

Letter

Oral decontamination with chlorhexidine reduces the incidence of nosocomial pneumoniaIlias I Siempos¹ and Matthew E Falagas^{1,2,3}¹Alfa Institute of Biomedical Sciences (AIBS), 9 Neapoleos Street, 151 23 Marousi, Athens, Greece²Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA³Department of Medicine, Henry Dunant Hospital, Athens, GreeceCorresponding author: Matthew E Falagas, m.falagas@aibs.gr

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Critical Care 2007, **11**:402 (doi:10.1186/cc5129)See related research by Pineda *et al.*, <http://ccforum.com/content/10/1/R35>

Pineda and colleagues [1] published a well-performed meta-analysis of four randomized controlled trials (RCTs) [2-5] exploring the effect of oral chlorhexidine (CHX) application on the incidence of nosocomial pneumonia (NP) in mechanically ventilated patients. They concluded that oral CHX decontamination did not reduce the incidence of NP in such patients; however, they clearly stated that the combined sample size of the four RCTs included may be inadequate for detecting important differences. Meanwhile, additional important data on this issue have been published; updating the findings of the above meta-analysis [1] is therefore warranted.

In detail, Koeman and colleagues [6] enrolled intensive care unit patients requiring mechanical ventilation in a large, multicenter, double-blind, three-arm RCT. Ventilator-associated pneumonia developed in 13 out of 127 (10%) patients treated with 2% CHX paste, in 16 out of 128 (13%) subjects treated with 2% CHX and 2% colistin paste, and in 23 out of 130 (18%) placebo recipients. One additional RCT (in fact, a pilot study) conducted by Bopp and colleagues [7] in patients intubated in the intensive care unit reported that neither of two (0%) patients treated with 0.12% CHX gluconate and one out of three (33%) patients who received standard oral care (with soft foam swab and hydrogen peroxide) developed NP.

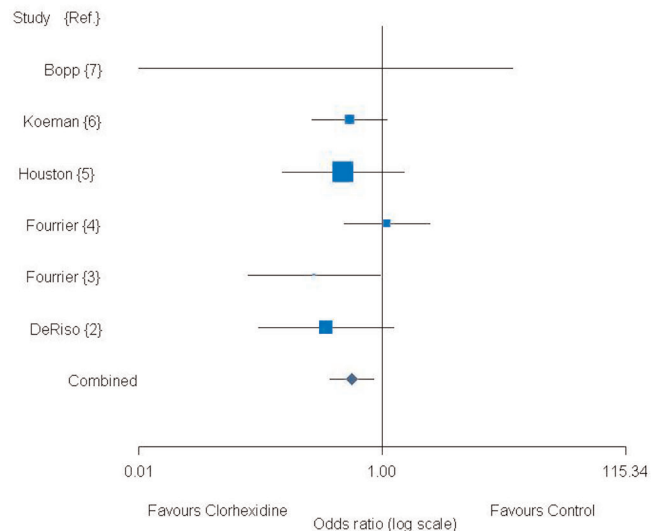
We used data from the four RCTs [2-5] included in the meta-analysis by Pineda and colleagues [1] as well as data from the two RCTs published later [6,7] to estimate the pooled odds ratio (OR) and 95% confidence intervals (CIs) for the incidence of NP. Both the Mantel-Haenszel fixed-effect model and the DerSimonian-Laird random effects model were employed. Heterogeneity between RCTs was assessed using both a chi-square test and the I^2 statistic. Statistical analyses were performed using the 'S-PLUS 6.1' software.

Oral application with CHX in mechanically ventilated patients was associated with reduced incidence of NP compared with control individuals (fixed-effect model, OR = 0.55, 95% CI = 0.36–0.84; random effects model, OR = 0.56, 95% CI = 0.36–0.86; data from six trials [2-7], Figure 1). No heterogeneity was detected between the trials ($P = 0.48$, $I^2 = 0$, 95% CI = 0–0.75). It should be mentioned that we omitted patients treated with CHX and antibiotic from our analysis in an attempt to avoid confounding. In addition, we performed a subgroup analysis by excluding RCTs conducted in a cardiac surgery population [2,5]. The rationale for this subanalysis was that cardiac surgery patients were at lower risk of developing NP than intensive care unit patients due to the shorter duration of mechanical ventilation [6]. Using the fixed-effect model, we found that oral decontamination with CHX was associated with lower NP incidence in intensive care unit patients compared with controls (OR = 0.61, 95% CI = 0.37–0.99; data from four RCTs [3,4,6,7]); however, the statistical significance of this finding did not remain when a random effects model was employed (OR = 0.60, 95% CI = 0.33–1.09; Figure 2). Employment of a fixed-effect model for this analysis seems reasonable because there was no heterogeneity between these four RCTs [3,4,6,7] ($P = 0.29$, $I^2 = 0.20$, 95% CI = 0–0.88).

