

Topical mupirocin, surgical wound infection, prevention

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Abstract

BACKGROUND : Mupirocin is a new topical antibiotic with broad spectrum germicidal activity. Therefore, it may represent a good agent for prevention of wound infection.

OBJECTIVE : The aim of this study was to analyze the effectiveness of topical mupirocin for prevention of surgical skin wound infections in the centrofacial area.

METHOD : A prospective study was performed on 273 patients. The patients were divided into two groups. Group A, 135 patients, was given no antibacterial prophylaxis. In group B, 138 patients, prophylactic medication with ointment containing 2% mupirocin was performed once a day for the 7 days before the surgery.

RESULTS : Eight of 273 patients had wound infections (2.93%). Seven of these 8 patients were in group A (2.95%) and one were in group B (0.48%) ($P < 0.01$).

CONCLUSION : Topical mupirocin is an efficacious, harmless, and inexpensive agent for prevention of wound infections in seborrhoeic regions.

(MJS 1999, 1 : 7 - 13)

บทคัดย่อ

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ได้ทำการศึกษาการป้องกันแผลผ่าตัดติดเชื้อบริเวณใบหน้าโดยใช้ 2% Mupirocin จากการศึกษาในผู้ป่วย 273 ราย พบว่าผู้ป่วยกลุ่มแรก (A) 135 ราย ซึ่งไม่ได้รับยาปฏิชีวนะป้องกันเปรียบเทียบกับ กลุ่ม (B) 138 ราย ซึ่งได้รับ 2% Mupirocin ทาป้องกันเป็นเวลา 7 วัน วันละ 1 ครั้ง ก่อนการผ่าตัด จากการศึกษาพบว่าอัตราการติดเชื้อในกลุ่ม B ต่ำกว่าในกลุ่ม A โดยมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ดังนั้นจึงสรุปได้ว่า topical mupirocin มีประสิทธิภาพในการป้องกันแผลผ่าตัดติดเชื้อบริเวณใบหน้านอกจากนั้น ราคาไม่แพงและผลข้างเคียงน้อย

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Introduction

The ideal means for prevention of surgical skin wound infections include absolute asepsis of the surgical environment and/or sterilization of the skin. The first can be achieved by adequate implementation of standard surgical techniques and procedures. The second goal is only a theoretical one because it is impossible to completely sterilize the skin. This structure is a selective environment in which various microorganisms live and grow. Moreover, 10–20% of the resident flora are in the pilosebaceous units and remain even after scrubbing and application of antiseptics.¹ It is important to stress that even *Staphylococcus epidermidis*, a common and innocent skin saprophyte, can under certain circumstances become virulent and cause minor or major infections.^{2,3} Moreover, the skin of the centofacial area is prone to be colonized by *S. aureus* due to nasal carriage of this organism.

The prevention of wound infection is very important when the surgical environment is the skin of the face. Here, the aesthetic result of any procedure is particularly compromised by wound infection. Last, in the central area of the face, direct closure of skin defects by approximation of the margins is often not feasible because of relative lack of tissue in this area. Here more aggressive techniques such as skin flap and/or free skin grafts are often needed. These procedures are subject to a higher risk of infection because of possible compromises in vascular supply and therefore prophylactic systemic antibiotic administration is often provided.

Mupirocin (Bactroban: pseudomonic acid A) is a new topical antibiotic with a unique chemical structure unrelated to that of any other group of

antibiotics.⁴ This naturally occurring antibiotic is produced by the anaerobic metabolism of a particular strain of *Pseudomonas fluorescens*.⁵ Mupirocin covers a broad spectrum of Gram-positive and Gram-negative bacteria and is particularly active against staphylococci (including methicillin and multiply resistant strains)⁶ and streptococci (minimum inhibitory concentrations, 0.12–0.5 mg/l).⁷

The mode of action by which this antibiotic inhibits bacterial growth is by inhibiting isoleucyl transfer-RNA synthetase which results in the inhibition of bacterial proteins.^{8,9} Because of its unique mode of action, mupirocin shows neither cross-reaction with, nor cross-resistance to, any other commonly used and clinically important antibiotic.¹⁰ The opportunity for the emergence of strains of *Staphylococcus aureus* that are less sensitive, and are resistant to antibiotics, exists in patients who receive longterm or frequent courses of antibiotic therapy, particularly patients with chronic inflammatory conditions such as atopic dermatitis.¹¹ When applied as ointment, systemic absorption of mupirocin is minimal.¹² The small amount that enters the blood is rapidly converted to an inactive metabolite, 90% of which is excreted in the urine,¹³ It may represent a better choice of prevention of wound infection in areas with a high density of sebaceous glands.

Therefore, the aim of this study was to analyze the effectiveness of topical mupirocin for the prevention of surgical skin wound infections in the centro facial area.

