

APPLICATION OF POLYHEXANIDE AS A NEW HIGHLY EFFECTIVE ANTISEPTIC COMPOSITION

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ABSTRACT

Currently, antiseptics are used at all stages of surgical treatment. Currently, the search continues for antiseptics that have effective properties in suppressing pathological microflora and as safe as possible in relation to tissues. One of the promising antiseptic solutions is a solution based on polyhexanide. The aim of this work was to study the available reports on the effectiveness of the polyhexanide solution, its safety, and experience of use.

To assess the effectiveness of using a polyhexanide solution as an antiseptic, a search was made for publications in the scientific databases "PubMed" and "Google Scholar".

A total of 2026 scientific articles were found during the search. When studying the content of the texts, 31 articles were accepted for consideration, corresponding to the given criteria.

Polyhexanide solution is widely used in surgical practice. In wound healing, antiseptic treatment is one of the key steps. The suppression of the reproduction of pathological microflora and the effect on the biofilm is extremely important. When analyzing the publications, different results were noted using the polyhexanide solution.

Studies of the effectiveness of the polyhexanide solution are currently being actively pursued. Due to its significant efficacy, safety, and ease of use, polyhexamethylene biguanide is promising for use in surgical practice.

KEYWORDS: antiseptic, polyhexanide, polyhexamethylene biguanide.

INTRODUCTION

Antiseptic solutions occupy a large portion of the surgical practice. Currently antiseptics are used at all stages of surgical treatment. For an example they are used on open wounds to reduce and suppress the development of microflora. There are many requirements for the antiseptic solutions that are used locally. They should create and maintain the necessary concentration of the substance that can effectively affect the pathogenic microflora, have minimal toxic effects on tissue cells, have a low risk of developing an antiseptic resistance, do

not irritate wound tissues, do not cause a lot of pain and be easy to use. However, when using antiseptic solutions, it is important to remember about some restrictions. So it is considered unjustified to use one antiseptic solution in the treatment of wounds for more than two weeks. Due to the poor penetration of solutions, it is necessary to carefully monitor the course of the treatment process in wounds with deep damage. [Privol'nev V et al., 2017; Pulatova Sh, Kambarova Sh, 2020; Nizamova G, 2021] Also, one of the problems is

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the constant changes in pathological microorganisms that lead to the formation of resistance. Currently, the search for antiseptics that have effective properties in suppressing pathological microflora and are as safe as possible in relation to tissues is continuing. One of the promising antiseptic solutions is a solution based on polyhexanide. The purpose of this work was to study the available reports on the effectiveness of polyhexanide solution, its safety and application experience.

MATERIALS AND METHODS

To evaluate the effectiveness of using a polyhexanide solution as an antiseptic, a search was performed for publications in the scientific databases "PubMed" and "Google Scholar". The search was performed by searching for the keywords "polyhexanide", "PHMB". The selection of articles was carried out according to the criteria: relevance (from 2017 to 2021), the presence in the publication of data on the effectiveness, experience of use, safety of polyhexanide, the presence of a full-text source.

A total of 2,026 scientific articles were found during the search, 771 publications were selected after selection according to the criterion of relevance, 14 articles were eliminated due to the absence of the full-text publications. When studying the content of the texts, 31 articles that meet the specified criteria were accepted for consideration.

DISCUSSION

Polyhexanide (polyhexamethylene biguanide (PHMB)) refers to polymer biguanides, is a cation $[-(\text{CH}_2)_6. \text{NH}. \text{C} (= \text{NH}). \text{NH}. \text{C} (= \text{NH}). \text{NH}-]_n$ ($n = 2-40$; average value = 11). It is a colorless, odorless solution, well soluble in water. [Chandki R et al., 2020]

Polyhexanide solution is widely used in surgical practice. When healing wounds, antiseptic treatment is one of the key stages. Suppression of the reproduction of pathological microflora and the effect on the biofilm is extremely important.

The study of the polyhexanide solution against microorganisms showed high efficiency. Ngaage L.M. and co-authors (2020) conducted a study of the activity of PHMB solution on the surface of breast implants. The authors noted a tenfold decrease in the number of bacteria of *S. Aureus* and

S. epidermidis strains resistant to methicillin. Loose M. and colleagues (2021) studied the effect of polyhexanide on biofilms formed by uropathogenic microorganisms at various dilutions of the solution. The polyhexanide-based antiseptic showed a broad effect against uropathogenic biofilms formed by *E. coli* and *P. mirabilis*, *P. Aeruginosa*, even with strong breeding. Salisbury A.M. and co-authors (2021) also investigated the activity of the effect of polyhexamethylene biguanide on biofilm in comparison with other antiseptics. According to the results of the evaluation of the effect of antiseptic solutions on *P. aeruginosa*, *S. aureus* and a multi-species biofilm, the PHMB solution demonstrated the highest efficiency.

