

Topical application of mupirocin to the exit site in haemodialysis patients or not?

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The following questions were answered by a systematic review of the literature:

Are certain mupirocin regimens to the exit site of an indwelling haemodialysis catheter better than others in terms of prevention of catheter-related infection and the development of mupirocin resistant *S.aureus* strains?

Specific comparisons to be addressed included:

- 1) Is topical exit site mupirocin prophylaxis superior to no prophylaxis or placebo in the prevention of exit site infection?
- 2) Is topical exit site mupirocin prophylaxis superior to other topical exit site disinfectant agents as defined by the trialists?

Data sources

Publications were retrieved by a search of Medline and the Cochrane Library up to May 2005. Terms included were (hemodialysis OR haemodialysis OR renal dialysis) AND exit-site AND mupirocin. To identify randomised controlled trials in Medline the search strategy developed by Robinson was used (1). Additionally, all reference lists of identified trials were examined.

Selection criteria

All randomised and quasi-randomised trials comparing the effects of different topical mupirocin application policies to the exit site in patients with an indwelling haemodialysis catheter and surgical wound infection as the outcome measure.

Review methods

Data were extracted by two reviewers independently and compared. Disagreements were resolved by discussion. Data from the original publications were used to calculate the relative risk of catheter-related infection. Data for similar outcomes were combined in the analysis where appropriate, using a random-effects model.

Results

Three parallel-group randomised controlled trials were included (2-4).

Study population, interventions and outcome definitions

See Table I

Validity assessment

See Table II

Summary estimates of associations between treatment and control group

See Table III

Table I: Study population, interventions and outcome definitions

Study	Participants	Interventions	Outcome definitions
<p>Johnson 2005</p>	<p>Incl: All (101) adult patients with acute or renal failure who required haemodialysis via a newly inserted tunnelled, cuffed central venous catheter. Catheters were not assessed for other purposes. A prophylactic preoperative antibiotic (cephazolin 1 g intravenously) was prescribed in all cases.</p> <p>Excl: Not reported</p>	<p>Treatment (51): Topical application of gamma-irradiated, commercially available, pooled antibacterial honeys including Leptospermum sp honey (Medihoney) to exit site thrice-weekly (Bactroban, SmithKline Beecham Pharmaceuticals).</p> <p>Control (50): Topical application of 2% calcium mupirocin ointment to exit site thrice-weekly (Bactroban, SmithKline Beecham Pharmaceuticals).</p> <p>Follow-up: Until catheter removal</p>	<p>Catheter-associated bacteraemia was defined as a) a single positive culture together with a positive culture of a catheter tip or exit site with an identical organism; b) two or more positive blood cultures (or a single positive blood culture for <i>S. aureus</i>) with no evidence of infection source other than the device.</p> <p>Catheter colonization was defined as the recovery of greater than 15 colony-forming units (semiquantitative method of Maki).</p> <p>Exit site infection was defined as either purulent exit site discharge or two out of three exit site erythema, tenderness and induration with a positive culture.</p>
<p>Johnson 2002</p>	<p>Incl: All (50) adult patients with acute or renal failure who required haemodialysis via a newly inserted tunnelled, cuffed internal jugular venous catheter. Catheters were not assessed for other purposes. No prophylactic antibiotics were given prior to catheter insertion.</p> <p>Excl: Not reported</p>	<p>Treatment (27): Application of topical 2% calcium mupirocin ointment to exit site thrice-weekly (Bactroban, SmithKline Beecham Pharmaceuticals) in addition to standard exit site care.</p> <p>Control (23): No ointment. Standard exit site care.</p> <p>Follow-up: Until catheter removal</p>	<p>Catheter-associated bacteraemia was defined as a) a single positive culture together with a positive culture of a catheter tip or exit site with an identical organism; b) two or more positive blood cultures (or a single positive blood culture for <i>S. aureus</i>) with no evidence of infection source other than the device.</p> <p>Catheter colonization was defined as the recovery of greater than 15 colony-forming units (semiquantitative method of Maki).</p> <p>Exit site infection was defined as either purulent exit site discharge or two out of three exit site erythema, tenderness</p>

