An integrated critique of the efficacy of topical mupirocin in preventing catheter-related Staphylococcus aureus infections in peritoneal dialysis clients

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Authors' objectives
To evaluate the quality of evidence for the effectiveness of topical mupirocin (Bactroban) in the prevention of Staphylococcus aureus (SA) exit-site infections in people undergoing peritoneal dialysis.

Searching
PubMed, CINAHL and Peritoneal Dialysis International (PDI) websites were searched; the search terms were provided but the search dates were not.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and prospective cohort studies with a historical control group were eligible for inclusion.

Specific interventions included in the review
Studies evaluating the use of mupirocin applied to either the nares or the catheter exit-site were eligible for inclusion. One of the included studies applied either intranasal mupirocin or 0.1% neomycin three times daily for 7 days, repeated monthly if the participant was still a carrier for the first 9 months, followed by all participants taking mupirocin for the next 15 months. Another study compared mupirocin and placebo applied to the nares twice daily for 5 days every 4 weeks. One study compared mupirocin applied to the exit-site either daily or three times a week with a historical control group. Another compared mupirocin applied at the exit-site daily with 300 mg rifampicin twice daily, for 5 days every 3 months. An exit-site procedure using water, antibacterial soap and gauze was used in two of the studies to ensure consistency in the application of mupirocin.

Participants included in the review
Studies investigating patients undergoing continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD) were eligible for inclusion. The participants in the included studies were: CAPD clients carrying SA in their nares; patients on CAPD who had not been screened for nasal carriage of nares; new CAPD patients who began using mupirocin one month after their catheter was implanted; or patients on peritoneal dialysis with or without nasal carriage of nares. The definitions of SA carriage used in the primary studies were reported. Two studies ensured patients did not have a catheter-related infection before collecting data, and excluded patients who had used antibiotics for peritoneal dialysis-related infections within one month of the study.

Outcomes assessed in the review
Studies with a primary outcome of SA exit-site infection and a secondary outcome of SA peritonitis were eligible for inclusion. The outcomes included in the review were SA exit-site infection, SA peritoneal infection, SA catheter infection, SA tunnel infection and the sensitivity of SA strains to mupirocin. In one study, resistance to mupirocin was defined as a minimum inhibitory concentration in the range of 8 to 256 mg/L (low resistance) or greater than 256 mg/L (high resistance).

How were decisions on the relevance of primary studies made?
The author did not state how the papers were selected for the review, or how many reviewers performed the selection. However, it appears one reviewer alone made the decisions.

Assessment of study quality
The validity of the studies was discussed in relation to sample size, selection bias, randomisation, blinding, treatment compliance, consistency of the intervention, nature of the control group, cointerventions, outcome measures, outcome
evaluators and the data analysis. The author did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment. However, it appears that one reviewer alone assessed the validity of the papers.

Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction. However, it appears that one reviewer alone extracted the data. The infection rates of two studies were recalculated to be expressed as the number of infections per patient-year, to make study results more comparable. The number-needed-to-treat (NNT) to prevent one infection was calculated from outcome data for the cohort studies.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
Differences between the studies could be seen in the table and were discussed in the text.

Results of the review
Four studies were included in the review: one prospective, randomised double-blind, placebo-controlled, multicentre trial (n=267); one prospective randomised comparison of two treatments compared with a historical period (n=82); one prospective randomised placebo-controlled study, which changed to an open prospective trial after the first 9 months; and one prospective double-blind, historically controlled cohort design. The latter study was divided into two separate studies. The total number of participants was not provided.

All studies investigating the effects of mupirocin on exit-site and catheter infections found a significant decrease in the rate of SA infections in the treatment group relative to the control (P<0.05; NNT range: 13 to 18). Three of the four studies found a significantly greater decrease in SA peritonitis in the mupirocin group than the control group (P<0.05; NNT range: 11 to 24). One study compared the effects of mupirocin and rifampicin for the prevention of peritonitis and catheter infections and found no significant differences between treatment groups.

Two studies investigated the sensitivity of SA strains to mupirocin. One study found both high and low resistant isolates of SA in both the mupirocin and control groups, which cleared at a similar rate during the trials. The other study found that the minimum inhibitory concentration of mupirocin for SA strains increased as the trial progressed.

Methodological quality varied across the studies. There was inconsistency across the studies in definitions of exit-site and catheter infections and SA nasal carriage. Three of the four studies reported use of randomisation, but selection of the participants was not fully described, suggesting that it may not have been true randomisation. Potential confounders were controlled for in all studies through participant exclusion criteria. One of the cohort studies and one of the RCTs took further measures to control confounders by matching treatment and control group participants on age, gender and diabetic status. Only one of the studies reported a sample size calculation, the requirements of which it met. In two studies, the experimenters and participants were blind to the treatment and to whom the SA nasal carriers were. Two studies measured compliance to treatment. Both RCTs used an intention-to-treat analysis.

Authors' conclusions
There was weak evidence to suggest that topical mupirocin was effective in the prevention of SA exit-site infection in patients on peritoneal dialysis. There was a relationship between SA nasal colonisation and SA exit-site infections. Mupirocin should be used with care, given the possibility of resistance. In addition, mupirocin should be used as part of a programme of good nutrition, hygiene, exit-site care, patient education and staff training. Further research using well-controlled prospective trials with an adequate sample size, as well as standard definitions of exit-site infections, is needed.
CRD commentary
The author set out a clear objective at the beginning of the review, and the inclusion criteria were defined for the participants, interventions, outcomes and study design. The search of two electronic databases and PDI websites was adequate, but the dates of the searches were not provided. In addition, it was not stated whether any language restrictions had been applied. It was unclear how many people selected the studies, assessed study quality and extracted the data, although it appears that the author alone carried out these tasks; this might have introduced bias into the review.

Little information on the participant numbers or characteristics was provided, which makes it difficult for the findings to be generalised to other patients. A discussion of methodological quality included appropriate criteria. However, this assessment did not appear to be systematic, so the critical evaluation may not have been applied equally to all studies. The narrative synthesis of the studies was appropriate given the small number of heterogeneous studies. The review was not set out clearly, which made it difficult to identify particular pieces of information and results. In light of the mixed quality of the primary studies, the author was rightly cautious in her conclusions about the efficacy of mupirocin for the prevention of SA exit-site infections. However, given the considerable potential for bias and small number of studies included, the review should be interpreted with caution.

Implications of the review for practice and research
Practice: The author stated that mupirocin should be used with care because of the possibility of resistance, and as part of a programme of good nutrition, hygiene and exit-site care. It is important that patients on dialysis receive education about the prevention of exit-site infections, including regular home follow-up visits from a nurse. Staff should be trained before providing this education, with continued evaluation. There was no reported evidence for a difference in the efficacy of nasal or exit-site application of mupirocin. However, exit-site application may be preferred by patients, as it does not have the unpleasant side-effects of nasal application.

Research: The author stated that further well-controlled, prospective studies with larger sample sizes are needed. Biases in sample selection and implementation of the intervention should be addressed. More trials with newly-diagnosed clients, who have not yet developed a routine of exit-site care, would help to increase compliance and reduce participant withdrawals. Future RCTs should control for the participants' nutritional status, as this may have an influence on SA infection rates. Further trials are needed to determine the optimal dosage for mupirocin and the appropriate duration of mupirocin treatment required to prevent mupirocin-resistant SA strains. RCTs with three treatment arms should be used to compare the benefits, adverse effects and cost-effectiveness of nasal application of mupirocin, exit-site application of mupirocin, and oral cephalosporin or rifampicin.

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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.