Some authors analyzed the activity of antiseptics on biofilms formed by *Candida albicans*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The results showed a high antibacterial activity of an antiseptic based on polyhexanide [Krasowski G et al., 2021]. Andreeva S.V. and colleagues (2018) evaluated the activity of several antiseptics against the biofilm formed by *S. aureus* and *P. Aeruginosa*. It was found that antibiotic-resistant wound colonies of *S. aureus* and *P. aeruginosa* are sensitive to a solution of polyhexamethylene biguanide, which showed the greatest antimicrobial activity.

Davis S.C. and co-authors (2017) compared solutions for wound irrigation. It was found that there was a significant decrease in methicillin-resistant *Staphylococcus aureus* (MRSA) in the wounds treated with polyhexanide solution. Treatment with PHMB solution was the only one in which a decrease in bacterial load was observed. Machuca J. and others (2019) also conducted studies aimed at studying the effectiveness of antiseptic solutions. Comparative characteristics of the effect of polyhexanide and 2% chlorhexidine on biofilms. The solution of polyhexamethylene biguanide showed higher efficiency compared to 2% chlorhexidine, both against gram-negative and gram-positive biofilms. Also, when studying the activity of a 0.02% poly-



*To overcome it
is possible, due to the
uniting the knowledge and
will of all doctors in the world*

hexanide solution on a microbial biofilm, the authors found that the solution is able to have a significant positive effect [Brill F et al., 2019].

The results of the conducted studies demonstrate the high efficiency of the polyhexamethylene biguanide solution against pathogenic microorganisms, as well as the biofilm formed by them. However, a number of studies demonstrate results of polyhexanide activity that are inferior to other antiseptic solutions. So O'Donnell J.A. and co-authors (2021), having tested the antiseptic property of PHMB and other antiseptics against the nascent 4-hour biofilm and mature three-day MRSA biofilm, found that the antiseptics povidone-iodine and Bactisur showed a significantly greater decrease compared to the polyhexanide solution. Günther F. and colleagues (2021) also found that polyhexanide is inferior to chlorhexidine in terms of activity against MRSA and vancomycin-resistant enterococcus isolates in their native biofilms. Such reports are few, but they prove the need for further study of the effectiveness of the PHMB solution.

Significant part of the publications on the study of the effectiveness of polyhexamethylene biguanide are data on the assessment of the state and the condition of wounds. Nunes C.A. and co-authors (2019) noted that the use of bandages with a polyhexanide solution showed high efficiency in the treatment of venous ulcers on the legs. In 2018 Ricci E., reported in his scientific work that the use of PHMB solution in 30 patients for the purpose of cleaning wounds showed an improvement in the skin in 29/30 cases. In 1 case, there was no significant improvement due to the complication of maceration. It was also found that the degree of effectiveness depends on the time of application. Dhoonmoon L.I. (2021) evaluated the use of a microfibre tampon of a conical design impregnated with a polyhexanide solution. 56 UK doctors sent 111 patient observation questionnaires when using a treatment regimen with polyhexamethylene biguanide, 90% of the observations showed high effectiveness of this treatment regimen. Some authors point to the high effectiveness of the use of PHMB in patients with acute chronic wounds. The solution promotes high-quality wound cleansing and pain reduction [Peghetti A et al., 2019].

Jie Gao and co-authors (2018) investigated the

effectiveness of using a polyhexanide-based wound irrigation solution in 62 patients with breast abscess. 33 patients had their wounds treated with PHMB solution, and the control group of 29 people had their wounds treated with saline solution. Polyhexanide showed a significant difference in the time of wound healing, the frequency of changing the dressing and the duration of the patient's stay in the hospital in comparison with saline solution. González-Porto S.A. reported that Prontosan showed high efficacy in a study on 17 patients with burns of the face, trunk and limbs [González-Porto S et al., 2018].

In the study of polyhexanide solution in 80 patients with breast abscess the authors observed a significant decrease in the level of pain, the wound healing time was shorter, the colic of dressings decreased, the level of relapses decreased [Ya-Yun M et al., 2018].

