Prophylactic mupirocin could reduce orthopedic wound infections

1,044 patients treated with mupirocin compared with 1,260 historical controls

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We analyzed the effect of perioperative elimination of nasal carriage of *Staphylococcus aureus* using mupirocin nasal ointment on the reduction of the postoperative wound infection rate in orthopedics. In an unblinded intervention trial, we compared 1,044 patients treated with mupirocin (intervention group) with 1,260 historical controls (control group). From each group a random sample of 50 patients was taken. Risk factors were analyzed in these random samples and we found it unlikely that different distributions of risk factors might have influenced the results.

The wound infection rates were 14/1,044 in the intervention group and 34/1,260 in the control group (p = 0.02). The rates of wound infections caused by *S. aureus* were subsequently 7/1,044 and 14/1,260 (p = 0.3). On checking the data we found that prophylaxis had unintentionally not been given to 172 patients in the intervention group. Correction of the data gave a comparable total infection rate, but a further reduced infection rate by *S. aureus*.

Our findings suggest that prophylactic treatment with mupirocin in orthopedic surgery can reduce the infection rate.

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Submitted 97-07-25. Accepted 98-04-17

It has been shown that nasal carriage with *Staphylococcus aureus* is a substantial risk factor in surgery and dialysis (Boelaert et al. 1991, Kluytmans et al. 1995). It is therefore likely that wound infections caused by *S. aureus* are mostly endogenous infections although the route of transmission is not yet clear (Wenzel and Perl 1995). Eradication of *S. aureus* nasal carriage can be effectively done with mupirocin (Hudson 1994). In an unblinded study, we evaluated the effect of intranasal mupirocin prophylaxis on the postoperative wound infection rate in orthopedics.

Patients and methods

Study population

The study was undertaken in the Canisius-Wilhelmina Ziekenhuis, a 653-bed teaching hospital in Nijmegen, The Netherlands. The study population comprised orthopedic patients who underwent arthroplasties, endoprosthetic surgery and internal fixations between 1 July 1992 and 1 January 1996. Perioperatively, all patients were given cefazoline as systemic antibiotics (1 g within 1 hour before operation and after 4 hours during the operation). The intervention group was defined as those patients who were given mupirocin calcium ointment (Bactroban Nasal, SmithKline Beecham Pharmaceuticals, London, U.K.) intranasally three times before surgery (at 18.00 and 22.00 o'clock on the day before and at 7.00 o'clock on the day of operation). They were operated on from 1 August 1994 to 1 January 1996 (1,044). The patients operated on from 1 July 1992 to 1 August 1994 (1,260) did not receive mupirocin. This group is called the historical control group. Apart from the addition in preoperative prophylaxis no changes were made in procedures in the operation theater.

Risk factor study

To assess possible differences in the baseline prognosis of patients in the intervention and control groups, we randomly sampled 50 patients in each. The medical records of these 100 patients were screened for the following risk factors (Simchen et al. 1984, Nicolle et al. 1992, Sherertz et al. 1992): diabetes mellitus, age, sex, use of immunosuppressive drugs, infections at

Risk factors

Risk factor	Historical control group (n 50)	Intervention group (n 50)	p-value
Duration of operation (≥ 2 hours)	3	5	0.7 [b]
Preoperative hospitalization (≥ 2 days)	8	6	0.6 [a]
Age (≥ 70 years)	10	18	0.08 [a]
Diabetes mellitus	2	3	1.0 [b]
Use of immunosuppressive drugs	0	1	
Sex (number of men)	22	23	0.8 [a]
Presence of infections at other sites	1	2	1.0 [b]

[a] chi-square, [b] Fisher exact two-tailed

other sites, length of preoperative hospitalization and duration of surgery. For all patients with postoperative wound infections, the following variables were recorded: location of the wound infection (superficial or deep), date of onset of infection and, when available, the micro-organisms causing the infection. Surgical wound class was recorded for all patients.

Definition of postoperative wound infections and registration

The criteria used for the diagnosis of postoperative wound infections were those set by the Centers for Disease Control and Prevention (Garner et al. 1988). All postoperative wound infections were recorded prospectively, using a computerized database.

Statistics

Data were analyzed with the Epi Info (version 5) statistical package. Differences in wound infection rates between the historical control group and the intervention group were tested with the relative risk ratio and 95% CI. Differences in risk factors between the random samples of the groups were tested with the chi-square or Fisher exact test and accessory p-values. Significance was accepted at p-value ≤ 0.05.

Results

Risk factor study

All patients with wound infections had had an operation in wound class clean. Among the groups, no clinically relevant differences were observed, apart from age (Table).

