteriostatic) and bactericidal concentrations (MIC and MBC, respectively) on isolates of opportunistic pathogens by the standard method of double serial dilutions, guided by guidelines for determining the sensitivity of Health of Ukraine № 167 from 05.04.2007 [9].

The research was conducted in accordance with the Helsinki Declaration of the World Medical Association on the Ethical Principles of Human-Based Medical Research. Patients' written consent was required to participate in a clinical trial [17].

Comparative characterization of the clinical efficacy of the studied antiseptic drugs against clinical strains of opportunistic pathogens was performed using a quantitative indicator - the index of antiseptic activity (IAA) according to A. P. Krasilnikov, which was calculated according to the method. IAA is the ratio of the working concentration of the drug to the MIC of the antiseptic relative to a particular type of pathogen or MIC+2σ in the study of several strains of one type of pathogen [6, 15].

Results

The study revealed significant advantages of bactericidal properties of decamethoxine compared with chlorhexidine over clinical strains of *Staphylococcus aureus* and *enterococci* (p<0.05). The data obtained showed that bactericidal concentrations of decamethoxine against *S. aureus* and *Enterococcus* spp. were lower than chlorhexidine by 3.5 and 10.5 times, respectively (Table 1).

Polyhexanide MBC was determined for staphylococci (16.51±1.75 µg/ml). Polyhexanide showed similar

Table 1. Quantitative characteristics of bacteriostatic, bactericidal action of antiseptics.

Clinical strains of microorganisms (number)	Decamethoxin	Chlorhexidine	Polyhexanide
	MBC *(µg/ml)		
<i>S. aureus</i> (n=56)	1.554±0.173	5.422±0.748**	16.51±1.75
<i>Enterococcus</i> spp. (n=22)	6.743±0.611	25.28±1.39**	4.080±0.392
<i>Enterobacter</i> spp. (n=23)	18.75±1.36	19.90±1.66**	14.83±2.20
<i>A.baumannii</i> (n=43)	51.13±7.40	70.54±16.55**	161.9±16.9
<i>P. aeruginosa</i> (n=44)	106.8±5.9	85.93± 6.30**	203.1±16.9

Notes: *MBC - minimum bactericidal concentration (in µg/ml); ** - p<0.05 compared with decamethoxine.

bactericidal properties against enterobacteria and staphylococci. It was found that the bactericidal effect of decamethoxine on clinical *A. baumannii* was manifested in the presence of MBC, which was 3.1 times less than those of polyhexanide and 2 times less than chlorhexidine. Chlorhexidine had a bactericidal effect on *Enterobacter* spp. in the presence of 19.90±1.66 µg/ml.

It was found that the antimicrobial properties of polyhexanide against *Pseudomonas aeruginosa* were twelve times weaker than against *Staphylococcus aureus*. Thus, isolates of *Enterobacter* spp. died in the presence of 14.83±2.20 µg/ml of polyhexanide, which were 10 times smaller than in the case of *A. baumannii* (p<0.001).

High bactericidal properties of decasan against *S. aureus* isolates, which were sensitive to 1.554±0.173 µg/ml of the drug, were proved. The bactericidal properties of chlorhexidine against *A. baumannii* were determined using a 2-fold higher concentration of antiseptic, which indicated a weaker activity against this type of microorganism. Clinical strains of *A. baumannii* were found to have a similar high sensitivity to polyhexanide as *Enterobacter* spp. (p>0.05).

Clinical strains of *P. aeruginosa* were endowed with high resistance properties. The vast majority of *Pseudomonas aeruginosa* isolates (85.4 %) were sensitive to decamethoxine (MBC 99.78±4.35 µg/ml). However, bactericidal properties against 14 (14.6 %) clinical strains of *P. aeruginosa* were not determined in 0.02 % decamethoxine solution, because the MBC of the drug exceeded 200 µg/ml. The obtained data showed the advantages of bactericidal properties of decane over sensitive strains of *P. aeruginosa* in comparison with polyhexanide in 2 times (p<0.001). Polyhexanide showed bactericidal antipseudomonad properties in the presence of high concentrations, which reached 203.1±16.9 µg/ml.

Given the significant differences in the quantitative content of the main active substances in the finished dosage forms of the studied antiseptics, it was considered insufficient to assess their antimicrobial efficacy only on the basis of MBC. A more detailed analysis of the antimicrobial efficacy of antiseptic drugs based on decamethoxine, chlorhexidine and polyhexanide was performed by calculating

Fig. 1. Characteristics of antimicrobial efficacy of antiseptic drugs against clinical strains of gram-positive, gram-negative microorganisms.

the IAA (Fig. 1). Thus, IAA of the official forms of 0.02 % decamethoxine, 0.05 % chlorhexidine and 0.1 % polyhexanide was determined. As a result of the analysis of IAA indicators, the high antimicrobial efficacy of decamethoxine against gram-positive and gram-negative opportunistic pathogens was established. Significant advantages of antimicrobial efficacy of this antiseptic against *S. aureus* in comparison with 0.05 % chlorhexidine and 0.1 % polyhexanide were proved 3.5 and 10.5 times, respectively ($p < 0.05$).