Taking into account the effectiveness of the polyhexamethylene biguanide solution, methods are being developed to strengthen it and increase the usability. So it was proposed to use a PHMB solution in the form of a gel for applying to wounds. Atkin L. When treating difficult-to-heal chronic wounds with a polyhexanide-based gel, there was an improvement in the condition of the wound surface after two days of exposure [Atkin L et al., 2020]. Chai W. and others (2020) in their study note that bandages with PHMB-based gel have shown high efficiency in the treatment of diabetic foot ulcers. When using a gel based on polyhexamethylene biguanide for wound treatment in 51 patients, 50 patients observed complete re-epithelization of wounds and also proved the high efficacy and safety of the gel [Kiefer J et al., 2018].

Another method of improving the activity of a polyhexanide-based antiseptic was to combine it with other antiseptic solutions. The authors evaluated the effectiveness of the use of PHMB in combination with betadine in patients with stoma. The combination showed high efficiency in the treatment of lesions around the stoma. [Rodríguez Maldonado Y, Naranjo Peña I, 2021].

Also, good results were shown by a combination of the use of a polyhexanide solution and physical influences. Thus, Zhang B.R. and co-authors (2021) note that in the treatment of necrotizing fasciitis with negative pressure therapy using a PHMB solution, it

significantly facilitates wound cleaning. The others state that polyhexanide hydrogel in combination with carbon photon therapy creates an optimal environment for wound healing [Yang F et al., 2020].

Also, during the study, several works were found on the use of a polyhexamethylene biguanide solution in dental practice. The use of PHMB solution for mouthwash was evaluated in order to study the activity against *Candida albicans*, *Streptococcus mutans*, *Actinomyces naeslundii*, *Aggregatibacter actinomycetemcomitans*, methicillin-resistant *Staphylococcus aureus* and *Fusobacterium nucleatum*. Polyhexanide significantly reduced the mass of the biofilm, the authors note a higher activity of the PHMB solution compared to the chlorhexidine solution [Kollmuss M et al., 2021]. Medvedec Mikić I. and others (2018) conducted an antimicrobial assessment of 0.2% polyhexamethylene biguanide in root canal models, and its effectiveness against *Enterococcus faecalis*, *Candida albicans* and *Staphylococcus epidermidis*. Comparison with sodium hypochlorite (NaOCl) (2.5%) and chlorhexidine (0.2%) was performed. The results showed that polyhexamethylene biguanide had significantly more pronounced efficacy against all 3 microorganisms. In their study the authors compared the effect of a 0.2% solution of polyhexanide and a 2% solution of chlorhexidine on the dentin of a human tooth. The results showed that the PHMB solution has a significantly greater effect on dentin. Based on the results of the work, the authors recommend using a polyhexanide solution as an irrigant for endodontic dental treatment [Chandki R et al., 2020]. The results of these studies demonstrate the great prospects for the use of polyhexamethylene biguanide solution in dentistry and the likelihood of its inclusion in treatment protocols.

Do not forget that an important condition for the use of any antiseptic solution is its safety in relation to the macroorganism. The polyhexanide solution is also being studied in this direction. The effect of antiseptic solutions on adipose tissue stem cells was also investigated. It was proved that among antiseptics, PHMB solution caused the least decrease in the viability, proliferation and

differentiation of adipose tissue cells. Thus, it was proved that the polyhexanide solution is preferably used in the treatment of wounds with open adipose tissue [Kim B et al., 2017].

Fernández-González A. and co-authors (2020) evaluated cell viability, structural integrity and function of the epidermal barrier when exposed to antiseptics. The study was performed on keratinocytes and dermal fibroblasts. The polyhexanide solution showed a high level of cell viability preservation (59.41%) compared to other antiseptics, the function of the epidermal barrier was not violated. Harnoss J.C. and colleagues tested the toxicity of antiseptics using the HET-CAM test. Compared with solutions of other antiseptics, the PHMB solution did not cause irritation, which means that it does not have toxic properties in relation to tissues. When studying the effect of PHMB solution in children from 4 years old with burn wounds, high efficacy and safety were noted, the authors recommend including the solution in the protocol of care for burns in children [Ciprandi G et al., 2018].

It is also important to note the absence of negative interaction with other drugs used in the treatment. The authors investigated the effect of antiseptic solutions used for pretreatment and cleaning of burn wounds on the activity of enzymatic preparations. It was proved that the polyhexanide solution has the greatest efficiency and inertia to enzymatic preparations. The authors recommend using a PHMB solution for pretreatment of burn wounds [Schulz A et al., 2018].

CONCLUSION

Studies of the effectiveness of the polyhexanide solution are actively being conducted at the present time. A significant part of the publications indicates a high activity of PHMB against pathogenic microorganisms and biofilms. Due to its significant effectiveness, safety and ease of use, polyhexamethylene biguanide is gradually being included in the treatment protocols of surgical patients. Also, PHMB has a great prospect of application in dental practice and requires further study in this direction.

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