Oral decontamination with chlorhexidine reduced ventilator-associated pneumonia in high-risk patients

Koeman M, van der Ven AJ, Hak E, et al. **Oral decontamination with chlorhexidine reduces the incidence of ventilator-associated pneumonia.** Am J Respir Crit Care Med. 2006;173:1348-55.

Clinical impact ratings: Infectious Disease ★★★★★☆☆ Critical Care ★★★★★★☆ Pulmonology ★★★★★★☆

QUESTION

In high-risk mechanically ventilated patients, how effective is oral decontamination with chlorhexidine for reducing ventilator-associated pneumonia (VAP)?

METHODS

Design: Randomized placebo-controlled trial.
Allocation: {Concealed}†.*
Blinding: Blinded (clinicians, patients, {outcome assessors, data collectors, data analysts, data safety and monitoring committee, manuscript writers, and pharmacists at participating centers}†).*
Follow-up period: Mean range 5.9 to 8.4 days (up to diagnosis of VAP, death, or extubation).
Setting: 2 mixed and 2 surgical intensive care units (ICUs) in 2 university hospitals, and mixed ICUs in 3 general hospitals in the Netherlands.
Patients: 385 patients > 18 years of age (mean age 62 y, 60% men) requiring mechanical ventilation for ≥ 48 hours. Exclusion criteria were inability to take oral medication, preadmission immune compromise (defined as leukopenia < 3×10^9/L, cumulative dose of corticosteroids > 750 mg/y, or HIV), or pregnancy.
Intervention: 2% chlorhexidine (n = 127), 2% chlorhexidine plus 2% colistin (n = 128), or placebo (n = 130). All medications were mixed with petroleum jelly FNA to form a paste, and 0.5 g was applied 4 times/d to each side of the mouth.
Outcomes: Incidence of VAP. Secondary outcomes were all-cause ICU mortality, and oral and endotracheal tube (ETT) colonization.
Patient follow-up: 100% (intention-to-treat analysis). Follow-up for oral and ETT colonization was < 80% for both.

MAIN RESULTS

The chlorhexidine and chlorhexidine plus colistin groups had lower incidences of VAP than did the placebo group (Table). Groups did not differ for all-cause ICU mortality (chlorhexidine vs placebo, hazard ratio [HR] 1.12, 95% CI 0.72 to 1.17; chlorhexidine + colistin vs placebo, HR 1.02, CI 0.66 to 1.59). Results for oral and ETT colonization are not reported because < 80% of patients were included in the analysis.

CONCLUSION

In high-risk mechanically ventilated patients, oral decontamination with chlorhexidine reduced ventilator-associated pneumonia.

Source of funding: Netherlands Organization for Health Research and Development.

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*See Glossary.
†Information provided by author.

Chlorhexidine or chlorhexidine plus colistin vs placebo in high-risk mechanically ventilated patients at mean 5.9 to 8.4 days‡

Outcome	Chlorhexidine	Chlorhexidine + colistin	Placebo	RRR (95% CI)	NNT (CI)
Ventilator-associated pneumonia	10%	–	18%	63% (19 to 83)	10 (7 to 30)
	–	13%	18%	52% (6.8 to 76)	11 (8 to 83)

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from control event rates and hazard ratios in article.

COMMENTARY

The study by Koeman and colleagues is the largest multicenter, blinded, placebo-controlled trial to date on the effectiveness of prophylactic oral chlorhexidine to prevent VAP in medicosurgical ICU patients (1), and it was the first to show a beneficial effect. In this trial, chlorhexidine with or without colistin was effective for decreasing the daily risk for VAP. The hypothesized advantage conferred by the addition of colistin for preventing late-onset VAP, usually caused by gram-negative microorganisms, could not be confirmed, possibly because of insufficient power.

This trial had several methodological strengths, including concealed allocation, intention-to-treat analysis for the primary outcome, blinded VAP adjudication by 3 independent experts, and correlation with a modified Clinical Pulmonary Infection Score to validate diagnosis of VAP.

Oral decontamination with chlorhexidine is an inexpensive pneumonia prevention strategy compared with some other prophylactic strategies. To date, randomized trial evidence favors chlorhexidine in patients at high risk for VAP, but inferences would be stronger from larger trials, increasing the total number of events and patients on which clinical policy can be based. Future studies evaluating whether routine long-term use of chlorhexidine with or without colistin influences ICU microbial flora will also inform us about its role in practice.

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Reference

1. **Fourrier F, Dubois D, Pronnier P, et al.** Effect of gingival and dental plaque antiseptic decontamination on nosocomial infections acquired in the intensive care unit: a double-blind placebo-controlled multicenter study. Crit Care Med. 2005;33:1728-35.