In terms of antimicrobial efficacy against enterococci, 0.1 % polyhexanide and 0.05 % chlorhexidine were superior to IAA 0.02 % decamethoxine (6.2 and 3.7 times, respectively; $p < 0.001$). It was found that the application of polyhexanide was not effective against *S. aureus*, *Enterococcus spp.*, because the IAA in both cases was much lower than the maximum allowable level of this indicator, which must be at least "4".

It was shown that the IAA of polyhexanide relative to *Enterobacter spp.* and *A. baumannii* significantly exceeded the corresponding index of 0.02 % decamethoxine (3.4 and 0.95 times, respectively; $p < 0.001$) and chlorhexidine (2.8 and 0.3 times, respectively; $p < 0.001$). No significant differences in the antimicrobial activity of 0.02 % decamethoxine, 0.05 % chlorhexidine and 0.1 % polyhexanide against acinetobacter and enterobacteria were found, as IAA values did not differ significantly and exceeded the maximum allowable threshold, indicating their high efficiency against these species.

The advantages of antimicrobial efficacy of polyhexanide in the concentrations of the finished dosage form in relation to clinical strains of *P. aeruginosa* have been established. 0.02 % decamethoxine and 0.05 % chlorhexidine showed 5-2 times less pronounced antipseudomonad activity than polyhexanide ($p < 0.001$).

Discussion

With the rapid formation and spread of antibiotic resistance among the causative agents of infectious

complications, scientists around the world have focused significant efforts on finding ways to overcome this problem. Among the alternative ways to control antibiotic-resistant pathogens, the active use of antiseptics, which have different mechanisms of action on microorganisms than antibiotics, is considered effective and promising [14]. Scientists have proven that microorganisms are much slower to form resistance to antiseptics [8, 12, 13, 16, 19, 20].

The use of antiseptics is recommended and regulated by the international scientific community in a set of measures for the prevention and treatment of infectious complications in the postoperative period in intensive care units and surgery caused by opportunistic pathogens [1, 4, 21]. Microbiological substantiation of the use of surfactant antiseptics based on decamethoxine, chlorhexidine is based on their proven high efficiency against a wide range of gram-positive, gram-negative microorganisms, which are problematic pathogens of infectious complications [1, 5, 12, 14]. Thus, as a result of the conducted researches the high bactericidal action of decasan against clinical strains of *S. aureus*, *Enterococcus spp.* was proved, which significantly exceeded the bactericidal properties of chlorhexidine by 3.3 and 3.7 times, respectively. The advantages of antimicrobial efficacy against these gram-positive bacteria in the antiseptic on the basis of decamethoxine in comparison with polyhexanide ($p < 0.001$) were established.

The obtained data correlate with the data of the literature in which the high antimicrobial effect of decamethoxine on gram-positive opportunistic pathogens was shown and the reduction of antimicrobial properties of polyhexanide against pathogens of infectious complications was proved [3, 13, 14].

Studies have proven the high antimicrobial properties of polyhexanide against a number of gram-negative microorganisms (*Enterobacter spp.*, *A. baumannii*, *P. aeruginosa*). At the same time, a significant decrease in the effectiveness of this antiseptic against clinical isolates of *S. aureus*.

The antimicrobial efficacy of decamethoxine and chlorhexidine against acinetobacteria has been proven, as evidenced by the IAA of these antiseptics, which did not differ significantly. However, according to a number of researchers and according to the study, a higher bactericidal effect on *A. baumannii* by decamethoxine was found, compared with chlorhexidine (3.7 times; $p < 0.05$).

Non-fermenting gram-negative bacteria *P. aeruginosa*, which have high resistance to antimicrobials, including antiseptics, were sensitive to decamethoxine, chlorhexidine and polyhexanide. Antiseptics containing decamethoxine (0.02 %) and chlorhexidine (0.05 %) were characterized by sufficient antimicrobial efficacy against this type of pathogen.

Conclusions

1. Surface-active antiseptics decamethoxine, chlorhexidine, polyhexanide have high bactericidal properties against clinical strains of gram-positive and

gram-negative opportunistic pathogens, with pronounced advantages of antimicrobial efficacy of the drug based on decamethoxine against *S. aureus* (3.5 and 3.7 times; $p < 0.05$), *Enterococcus* spp. (3.7 times; $p < 0.001$) and *Enterobacter* spp. (1.3 times; $p < 0.001$).

2. Polyhexanide exhibits high antimicrobial properties against a wide range of opportunistic pathogens, including enterococci, *Staphylococcus aureus*, enterobacteria.

3. High sensitivity of leading gram-positive pathogens (*Staphylococcus aureus*, enterococci), gram-negative

pathogens (enterobacteria, acinetobacteria, pseudomonads) to domestic antiseptic drug based on decamethoxine justifies its high effectiveness in the treatment of its antimicrobial treatment.

4. Given the high risk of infection with opportunistic pathogens after surgery, the risk of antibiotic resistance, and pronounced antimicrobial properties of local antiseptics, the use of the latter is appropriate in the perioperative period for the prevention of infectious complications.

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