Perioperative intranasal mupirocin for the prevention of surgical-site infections: systematic review of the literature and meta-analysis

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CRD summary
This review determined the efficacy of peri-operative intranasal mupirocin for the prevention of surgical-site infection (SSI) according to type of surgical procedure. The authors concluded that peri-operative intranasal mupirocin appeared to reduce the incidence of SSI in non-general surgery, but had no apparent effect in general surgery. Given the limited evidence base and small number of randomised controlled trials, the authors' conclusion may be overstated.

Authors' objectives
To determine the efficacy of peri-operative intranasal mupirocin for the prevention of surgical-site infection (SSI) by type of surgical procedure.

Searching
MEDLINE, CINAHL, BIOSIS Previews, the Cochrane Database of Systematic Reviews and the Cochrane CENTRAL Register were searched from inception to 2004, unrestricted by language; the search terms were reported. A bibliographic and cited reference search of relevant articles was also performed.

Study selection
Study designs of evaluations included in the review
Controlled studies with a follow-up of at least 28 days were eligible for inclusion.

Specific interventions included in the review
Studies of intranasal mupirocin monotherapy were eligible. At least one pre-operative dose of mupirocin was required, regardless of Staphylococcus aureus colonisation status. Mupirocin was administered two to three times daily for 3 to 5 days (with one to ten doses given pre-operatively). The comparators included 'standard therapy', antibiotics (pre- and/or post-operative), pre-operative chlorhexidine shower plus antibiotics, and pre-operative antiseptic shower plus pre-operative antibiotics. Studies performed during an outbreak of SSI were excluded from the review.

Participants included in the review
No inclusion criteria were specified, although the research question implied that participants were undergoing surgery. Participants undergoing various types of surgery were included in the review: classified as general surgery (including gastrointestinal, oncologic and gynaecologic surgery) and non-general surgery (cardiothoracic/neurosurgery or orthopaedic surgery). Studies solely about peritoneal dialysis catheter or central venous catheter placement were excluded. The mean age of the participants ranged from 53.8 years to older than 70 years. Where reported, the body mass index ranged from 18.8 to 29.0 and between 0.3% and 31.2% of the participants had diabetes mellitus. Pre-study colonisation with Staphylococcus aureus ranged from 12.0 to 30.3%.

Outcomes assessed in the review
The primary outcome was SSI rate. Studies in which SSI rates could not be determined, or where SSI was not defined by current Centers for Disease Control and Prevention (or equivalent) criteria, were excluded. Post-operative infections due to gastrointestinal leaks during gastrointestinal surgery were excluded from the review. Resistance and side-effects were also reported.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected studies for inclusion in the review; any discrepancies were resolved through discussion, or by a third reviewer.
Assessment of study quality
The authors assessed the primary studies using U.S. Preventive Services Task Force criteria for hierarchy of research design and internal validity. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Two reviewers independently extracted the data from the primary studies using a standardised form; any discrepancies were resolved through discussion, or by a third reviewer. Relative risks (RRs) and their 95% confidence intervals (CIs) were calculated for SSI. Where reported, data from intention-to-treat analysis were extracted.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis using a random-effects model. Efficacy estimates were reported as summary RRs with 95% CIs.

How were differences between studies investigated?
The studies were grouped by surgery (general or non-general, and cardiothoracic or orthopaedic) and by study design (RCT or non-randomised studies). The authors reported that statistical heterogeneity was assessed, but did not provide any further details.

Results of the review
Seven studies (n=11,088) were included in the review: 3 randomised controlled trials (RCTs; n=4,873) and 4 before-and-after studies (n=6,215).

The 3 RCTs were given a research design rating of I; internal validity was rated as ‘good’ in 2 RCTs and “fair” in the other. The 4 non-randomised studies were given a research design rating of II and an internal validity rating of ‘fair’.

General surgery.
In RCTs, the incidence of SSI ranged from 8.4 to 8.8% in the mupirocin group and from 6.9 to 8.3% in the control group; in the single non-randomised study, the incidence was 11.3% in the mupirocin group and 18.0% in the control group. No statistically significant difference in infection rate was found between mupirocin and the control group for RCTs (RR 1.04, 95% CI: 0.81, 1.33; 2 studies) or non-randomised studies (RR 0.63, 95% CI: 0.35, 1.14; 1 study). No statistically significant heterogeneity was found.

Non-general surgery.
In RCTs, the incidence of SSI ranged from 3.8 to 7.0% in the mupirocin group and from 4.7 to 8.8% in the control group; in non-randomised studies, SSI incidence ranged from 0.9 to 2.8% (mupirocin) and from 2.7 to 7.3% (control), respectively. When only RCTs were analysed, mupirocin use reduced infection (RR 0.80, 95% CI: 0.58, 1.10; 2 studies), although this was not statistically significant. A statistically significant reduction in infection rate was shown when only non-randomised studies were analysed (RR 0.40, 95% CI: 0.29, 0.56; 3 studies). No statistically significant heterogeneity was found.

When cardiothoracic surgery studies were analysed, mupirocin was found to reduce infection compared with controls in both RCTs (RR 0.69, 95% CI: 0.46, 1.03; 1 study) and non-randomised studies (RR 0.37, 95% CI: 0.25, 0.55; 2 studies), although the difference was not statistically significant in the former. No statistically significant heterogeneity was found.

When orthopaedic surgery studies were analysed, mupirocin was found to reduce infection compared with controls in both RCTs (RR 0.81, 95% CI: 0.38, 1.73; 1 study) and non-randomised studies (RR 0.50, 95% CI: 0.27, 0.92; 1 study), although the difference was not statistically significant in the former.

Resistance and adverse events.
Of 4 studies reporting mupirocin resistance, sensitivity to mupirocin was reported in 2 studies (99.4% and 96.2%), while no mupirocin resistance was reported in the remaining 2 studies. Side-effects, primarily rhinorrhea and itching at site of application, were reported by 4.8% of mupirocin recipients and 4.8% of placebo recipients in 1 study.

**Cost information**
One trial estimated the cost of intranasal mupirocin to be less than $15.

**Authors' conclusions**
The use of peri-operative intranasal mupirocin in non-general surgery appeared to reduce the incidence of SSI, but had no apparent effect in general surgery.

**CRD commentary**
The review question was supported by clear inclusion criteria that were defined in terms of the study design, intervention and outcome; participants were not specifically defined. A number of relevant databases and reference lists were searched without language restriction. However, no specific attempts were made to locate unpublished data, which the authors acknowledged may lead to publication bias. The methods employed for the study selection and data extraction processes were likely to have minimised reviewer error or bias; the quality of the included studies was also assessed, but it was unclear whether similar steps were taken to reduce error and bias. The quantitative synthesis seemed appropriate; statistical heterogeneity was assessed, and potential differences between the studies in terms of the study design and type of surgery were examined. Studies using different doses of mupirocin and different comparators were, however, combined. The authors highlighted that significant baseline differences (age and pre-study colonisation with Staphylococcus aureus) were found between populations in a number of the non-randomised studies. Given the limited evidence base, heterogeneity between studies and the small number of RCTs, the authors' conclusion may be overstated.

**Implications of the review for practice and research**
Practice: The authors stated that the peri-operative use of intranasal mupirocin should be considered in clean surgeries where the risk of Staphylococcus aureus is high.

Research: The authors did not state any implications for further research.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.