PHARMACOLOGY AND TOXICOLOGY

Efficiency of Magnesium-Containing Preparation Polykatan in Therapy of Purulent Wounds

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Local treatment with polykatan, a magnesium-containing drug based on bischofite mineral, promoted healing of infected skin wounds. Wound cleansing from bacteria was due to a direct antibacterial effect of the drug.

Key Words: *magnesium chloride; bischofite; polykatan; infected wounds; rats*

The agents inducing purulent and inflammatory diseases have changed in recent years. The appearance of numerous bacterial strains of with multiple drug resistance and perverted immunological reactions of the organism result in poor efficiency of antibiotic therapy of purulent infections, despite introduction of new drugs and therapeutic methods in clinical practice. Increased incidence of severe complicated forms of purulent infections is paralleled by the appearance of numerous maxillofacial inflammatory diseases running an atypical course, resistant to traditional therapy, and liable to chronic transformation [1,10]. Therefore, the development of new drugs for local therapy of purulent wounds acquires special attention.

Recently, a magnesium-containing drug polykatan based on bischofite mineral was used for the treatment of inflammations of the buccal mucosa [9]. The use of preparations based on salt solutions in purulent surgery promotes wound cleansing and healing [4]. Ukrainian scientists showed that aqueous solution of bischofite activates monocyte and neutrophil redox metabolism, thus stimulating their phagocytic activity [2]. Magnesium ions stimulate production of C_3b complement component [5], thus activating phagocytosis and promoting cleansing of the wound. Hence, polykatan can indirectly affect the immunity.

The use of polykatan for the treatment of purulent and inflammatory diseases is dictated by its antibacterial and inflammatory effects [2,7].

We evaluated the efficiency of polykatan treatment of experimental infected wounds of the skin and studied the mechanism of action of this drug.

MATERIALS AND METHODS

Polykatan (Volgograd Pharmaceutical Plant) solution including standard solution of magnesium-containing mineral bischofite (up to 95-96% $MgCl_2 \times 6H_2O$ in dry residue) and corrective and stabilizing trace additives was used. Experiments were carried out on 108 random-bred male and female rats weighing 160-200 g as described previously [6]. Standard tangential skin wounds (200 mm^2) inflicted under sodium ethaminal narcosis (40 mg/kg) were infected with bacterial suspension (24-h culture of *Staphylococcus aureus*, 10^9 bacterial cells). *S. aureus* culture was identified using a staphy-test (Lachema). The wounds were washed with 10% polykatan solution. In control group 1 polykatan was not used, in control group 2 the wounds were washed with NaCl solution isotonic to polyka-

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tan solution with molar concentration of 1.8756 M or 54.808 g/liter.

The dynamics of the wound process was evaluated by the following clinical parameters: terms of wound cleansing from pyonecrotic tissue, granulation, and rate of wound healing (reduction of wound area and time of epithelialization). Planimetry of the wound was carried out as described previously [8].

The rate of wound surface decrease was estimated by the formula:

$$V_S = \frac{S\text{-}Sn}{t} \times 100,$$

where S is the initial area of the wound, Sn wound area on the day of measurement, and t time in days between the day when the wound was inflicted and the day of investigation.

Tissue microflora was quantitatively studied in biopsy specimens from the wound edge (number of bacterial cells in bacterial suspension containing 24-h *St. aureus* culture) and in impressions. In bacterial control, bacterial cells per g tissue on days 3, 5, 7, 10, 12, 15, and 18 after wound infection were counted as described previously [3]. The criterion of wound cleansing was a decrease of this parameter to at least 10^5 bacterial cells per gram g tissue.

Antibacterial effect of polykatan was studied *in vitro* on reference pathogenic *St. aureus, Streptococcus mutans,* and *Candida albicans* in liquid nutrient media: Hottinger broth (pH 7.4) for staphylococci and streptococci and Sabur broth (pH 6.8) for Candida. Bactericidal activity of the preparation was evaluated for a final concentration of 10^6 bacterial cells/ml medium and its bacteriostatic effect at concentrations 10^4 and 10^2 bacterial cells/ml medium. The antibacterial effect of polykatan was evaluated by growth of bacterial colonies.