Wound infections in the patient population

In the historical control group, 2.7% (34/1,260) developed a wound infection, in the intervention group, 1.3% (14/1,044). This means a relative risk ratio of 2.0, with a 95% CI of 1.1–3.7, and a p-value of 0.02, which is a significant reduction by 50%.

In the historical control group, 14 wound infections were caused by *S. aureus*, in the intervention group 7. This means a relative risk ratio of 1.7, with a 95% CI of 0.7–4.1, and a p-value of 0.3.

In the intervention group, it was found that although it was the intention to treat all patients, 84% (872/1,044) really received the mupirocin prophylaxis. In the intervention group, the number of patients who developed a postoperative wound infection and really received the mupirocin prophylaxis, was 11/872. This gives to a corrected relative risk ratio of 2.1, with a 95% CI of 1.1–4.2, and a p-value of 0.02. The number of patients who developed a postoperative wound infection with *S. aureus* and received the mupirocin prophylaxis was 5/872. This leads to a corrected relative risk ratio of 1.9, with a 95% CI of 0.7–5.4, and a p-value of 0.2.

In the intervention group, 7 wound infections were superficial (of which 4 were caused by *S. aureus*); in the historical control group, 22 (11 were caused by *S. aureus*). In the intervention group, 6 wound infections were deep (of which 3 were caused by *S. aureus*); in the historical control group, 11 had deep infections (3 caused by *S. aureus*). In each group, it was not stated whether 1 wound infection was deep or superficial.

Discussion

We found a marked decrease in the number of postoperative wound infections after the introduction of mupirocin. Although mupirocin was given to eliminate nasal carriage of *S. aureus*, we found that the total number of postoperative wound infections decreased, as well as infections caused by *S. aureus*. An explanation may be the elimination of other micro-organisms as well (other staphylococci, including methicillin-resistant strains, streptococci and certain Gram-negative micro-organisms). The numbers of wound infections caused by *S. aureus* were too small to reach significance.

The same results in the "intention to treat" analysis and the analysis based on the actual numbers of treated and un-treated patients suggest that patients who unintentionally did not receive the treatment, were not selected. Why was no treatment given? Usually because nurses had never known or had forgotten it.

Comparison of the intervention group with a historical control group means that temporal and undetected factors may have reduced the number of infections. However, an important and constant factor in this study is the medical staff, which remained unchanged. No changes in surgical procedures or in the operation theater had occurred. The infection control practitioner who registered the infections had been replaced for 7 months. This might have led to an underestimate of infections in the intervention group.

Analysis of risk factors showed that it is unlikely that these influenced the results. Although more elderly persons were present in the intervention group, this should have led only to underestimates of the effectiveness. Estimation of the risk for sustaining a wound infection among patients older than 70 years by correction of this variable on the basis of the sample study resulted in a risk ratio of 1.4, with a 95% CI of 0.8–2.6, and a p-value of 0.2, which suggests that age is not a confounder in our study.

We also analyzed the results of wound infections in the group of patients who, in accordance with the procedure, did not receive mupirocin. These were patients who underwent operations other than those described in the section Patients and methods. In the first period, 0.7% (7/955) developed a postoperative wound infection, in the second period, 0.9% (5/587). This indicates there is no temporal decline in wound infections because of undetected factors.

In this study, it was not possible to identify patients who did not develop a wound infection and underwent two or more operations. Therefore we do not know whether such patients were counted at least twice in this study. In the intervention group, 1 patient had 2 wound infections (after several operations) and was also included twice. Screening the random samples of the 2 cohorts gave the following results. In the random sample of the historical control group (n 50), 10 patients were counted twice and 1 patient 3 times. In the random sample of the historical control group, 11/50 patients were counted twice and 1 patient 3 times. The risk ratio adjusted for these findings was 2.1, with a 95% CI of 1.1–3.8, and a p-value of 0.02. This suggests that the risk ratio did not change.

The decrease in the total number of wound infections was statistically significant, but the decrease in wound infections caused by *S. aureus* was not. Mupirocin administered in thoracic surgery gave almost the same results: a clear decrease in the total number of infections and also in infections caused by *S. aureus* (Kluytmans et al. 1996).

It is easy to use mupirocin as preoperative prophylaxis in orthopedics. It does not harm the patient and although the procedure has not been proved by a randomized controlled trial it seems to reduce postoperative infections. The risk of developing resistance with a short use is probably low.

We thank Mr. Eelko Hak, epidemiologist at the Department of General Practice, University of Utrecht, for advice about epidemiology and useful comments on the methodological part of the manuscript.

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