ANNEXES TO CHAPTER 6

Clinical Question XXXIII. Does the detection and eradication of Staphylococcus aureus in nasal carriers reduce episodes of catheter-related bacteraemia? Is it cost-effective?

The available evidence from RCT only addresses findings that relate to bacteraemia, without providing information on mortality, hospitalisation or antibacterial resistance. A Cochrane review was found that analyses the impact of local treatment of nasal carriers with mupirocin (van Rijen 2008) on the prevention of Staphylococcus aureus bacteraemia.

Nasal mupirocin

A Cochrane review (van Rijen 2008) which analysed the effectiveness of nasal mupirocin in the prevention of infections by Staphylococcus aureus in nasal carriers identified nine RCT with 3396 patients. There was a great deal of clinical heterogeneity among patients in the different studies, with patients on haemodialysis, on peritoneal dialysis and both surgical and non-surgical patients. **S. aureus infection rates** The meta-analysis of the eight studies, with 3374 participants, comparing mupirocin with placebo or with no treatment, found a statistically significant reduction in those treated with intranasal mupirocin (RR 0.55, 95% CI: 0.43-0.70). **Infection rates caused by microorganisms other than S. aureus** The meta-analysis of three studies, with 1393 patients, found a significantly higher rate in patients treated with mupirocin than in the placebo group (RR 1.38, 95% CI: 1.118 to 1.72). **Mortality** The meta-analysis of five studies, with 2161 patients, found no statistically significant differences between those treated with mupirocin or placebo (HR 0.91, 95% CI: 0.64 to 1.31).	**Moderate quality**
The only RCT in patients on haemodialysis (Boelaert 1989), included in the van Rijen review (2008), with 17 patients treated with nasal mupirocin and 18 with placebo three times a week for 9 months, found fewer *infections* in patients treated with mupirocin, although the difference was not statistically significant (RR 0.18, 95% CI: 0.02 to 1.32), but not in relation to the incidence of *bacteraemia*. The review by Laupland (2003) reported that the results from the above study by Boelaert may have been biased due to the shorter duration of follow-up of the mupirocin group compared to the placebo group (104 vs 147 patient-months respectively). They also point out the failure of Boelaert to provide a strict definition for infection beforehand, and that the blinding process was not well described.	**Low quality**

Oral rifampicin + intranasal bacitracin

Several published reviews (Herwaldt 1998; Barraclough 2009; Ammerlaan 2009) identified a single RCT on haemodialysis patients who were nasal carriers of S. aureus, comparing not treating vs treatment with oral rifampicin 600 mg twice weekly plus intranasal bacitracin four times daily for one week, repeated every three months (Yu 1986).	**Moderate quality**

They found a lower rate of infections in those treated actively (2/18: 11% vs 12/26: 46%; RR 0.24. 95% CI: 0.06-0.95; p: 0.02). Barraclough (2009) reports that strains resistant to rifampicin were identified in the above study, limiting the application of that intervention. They go on to say that the study also looked at whether or not the use of rifampicin for one week was effective in the eradication of carrier status, and point out that a high recurrence rate of colonisation by S. aureus was found at three months. The Ammerlaan review (2009) discusses the fact that the follow-up in the Yu RCT was 90 days and that at the end of the study the eradication of the bacillus in the nose was sustained in 67% of those treated with rifampicin and in only 27% of those not treated.	
Summary of evidence	
A meta-analysis of 8 RCT, only one of which was on haemodialysis patients, found that treating carriers of Staphylococcus aureus with nasal mupirocin was associated with a lower rate of hospital-acquired infection by S. aureus, but was accompanied by an increase in the rate of infection caused by microorganisms other than S. aureus.	**Moderate quality**
An RCT analysing treatment with oral rifampicin vs no treatment found a lower rate of infections, but also a high rate of recurrence of colonisation by S. aureus at three months and the development of strains resistant to rifampicin.	**Moderate quality**
Patients' values and preferences *No relevant studies related to this aspect have been identified.*	
Use of resources and costs Two old economic evaluations were identified, one carried out in the USA and the other in Belgium. The study conducted in 1996 in the USA (Bloom 1996) concluded that the strategy of treating all patients with mupirocin without screening for infection was more cost-effective than screening and only treating carriers. The Belgian study (Boelaert 1991) compared screening vs not screening for carriers and treating them with mupirocin, concluding that the strategy of screening patients resulted in savings of $665 per patient-year on haemodialysis. However, Davey (1998) considered that the problems of infections by other microorganisms and the negative effect of potential antimicrobial resistance had not been taken into account in this study.	
Recommendations [Proposal]	
Weak	We do not recommend routine use of detection and local or systemic antibiotic treatment for the eradication of Staphylococcus aureus in nasal carriers on haemodialysis.
References	
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van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. Cochrane Database Syst Rev. 2008 Oct 8; (4):CD006216.

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Table 1. STUDIES EXCLUDED

Study	Cause for exclusion
Bode 2012	Study in patients with planned hospital admission in hospital for at least four days. Were not patients on haemodialysis.
Johnson 2002	Does not analyse anything related to nasal carriers of S. aureus.
Kang 2012	Prevalence study. Does not compare interventions.
Kaplowitz (1998)	RCT comparing two local treatments in the area of skin where the catheter is inserted.
Katneni 2007	Narrative review, from 2007.
Lederer 2007	Clinical series, without comparator group.
Schmid 2013	Clinical series, without comparator group.
Whertein 2005	Narrative review, from 2005.

GRADE TABLES

Date: 2013-12-08
Question: Should nasal mupirocin vs placebo be used in nasal carriers of *Staphylococcus aureus* ?
Bibliography: van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. Cochrane Database Syst Rev. 2008 Oct 8; (4):CD006216. doi: 10.1002/14651858.CD006216.pub2.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nasal Mupirocin	Placebo	Relative (95% CI)	Absolute		
***S. aureus* infection rate**												
8	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	82/1678 (4.9%)	150/1696 (8.8%)	RR 0.55 (0.43 to 0.7)	40 fewer per 1000 (from 27 fewer to 50 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Infection rate by bacteria other than *S. aureus*												
3	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	131/694 (18.9%)	95/699 (13.6%)	RR 1.38 (1.11 to 1.72)	52 more per 1000 (from 15 more to 98 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Mortality												
5	randomised trials	no serious risk of bias	no serious inconsistency	serious	no serious imprecision	none	50/1074 (4.7%)	55/1087 (5.1%)	RR 0.91 (0.64 to 1.31)	5 fewer per 1000 (from 18 fewer to 16 more)	⨁⨁⨁◯ MODERATE	CRITICAL

[1] Only one of the studies in patients on haemodialysis.

Date: 2013-12-08
Question: Should oral rifampicin vs no-intervention be used in nasal carriers of *Staphylococcus aureus* ?
Bibliography: van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. Cochrane Database Syst Rev. 2008 Oct 8; (4):CD006216. doi: 10.1002/14651858.CD006216.pub2.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Oral rifampicin**	**No-intervention**	**Relative (95% CI)**	**Absolute**		
***S. aureus* infection rate**												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	2/18 (11.1%)	12/26 (46.2%)	RR 0.24 (0.06 to 0.95)	351 fewer per 1000 (from 23 more to 434 more)	⨁⨁⨁◯ MODERATE	CRITICAL

[1] Wide confidence interval.