Materials and Methods

A prospective study was performed on 273 patients. One hundred fifty-three were men and 120 were women. Mean age was 45 ± 18 years (range,

20–63 years). All patients underwent outpatient surgery for cutaneous proliferative lesions arising in the centrofacial area (nose, naso–labial folds, prolabium, and chin). Lesions arising on the lips were not included. The types and the incidence of the lesions are listed in Table 1.

centers, referred to the same operating unit, and assigned to one of the two study groups using the method of random allocation by random number tables. Therefore, there was a single central list. These groups were equivalent in number, age and sex of patients. In group A, there were 135 patients,

TABLE 1. Type of Lesion

Pathology	GROUP A		GROUP B	
	Patient Number	Percent	Patient Number	Percent
Nevi	81	60	79	57.2
Sebaceous adenomas	15	11.1	23	16.7
Fibromas	25	18.5	21	15.3
Seborrheic keratosis	13	9.7	14	10.1
Trichoepitheliomas	1	0.7	1	0.7
Total	135		138	

The following patients were excluded from the study: those with infected eczema, infected burns or scalds, systemic lupus erythematosus or severe skin disease requiring the use of a systemic antibiotic; those who had received topical or systemic antibiotics within the preceding 48 h; those receiving steroids; those with an associated disease that might interfere with the study (e.g. diabetes); those with renal insufficiency; those with suspected pregnancy or lactation; and those who were hypersensitive to mupirocin or preparations containing polyethylene glycols.

Investigators had to explain to the patient, orally and in writing, the nature, duration and purpose of the study, and the possible side-effects. Patients were informed that they might withdraw from the study at any time, without this affecting their future status.

The patients were divided into two groups. They were selected from the different participating

78 men and 57 women. The mean age was 44 ± 13 years (range, 20–61 years). This group was given no antibacterial prophylaxis. In group B, there were 138 patients, 75 men and 63 women. Mean age was 42 ± 13 years (range, 20–63 years). In this group, prophylactic application of an ointment containing 2% mupirocin (Bactroban ointment) was performed once a day for 7 days prior to surgery. The patients were instructed to apply it on the lesion and 3 cm around it with light massage.

To avoid extraneous variables, the operating room, the sterilization techniques, the preparation of the patients, the surgical staff, and the surgeons were identical for every operation. Immediately before the surgery the operative area was scrubbed with 0.25% benzalkonium chloride in alcoholic solution (Citrosil) starting from the center to peripheral areas. After scrubbing, the skin was blotted with sterile gauze and draped

with sterile towels. No occlusive adhesive drape was employed. All the operative personnel wore caps, masks, and sterile disposable gloves and gowns. Polyglactin 910 (Vicryl; Ethicon) was the suture material for the dermis and monofilament nylon (Ethilon; Ethicon) for the skin.

The size of the lesions excised ranged from 4 to 22 mm (mean, 13.3 ± 8.7 mm). There were no significant differences between the two groups in mean size of the lesions excised (13.1 ± 9.2 mm for the major diameter in group A; 13.4 ± 8.5 mm in group B).

All lesions treated were limited in thickness to the dermis and excision depth was to the subcutaneous plane. Direct approximations are the types of surgical procedures for closure of the various defects. Subcuticular sutures were performed in 105 group A patients and in 86 group B patients.

The dressings were applied by the same physician on the days 2–4 and 6 after surgery. Further inspection and dressing changes were performed subsequently every second day when needed. At each dressing change, the wounds were cleansed with 0.25% benzalkonium chloride in alcoholic solution and covered with sterile gauze. The evaluation of the wounds was made independently, by the investigator, the investigator had to record on the casereport form, demographic data such as the patient's age and sex, the nature of the infection, the site of infection, the presence or absence of systemic complications (e.g. lymphadenopathy and pyrexia), and all previous and/or concomitant treatments. A swab was also taken from each appropriate site for bacteriological evaluation; isolated organisms were cultured and their sensitivities to mupirocin, penicillin G, tetracycline, chloramphenicol and

fusidic acid were assessed using the disk diffusion susceptibility test.

ADVERSE EVENTS

Any adverse events observed by the investigator or reported spontaneously by the patient were recorded on the patient's case report form. The date of onset, duration, intensity, course, action taken, outcome and relation to the study drug were recorded. The relationship of the adverse event to the study drug was categorized as: unassessable, unrelated, probably unrelated, probably related or related. For each adverse event, the decision of whether to withdraw the patient from the study and initiate appropriate treatment or to continue the study medication was made by the investigator.

STATISTICAL ANALYSIS

In every case, infection was confirmed by cultures. The data were analyzed statistically by the corrected chisquare test, the odds ratio, confidence interval, and Student's t-test.

Results

A total of 273 patients were enrolled in the study comprising 120 women (aged 2 months–50 years; mean, 12.7 years) and 153 men (aged 3 months–64 years; mean, 20 years). There was no statistically significant difference between the ages of the women and men enrolled in the study (Student's t-test, $P > 0.05$).