We believe current evidence suggests that oral decontamination with CHX may reduce the NP incidence in mechanically ventilated patients. Given its low cost and safety, CHX may be considered among the preventive measures for NP. Further investigation is warranted to confirm these promising findings as well as to evaluate the potential impact of CHX overuse on induction of antimicrobial resistance.

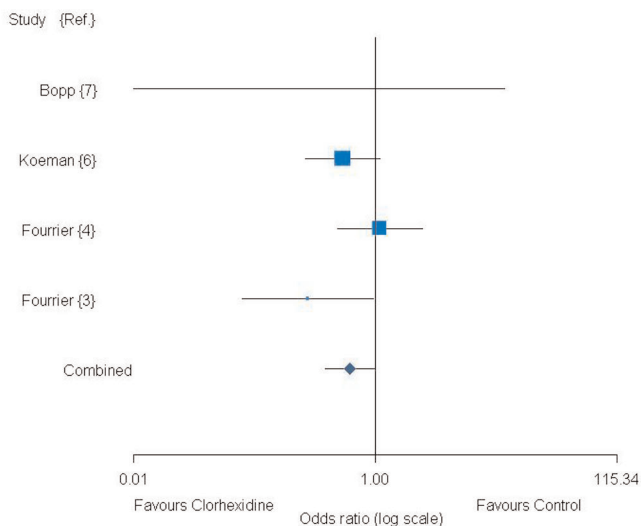
CHX = chlorhexidine; CI = confidence interval; NP = nosocomial pneumonia; OR = odds ratio; RCT = randomized controlled trial.

Figure 1



Odds ratios of the incidence of nosocomial pneumonia for the individual randomized controlled trials comparing chlorhexidine and controls for the management of mechanically ventilated patients and the pooled analysis. Vertical line, 'no difference' point between the two regimens; square, odds ratio (size of each square denotes the proportion of information given by each trial); diamond, pooled odds ratio for all randomized controlled trials; horizontal lines, 95% confidence intervals.

Figure 2



Odds ratios of the incidence of nosocomial pneumonia for the individual randomized controlled trials comparing chlorhexidine and controls for the management of mechanically ventilated patients in the intensive care unit setting and the pooled analysis. Vertical line, 'no difference' point between the two regimens; square, odds ratio (size of each square denotes the proportion of information given by each trial); diamond, pooled odds ratio for all randomized controlled trials; horizontal lines, 95% confidence intervals.

Reply from the authors

Lilibeth A Pineda, Brydon JB Grant and Ali A El Solh

We would like to thank Dr Siempos and Dr Falagas for their comments on our study [1].

In our meta-analysis, we set up *a priori* to use a random effects model to account for the between-study variations with regard to an overall mean of the effects of all the studies [8]. There were variations among the studies in terms of the CHX dose, the clinical setting, and the criteria of ventilator-associated pneumonia. We therefore felt that these variations should be taken into account despite the fact that we did not detect any heterogeneity between the selected trials.

Inherent to any meta-analysis, new trials will become available – warranting an update of the analysis. With the addition of two recent trials favoring the use of CHX [6,7] the sample size increased by 21%, yet the results of the subgroup analysis showed a significant reduction in ventilator-associated

pneumonia only when a fixed-effect model was applied. It is noteworthy to mention that the study of Bopp and colleagues [7] was a pilot study that included only five patients. In their methods, Bopp and colleagues [7] stated that, due to the small sample size, their investigation was modified to a case study and they mainly used descriptive statistics.

Finally, we would like to point out that the diagnosis of ventilator-associated pneumonia in these trials was, in the majority, based on clinical criteria and endotracheal aspirates rather than on quantitative cultures of the lower respiratory tract. Given the limitations of these diagnostic criteria, the proof of CHX efficacy in reducing the rate of ventilator-associated pneumonia remains elusive. Nonetheless, because of the low risk and cost of CHX, we feel that CHX may be added to the oral care of intubated patients while awaiting the results of future RCTs.

Competing interests

The authors declare that they have no competing interests.

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