The results were statistically processed using Student's t test.

RESULTS

Pronounced inflammation around the skin defect, edema of the adjacent tissues, infiltration, hyperemia, marginal shaft, and uneven whitish crusts were observed in untreated animals. In control group 1, the area of the wound decreased due to retraction of wound edges; after 24 h the wound area decreased by 12.5%, after 2 days by 30%, after 5 days by 52.7%, and after 11 days by 80%.

The rate of wound retraction in control group 1 was the highest 2 days after infection with *St. aureus* (Fig. 1, *a*). The wound gradually decreased during the next 10 days, with slight fluctuations in rate of healing. On days 17-18 the wound crust was detached. Complete epithelialization with coarse cicatrices was observed after 18 days.

The time course of wound healing under the effect of hypertonic NaCl solution was well expressed: during the first 3 days the wound area decreased by 40% (Fig. 1, *a*). Pronounced inflammation around the skin defect with edema of the adjacent tissues, infiltration, and hyperthermia were observed. The wounds were covered with uneven whitish crusts, the crusts were surrounded with a shaft. After 5 days the wound area decreased by 50%, after 9 days by 84%, after which the wound area continued to decrease.

In control group 2 similarly to control 1 the rate of wound healing was most pronounced after 2 days (35%). During subsequent 3 days the rate of wound healing under the effect of hypertonic NaCl solution decreased (Fig. 1, *b*). After 5 days the rate of healing was virtually the same. After 18 days complete epithelialization with coarse cicatrices was observed in 71.4% rats.

In experimental group purulent and inflammatory processes, especially the hydration phase, were less

TABLE 1. Effect of Polykatan on Wound Cleansing from Bacteria (Number of Bacterial Cells per Gram Tissue)

Term after treatment, day	No treatment		NaCl		Polykatan	
	impression	suspension	impression	suspension	impression	suspension
1	10^8	3×10^9	10^7	4×10^8	10^6	3×10^7
3	10^6	3×10^8	10^5	1.9×10^7	10^3	4×10^6
5	10^5	4.4×10^7	10^3	2×10^6	10	7×10^2
8	10^3	8×10^5	10^3	2×10^5	0	0
10	10^2	3×10^5	10^2	3×10^5	0	0
13	10^2	10^6	10^2	5×10^5	0	0
16	10^2	6×10^5	10^2	2×10^3	0	0

Note. 0: no growth.

TABLE 2. Effect of Polykatan on Growth of Opportunistic Microorganisms in Solid Nutrient Media

Microorganism; inoculation dose, bacterial cells/ml medium	Control	Polykatan, %			
		30	20	10	5
Staphilococcus aureus					
10^6	+++	+	+	+++	+++
10^4	+++	+	+	+++	+++
10^2	++	0	0	+	++
Streptococcus mutans					
10^6	+++	0	+	++	+++
10^4	+++	0	+	++	+++
10^2	++	0	0	0	++
Candida albicans					
10^6	+++	0	+	+	+++
10^4	+++	0	0	+	++
10^2	++	0	0	0	+

Note. 0: no growth; +: 10-50 CFU/dish; ++: 50-100 CFU/dish; +++: more than 100 CFU/dish.

expressed. Wound edges were moderately hyperemic with slight edema starting from the very first days. The wound area decreased starting from day 1 of treatment (Fig. 1, *a*). The most rapid decrease of the wound area was observed after 2 days: by 71.9% *vs.* 30.04 and 35% in control groups 1 and 2, respectively. During subsequent 3 days the wound area gradually decreased with a constant rate. Five days after treatment the wound area in experimental group decreased by 94% *vs.* 50% in both control groups. Moreover, wounds in the experimental groups more rapidly cleansed from pyonecrotic mass and by days 3-4 presented as clean granulated surface without signs of acute inflammation, with good marginal epithelialization. The wounds were covered with thin dry crusts; after detachment of the crusts on days 8-9 the wound bottom was clean and pink. Hence, wound process was markedly accelerated in comparison with both control groups (Fig. 1, *b*).