			and induration with a positive culture.
Sesso 1998	<p>Incl: 136 end-stage renal disease patients who required haemodialysis via a newly inserted internal jugular or subclavian venous catheter (without a subcutaneous tunnel; aseptic Seldinger technique). Catheters were not assessed for other purposes. No prophylactic antibiotics were given prior to catheter insertion.</p> <p>Excl: Patients with acute renal failure, use of a central venous catheter within 1 month prior to study, septicaemia or a life-threatening infection.</p>	<p>Treatment (69): Application of topical 2% calcium mupirocin ointment to exit site thrice-weekly (Bactroban, SmithKline Beecham Pharmaceuticals) in addition to standard exit site care.</p> <p>Control (67): No ointment. Standard exit site care.</p> <p>Follow-up: Until catheter removal</p>	<p>S. aureus catheter-associated bacteraemia was defined as 1) one or more blood cultures yielded S. aureus while the catheter was in place and 2) fever > 37.8 C accompanied by rigors and 3) no evidence of infection source other than the device (clinical examination, chest radiography, laboratory investigation, microbiologic data) and 4) recovery of S. aureus on catheter tip culture.</p> <p>Catheter colonization was defined as the recovery of greater than 15 colony-forming units (semiquantitative method of Maki).</p> <p>Exit site S. aureus infection was defined as presence of objective clinical signs (erythema, drainage of purulent exsudate at the catheter site) and a positive culture with S. aureus.</p>

Table II: Data on quality assessment

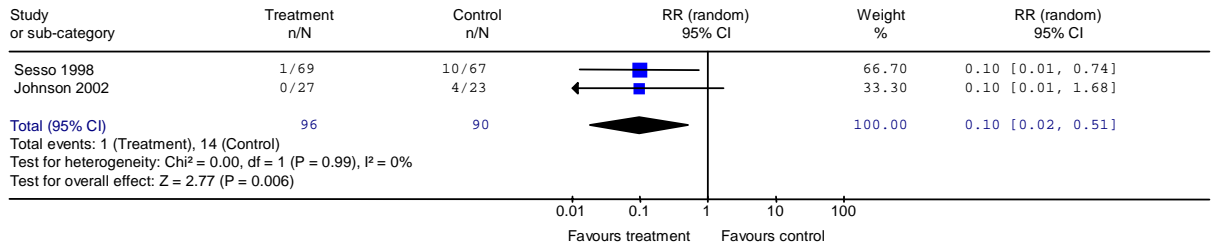
General quality assessment		
Johnson 2005	<i>Generation of allocation sequence:</i> <i>Concealment of allocation:</i> <i>Blinding patients:</i> <i>Blinding attending physician:</i> <i>Blinding outcome assessors:</i> <i>Description of dropouts:</i> <i>Analysis by intention-to-treat:</i>	Randomisation by sequentially numbered, opaque, sealed envelopes before catheter insertion; the sequence of interventions was obtained from a computer-generated random number list with randomization blocks of 10 Adequate No No Yes None were lost Yes
Johnson 2002	<i>Generation of allocation sequence:</i> <i>Concealment of allocation:</i> <i>Blinding patients:</i> <i>Blinding attending physician:</i> <i>Blinding outcome assessors:</i> <i>Description of dropouts:</i> <i>Analysis by intention-to-treat:</i>	Randomisation by sequentially numbered, opaque, sealed envelopes; the sequence of interventions was obtained from a computer-generated random number list Adequate No No Yes No losses Yes
Sesso 1998	<i>Generation of allocation sequence:</i> <i>Concealment of allocation:</i> <i>Blinding patients:</i> <i>Blinding attending physician:</i> <i>Blinding outcome assessors:</i> <i>Description of dropouts:</i> <i>Analysis by intention-to-treat:</i>	Randomisation by sequentially numbered, opaque, sealed envelopes; the sequence of interventions was obtained from a computer-generated random number list, using blocked randomizations (blocking size varying from 4 to 6) Yes No No No No losses Yes

Table III: Summary estimates of associations between treatment and control group expressed as relative risk (RR) and 95% confidence interval (CI) using a random effects model

