Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis
Chan E Y, Ruest A, Meade M O, Cook D J

CRD summary
This review concluded that oral decontamination is associated with a lower risk of ventilator-associated pneumonia in mechanically ventilated adults, but not reduced mortality or shorter duration of ventilation or length of stay in intensive care. The authors are right, however, to suggest a cautious interpretation of their results given the presence of significant variation between the studies.

Authors' objectives
To investigate the effect of oral decontamination on the incidence of ventilator-associated pneumonia (VAP) and mortality in mechanically ventilated adults.

Searching
MEDLINE, EMBASE, CINAHL, the Cochrane CENTRAL Register and the Cochrane Database of Systematic Reviews were searched from inception to May 2006; the search terms were not reported. In addition, references from retrieved articles and meta-analyses were screened; trials registers and web postings from conference proceedings, abstracts and poster presentations were searched; and experts and pertinent authors were contacted. No language restrictions were applied. Editorials and commentaries were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies investigating the effect of oral decontamination using any type or combination of antibiotics or antiseptics were eligible for inclusion. Studies evaluating the selective decontamination of the digestive tract were excluded. The included studies evaluated various interventions: Orabase with gentamicin, colistin and vancomycin; chlorhexidine with or without oropharynx rinse or colistin; gentamicin with polymyxin B or with amphotericin B plus oral disinfection with phenylhydragryum boricom and hexetidine; and Iseganan. The majority of the control groups used placebo. One study used placebo with or without topical antimicrobial prophylaxis; another used standard care; a third used 'standard oral care' or saline rinse.

Participants included in the review
Studies with adults requiring mechanical ventilation in an intensive care unit were eligible. Most of the included studies evaluated mixed populations of patients in general intensive care facilities; others included specific medical, surgical or cardiothoracic populations.

Outcomes assessed in the review
Studies had to report the incidence of pneumonia and mortality to be eligible. The authors' definition for VAP was used if it included clinical and radiological criteria; studies using the clinical pulmonary infection score alone were excluded. The review also assessed the duration of mechanical ventilation and stay in the intensive care unit.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies; one reviewer was blinded to the author, journal, institutional affiliation and date of publication.
Assessment of study quality
Two reviewers independently assessed randomisation, allocation concealment, blinding, clarity of the inclusion and exclusion criteria and outcome definitions, similarity of baseline characteristics, and completeness of follow-up. Authors were contacted to clarify methods where necessary.

Data extraction
Two reviewers independently abstracted the data, and any disagreements were resolved by discussion. Authors were contacted for clarification where necessary.

Methods of synthesis
How were the studies combined?
The studies were grouped according to prophylactic agent and combined in a random-effects model. Binary variables were pooled as relative risks (RRs), together with the 95% confidence intervals (CIs); continuous outcomes were pooled as mean differences. The number-needed-to-treat was also computed. Egger’s regression intercept and Begg’s rank correlation tests were used to assess publication bias.

How were differences between studies investigated?
Cochran’s Q and the I-squared statistic were used to investigate heterogeneity. I-squared values of above 25% were considered to indicate low heterogeneity, 50% moderate heterogeneity and 75% high heterogeneity. The effects of method of allocation, blinding, patient population and duration of ventilator treatment were investigated. A subgroup analysis compared alternative approaches to the diagnosis of pneumonia.

Results of the review
Eleven RCTs (n=3,242) were included.

Most of the studies were double-blind, used a computer-generated sequence for the randomisation, and used pharmacy-controlled allocation. All of the studies had explicit inclusion and exclusion criteria. All but one unclear study showed similar baselines of the treatment arms. The majority of the studies described the patients excluded after randomisation.

Oral application of antibiotics (4 trials) did not significantly reduce the incidence of VAP (RR 0.69, 95% CI: 0.41, 1.18) or mortality (RR 0.94, 95% CI: 0.73, 1.21).

Oral application of antiseptics (7 trials) significantly reduced the incidence of VAP (RR 0.56, 95% CI: 0.39, 0.81), but showed no effect on mortality (RR 0.96, 95% CI: 0.69, 1.33). There was evidence of statistical heterogeneity.

The pooled results of antibiotic and antiseptic interventions (11 trials) showed a significant effect on the incidence of VAP in favour of oral decontamination (RR 0.61, 95% CI: 0.45, 0.82), but still no significant effect on mortality.

There were no differences in terms of the duration of mechanical ventilation or the length of stay in intensive care.

The funnel plot showed some asymmetry, but both statistical tests were negative (p=0.111, p=0.175).

Authors’ conclusions
Oral decontamination is associated with a lower risk of VAP in mechanically ventilated adults; however, neither antiseptic nor antibiotic oral decontamination reduced mortality or the duration of ventilation or stay in the intensive care unit. More evidence is needed to confirm these conclusions in light of the heterogeneity and possible risk of publication bias.

CRD commentary
This review addressed a clear research question with explicit inclusion criteria. The searches were thorough, with no language restrictions applied and with explicit strategies to identify unpublished material. Tests for publication bias did
suggest a moderate risk of bias, but their reliability is unclear given the relatively small number of included studies. Procedures to minimise reviewer bias and error were reported for critical stages of the review. The quality of the included studies was documented and the effects of some variables were investigated. Other sources of heterogeneity were also explored, but the overall positive findings were dominated by a small number of strongly positive trials. Overall, the conclusions are likely to be reliable but, as the authors pointed out, the level of statistical heterogeneity between the studies and the potential risk of publication bias suggest that they should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that, while the results are promising, it may not be prudent to adopt a practice of oral decontamination routinely for critically ill patients.

Research: The authors stated that trials comparing antibiotic with antiseptic oral decontamination while incorporating stringent infection surveillance are desirable. The influence on patient outcomes such as duration of ventilation or stay in the intensive care unit should also be evaluated in rigorously designed and adequately powered RCTs. In addition, long-term risk assessments of selecting antiseptic- and antibiotic-resistant organisms are needed.

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