After 1 day bacterial contamination in impressions and suspensions in the experimental group decreased 10 and 100 times compared to control groups 1 and 2, respectively (Table 1). After 3 days the number of bacterial cells in the suspension decreased 10-fold and in impression 1000-fold. In comparison with control group 2, the number of bacterial cells in impression decreased 100 times and in suspension 5-fold.

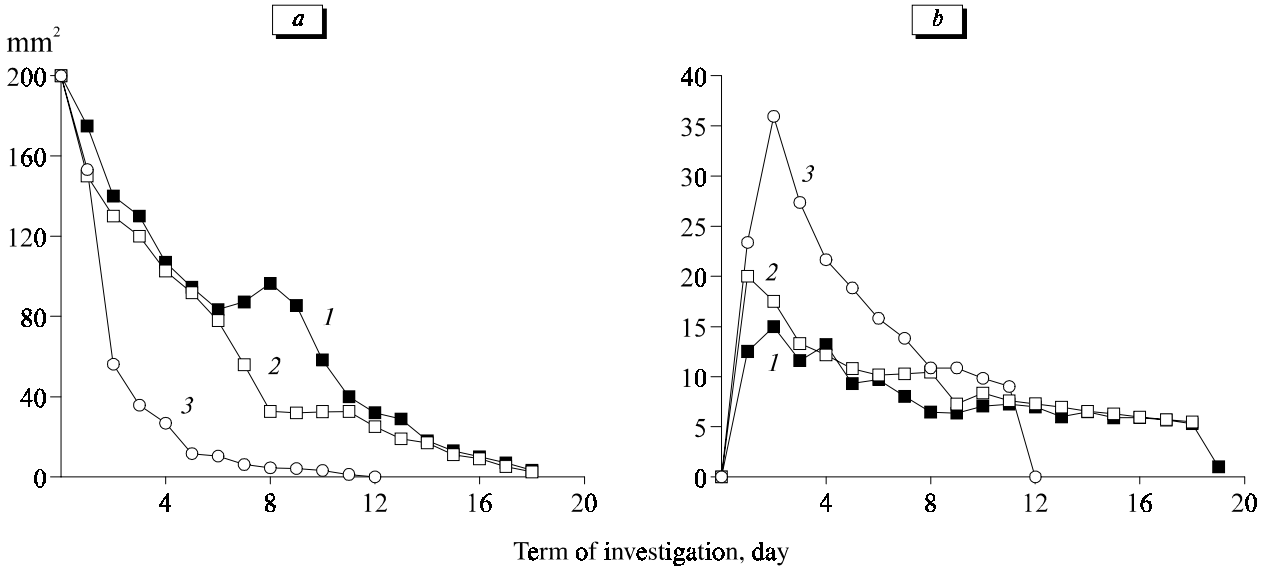

Fig. 1. Effect of polykatan on area (*a*) and rate of healing (*b*) of infected purulent wounds. *1*) control group 1; *2*) control group 2; *3*) experimental group.

Three days after the treatment, the number of bacterial cells in impression in control group 1 remained 1000 times higher and in suspension 100 times higher than in the experimental group. In control groups the criterion of wound cleansing was attained on day 8 and the parameters of contamination persisted at this level until day 13 (Table 1), while in experimental group no bacterial colonies were observed after 5 days. The decrease of bacterial contamination in experimental group was due to polykatan effect on the growth of opportunistic microorganisms. Planimetry and parameters of opportunistic microflora growth in wounds treated with polykatan were in good correlation. Hence, polykatan had a pronounced necrolytic and healing effect on infected experimental wounds on days 3-5.

Bacteriostatic effect towards staphylococci was observed when polykatan was used in concentrations 10% and higher (Table 2). For streptococci, the bactericidal effect manifested at a concentration of 30% and bacteriostatic effect at concentrations of 10 and 20%. For candida the bactericidal effect was observed at a concentration of 10-20%, while 5% preparation exerted a bacteriostatic effect. Purulent wounds were washed with 10% solution of polykatan, and therefore its bacteriostatic effect cannot be neglected.

Hence, polykatan exerts a wound-healing effect, inhibits growth of microorganisms, and shows bacteriostatic activity. Presumably, accelerated healing of skin wounds is due to Mg ions and not to isotonic solution.

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