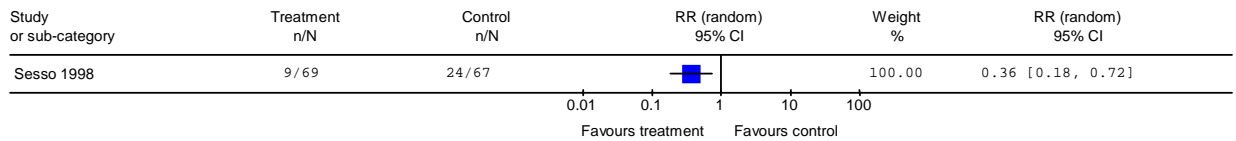
TREATMENT: Mupirocin

CONTROL: No Mupirocin

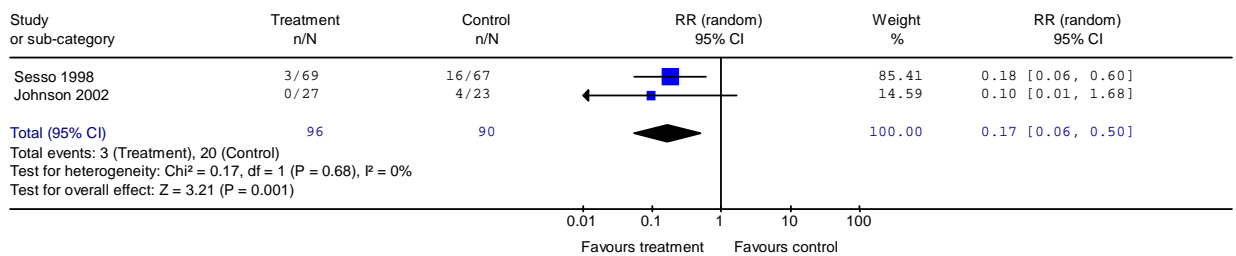
Outcome: S. aureus catheter-related bacteremia



OutcomeL Colonisation catheter tip with S. aureus



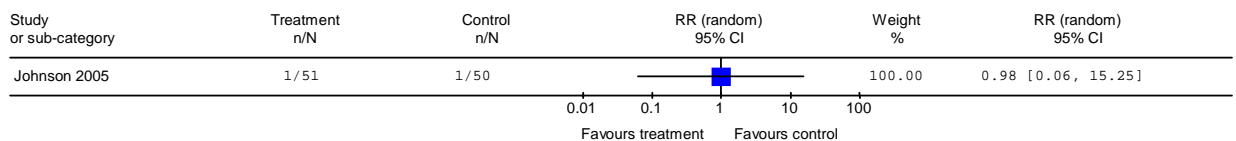
Outcome: S. aureus exit site infection



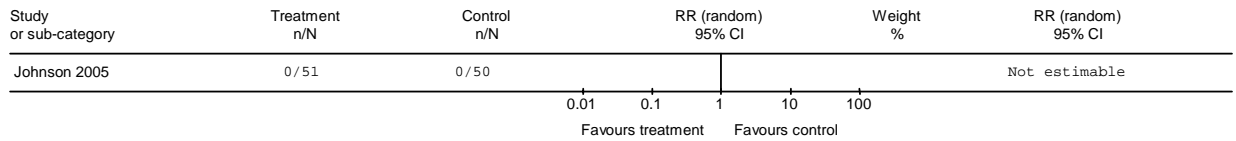
TREATMENT: Mupirocin

CONTROL: Honey

Outcome: S. aureus catheter-related bacteremia



Outcome: S. aureus exit site infection



Comments (points of criticism)

One concern about methodological quality is the possibility of performance bias because of the open label design used by all trials. Another major concern is that none of the trials investigated development of mupirocin resistant staphylococcal isolates in an adequate way (small numbers, too short follow-up).

Conclusion

1) Is topical exit site mupirocin prophylaxis superior to no prophylaxis or placebo in the prevention of exit site infection?

There is limited evidence that topical exit site mupirocin prophylaxis is significantly better than no prophylaxis in terms of catheter-related infections. Two open-label trials of methodological good quality addressed this issue. Because of the few data on development of antibiotic resistance, the results should be interpreted with caution.

2) Is topical exit site mupirocin prophylaxis superior to other topical exit site disinfectant agents as defined by the trialists?

The evidence available is not sufficient as a basis for determining practice. One trial of good methodological quality comparing mupirocin with honey addressed this issue.

References

1. Robinson KA, Dickersin K. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. *Int J Epidemiol* 2002;31:150-53.
2. Johnson DW, Eps van C, Mudge DW, Wiggins KJ, Armstrong K, Hawley CM, et al. Randomized, controlled trial of topical exit-site application of honey (medihoney) versus Mupirocin for the prevention of catheter-associated infections in hemodialysis patients. *J Am Soc Nephrol* 2005;16:1-7.
3. Johnson DW, MacGinley R, Kay TD, Hawley CM, Campbell SB, Isbel NM, et al. A randomized controlled trial of topical exit site mupirocin application in patients with tunnelled, cuffed haemodialysis catheters. *Nephrol Dial Transplant* 2002;17:1802-1807.
4. Sesso R, Barbosa D, Leme IL, Sader H, Canziani ME, Manfredi S, et al. S. aureus prophylaxis in hemodialysis patients using central venous catheter: effect of mupirocin ointment. *J Am Soc Nephrol* 1998;9:1085-92.