Use of Polyhexanidine in Treating Chronic Wounds

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Chronic wounds have a long period of healing, being impeded by numerous factors, as infections. Polyhexanidine is a new broad spectrum antiseptic with non-toxic action which is used lately in wound cleaning solutions. A case control study was realized with two groups of patients treated with silver sulfodiazine and with polyhexanidine, the last group having an accelerated healing evolution. Besides the bactericide action, polyhexanidine has also no cytotoxicity, good tolerability and anti-inflammatory proprieties.

Keywords: polihexanidine, sulfodiazine, cytotoxicity, anti-inflammatory

Chronic wounds are defined as wounds that do not heal in a predictable amount of time, usually within three months [1]. Their evolution stops in one of healing phases, commonly in the inflammatory phase, due to action of numerous factors such as inflammatory mediators, infections, biofilm, hypoxia or poor nutrition [2]. Chronic wounds became a challenge to every country healthcare system, affecting a high percentage of patients with diabetes and arterial disease, having a long evolution and lowering the quality of life [3]. Common chronic wounds are considered diabetic foot ulcer, vascular ulcers (arterial or venous) and pressure ulcers [1]. Besides the intrinsic factors determined by the underlying disease, chronic wounds have in common extrinsic factors that impair healing, like persistent infections and presence of a drug resistant biofilm which creates a failure in response of epidermal cells to reparative stimuli [4].

Wound standard of care improves the healing of chronic wounds and consists of debridement, irrigation and cleaning [4]. Cleaning has an important role in improving wound status and accelerating healing. Numerous wound cleaning solutions are available nowadays like povidone iodine, ionized silver, clorhexidine, alcohol, hydroxide peroxide or chlorine based agents [5-7]. All of these agents reduce bacterial load of the wound, but it has been shown that does not promote wound healing, in some cases are even delay it (clorhexidine, povidine iodine, hydrogen peroxide) [5].

Having the aim to reduce bacterial load and also promote wound healing a new molecule has been discovered and used [8]. Polyhexanidine or Polyhexamethylene biguanide is a polymer that was frequently used as an antiseptic, bactericid and fungicide in swimming pools. The molecular formula is $(C_8H_{19}N_5)_n$ and the molecular weight 185.27g/mol [9].

The first approval as a medical product was realized in 1991 in Switzerland, but only further studies showed its efficiency and created the today's acknowledged substance for wound treatment [10,11].

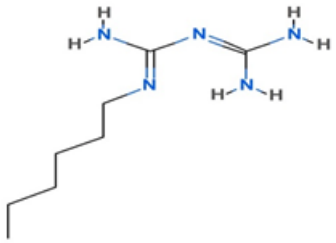

Fig. 1. Chemical formula of Polyhexanidine

Experimental part

A case control series of ten patients with chronic wounds were treated in the Plastic Surgery Department of Emergency Clinical Hospital Prof. Dr. Agrippa Ionescu over a six month period. Inclusion criteria were chronic wounds of diabetic or vascular etiology older than 3 months. Exclusion criteria were uncontrolled glycemia, pregnant women and hemoglobin value less than 12mg/dL.

The patients were divided in two groups, of five patients each. In one group the patients' wounds were treated with polihexanidine and in the other group, considered a control group, with usual local therapies.

At admission usual blood tests and bacterial wound cultures were realized. In the polyhexanidine group, patient's wounds were cleaned daily with 0.1% polyhexanidine solution and a polyhexanidine gel was applied with a dry gauze. In the control group, the wound were cleaned with betadine soap and saline solution and a dressing with silver sulfadiazine was applied. Wound cultures were repeated after one week from the treatment start and the wound dimensions and evolution were evaluated weekly.

Results and discussions

At admission all wound cultures were positive, the most common bacteria being Staphilococcus aureus in 6 out of 10 cases, in 3 of the cases being meticilin resistant (MRSA). Other encountered bacteria were: Escherichia coli, Enterococcus faecalis, Enterococcus faecium, Proteus mirabilis and Pseudomonas aeruginosa. After one week of cleaning and dressing with polihexanidine, in 4 out of 5

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patients the wound cultures become sterile and no systemic antibiotic was necessary compared with the control group where antibiogram was still positive in all patients and systemic antibiotherapy was started.

Fig. 2. Chronic wound older than 3 months

The polyhexanidine dressing provided also a moist environment promoting wound healing. Wounds started to epithelise from the periphery after one week, and a pink granulation appeared after 10 days. The patients have been skin grafted one week earlier comparing with the control group.

Fig.3. Chronic wound treated with Polyhexanidine

Polyhexanidine is a commonly used antiseptic and bactericid and can be used in wound cleansing solutions at concentrations of 0.1, 0.02 and 0.04 % [12]. Another application form is the 0.04% concentration gel that is used in wound dressings. This polymer has a lot of properties: broad antibacterial spectrum, sustained antiseptic effect, no effect in lipids from the human cell membrane with no cytotoxicity, biofilm reduction, good tolerability with no known toxic risks and anti-inflammatory properties [12].

Regarding its chemical properties polyhexanidine has hydrophilic biguanide residues and hydrophobic hexamethylene spacers, being soluble in water and poor soluble in lipids [13]. The antibacterial actions have been studied; polyhexanide disorganizes the microbes' cytoplasmic membrane, increases its permeability and is absorbed in the bacterial cell, finally causing cell death [5]. This antimicrobial property increases by combing small oligomers (n=4) that start the cell wall disintegration and permit a more easily passing into the cell of large oligomers (n=35) [13].

Polyhexanidine acts also on gram negative and gram positive bacteria having a higher natural affinity for their envelopes by replacing the cations that stabilize their membrane [14].

Apart from the local colonization, bacteria create also a natural habitat with a matrix made of biopolymers and polysaccharides that realize a shield from biocides and host defense mechanisms [15]. One of the main opportunistic pathogens that create this biofilm are staphylococcus aureus and pseudomonas aeruginosa, being also responsible for transition in a chronic wound [16]. Polyhexanidine has been demonstrated that reduces this biofilm by binding of the matrix polysaccharides, accumulating in the matrix and making it toxic for the resident bacteria [13].

This biocide has been considered one of the strongest antiseptic, being effective on gram negative bacteria, gram positive bacteria, fungi (Candida albicans, Aspergillus niger), protozoa pathogens (acanthamoeba spp) and even HIV virus [13].

Polyhexanidine has also a non-toxic profile, superior to other antiseptics and also a safety margin greater than the used antibiotics. Also, until present there is no known development of bacterial resistance, probably due to its heterogeneity [12].

Conclusions

Polyhexanidine is a broad spectrum antimicrobial substance used in treating colonized or infected chronic wound having a good impact on multidrug resistant bacteria. Having the ability to act on bacterial membrane and biofilm matrix prevents the development of bacteria resistance.

Contrast to other antiseptic agents that have poor tissue tolerability and decrease healing, polyhexanidine has a low risk profile, a good tissue tolerability creating a moist environment that promotes wound healing.

Today, polyhexanidine is an accepted substance for reducing bacterial load in infected acute and chronic wounds, but is not the only therapy option. Surgical debridement and treatment of the underlying disease remain still the first priority.

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