The topical administration of the mupirocin ointment was moderately well tolerated by all 138 group B patients. Ninety two patients had mild erythema. Mild to moderate itching was noted by

32 patients. No patient stopped the medication. Eight of 273 patients had wound infections (2.93%). The mean age of these 8 patients was 42.7 ± 6.5 years versus 44.1 ± 5.5 years ($P=NS$) for the 265 noninfected patients. Seven of these 8 patients were in group A (2.95%) and one in group B (0.48%) ($P < 0.01$) (see Table 2).

TABLE 2. Comparison of rates infection on the groups

	Group A	Group B	Total
I ⁺	7	1	8
%	2.95	0.48	2.93
I ⁻	128	137	265
Total	135	138	273

Odds ratio: 6.043; confidence interval (95%): 1.32924.470; chi square: 6.981; $P < 0.01$. I⁺ = infection; I⁻ = no infection.

A positive culture was obtained from all infected patients: a total of 8 bacterial strains were isolated from the lesions, predominantly staphylococci (87.5%) and streptococci (12.5%). (Table 3).

TABLE 3 Bacteriological findings of patients with skin infections

Bacteriological findings	No. of patients affected (8)
<i>Staphylococcus aureus</i>	7
streptococci	1

Discussion

Surgical infections may be caused by pathogens reaching the wound from the patient's own skin flora.² Since there is no way to completely sterilize the skin, some degree of wound contamination is inevitable. Therefore, it is important to lower the amount of bacterial inoculum as much as possible.¹⁴ Until now, pharmacological prophylaxis of wound infections depended on the use of systemic antibiotics.^{1,3} Their use for clean surgical procedures is controversial.¹⁵ We have recently shown in a large series of patients that antibiotic prophylaxis reduces significantly the rate of infection in clean surgical wounds.³ However, when the risk of wound infection is slight, the use of antibiotics may not be justified for clean wounds due to the possibility of emergence of bacterial antibiotic resistance, risk of systemic allergic reactions, and monetary cost.¹⁵ Therefore, the use of an effective manageable antimicrobial topical agent may be of value especially when operating on the face, where an optimal aesthetic result is extremely important. The ideal antiseptic should accomplish the following goals: 1) removal of as many bacteria as possible from the skin surface and destruction of pathogens; 2) persistent antibacterial effect; 3) low cost; and 4) aesthetic acceptability.²

The use of topical antibiotics is appropriate in superficial skin wound infections since the agents are directly active at the infection site. The excessive use of topical antibiotics for such infections has increased bacterial resistance both to current and to new drugs due to the development of cross resistance. As a result many topical drugs are not effective. Topical antibiotics should, where possible, meet the following requirements: the

development of bacterial resistance during therapy should be slow, they should either have no or have only slow patient sensitization potential and it should not be necessary to apply antibacterial agents that are also used systemically (because of the risk of resistance development). Mupirocin meets all these requirements. Owing to its unique mode of action and the fact that it is designed for topical use only, the risk of resistance development is minimal compared with that of other topical antibiotics. In vitro experiments with susceptible strains of *Staphylococcus aureus* revealed that in the presence of mupirocin spontaneous resistant mutants developed only at a frequency of 10^{-8} to 10^{-9} .¹⁶ A recent UK multicentre survey examined 8220 strains of staphylococci (7173 strains of *Staphylococcus aureus* and 1083 strains of coagulase-negative staphylococci) and showed that only 0.3% of the isolates of *S.aureus* were resistant (minimum inhibitory concentration > 4 mg/l).¹¹ The potential for sensitization and the development of allergy to 2% mupirocin ointment is minimal. In studies with healthy volunteers, no evidence of phototoxic or photoallergic reactions was observed.¹⁷ In addition, the safety and tolerance were particularly good: no adverse events were reported among the 48 patients treated with mupirocin ointment.

This study highlighted the importance of staphylococci and streptococci in bacterial surgical skin infections and the emergence of resistance to common drugs, although some of the results must be interpreted with care because of the small number of strains isolated.

Mupirocin is particularly valuable against staphylococci and streptococci owing to its unique mode of action, together with its lack of cross-resistance to other antibiotics, and its unavailability

in systemic form.

In our study, 2% mupirocin was moderately well tolerated by all patients and no allergic contact dermatitis was observed. It has a broad spectrum germicidal activity that persists for at least 48 hours on human skin and is increased by a high lipid environment.^{18,19,20} In our study most infections were caused by strains of *S. aureus*, the usual source of wound infection in cutaneous surgery. Even though this organism is not normally found in pilosebaceous units, 2% Mupirocin may reduce the incidence of *S. aureus* as a transient pathogen. This may be due to the drug's high solubility and persistence in lipid rich areas, or because it also acts as a peeling agent allowing the nonselective physical removal of a variety of microorganisms.

In our study, topical mupirocin was an efficacious, safe, and inexpensive agent for the prevention of surgical wound infection in the seborrhic, centofacial area.

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