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REVIEW

Efficacy of oral chlorhexidine in preventing lower respiratory tract infections. Meta-analysis of randomized controlled trials

A. Kola*, P. Gastmeier

Institute for Medical Microbiology and Hospital Epidemiology, Hannover Medical School, Hannover, Germany

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KEYWORDS
Lower respiratory tract infections; Oral decontamination; Chlorhexidine; Meta-analysis

Summary Several randomized controlled trials (RCTs) have examined the influence of oral chlorhexidine (CHX) in preventing nosocomial lower respiratory tract infection (LRTI). Most have failed to demonstrate a reduction in the incidence of LRTI. The present meta-analysis summarizes the effect of oral CHX on the development of LRTI. RCTs were identified through searching PubMed, MEDLINE and the Cochrane Central Register of Controlled Trials databases. Those describing the use of chlorhexidine for oral decontamination and reporting the incidence of LRTI as a study outcome were included in the meta-analysis. Seven RCTs met the inclusion criteria; pooling the results from these reveals a reduction in the relative risk (RR) of LRTI in the CHX group [RR_{random}: 0.58, 95% confidence interval (CI): 0.45–0.74; and RR_{fixed}: 0.56, CI95: 0.44–0.72, respectively]. Further analyses showed that this result applied only to patients ventilated for up to 48 h (RR_{random}: 0.58, CI95: 0.45–0.74; and RR_{fixed}: 0.56, 95% CI: 0.44–0.72). Oral CHX should be included among preventive measures performed to reduce nosocomial LRTI. Whether it has an impact on the development of LRTI in patients requiring mechanical ventilation for a longer period of time remains unresolved.

Introduction

Nosocomial lower respiratory tract infections (LRTIs) are a major problem in intensive care medicine. Nosocomial pneumonia among patients receiving mechanical ventilation (MV), also termed ventilator-associated pneumonia (VAP), is the

* Corresponding author. Address: Institute for Medical Microbiology and Hospital Epidemiology, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany. Tel.: +49 (0)511 532 4249; fax: +49 (0)511 532 8174.
E-mail address: kola.axel@mh-hannover.de

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most important nosocomial infection in intensive care units (ICUs), accounting for eight cases per 1000 ventilation-days in Germany.[1] VAP is leading to lengthening of hospital stay, increased costs and a doubled risk for mortality.[2]

Numerous factors have been found to increase the risk of developing VAP. Beside MV itself, there are reintubation, aspiration, coma, supine positioning, enteral nutrition, failed subglottic aspiration, antibiotics, and others.[3,4] As the defence mechanisms that usually protect the lung from infection are compromised by patients' underlying disease [chronic obstructive pumonary disease (COPD), acquired respiratory distress syndrome (ARDS)] or MV (local trauma, epithelial damage), the colonization of the upper respiratory tract of ICU patients becomes another important risk factor for VAP.[5–7]

Preventive strategies to reduce the colonization of the upper respiratory tract are the selective decontamination of the digestive tract (SDD), oropharyngeal decontamination and combinations of these with or without the use of systemic antibiotics. Oropharyngeal decontamination can be achieved using topical antibiotics, which may increase the risk of antibiotic resistance, or using topical antiseptics. Until recently, oropharyngeal decontamination using the topical application of chlorhexidine (CHX), an antimicrobial cationic compound active against aerobic and anaerobic bacteria, has failed to prove its efficacy in preventing LRTI.[8–11] As the use of antiseptics avoids the problem of antibiotic resistance, it might offer significant advantages over the use of SDD. Therefore, we performed a meta-analysis including recently published studies to determine the efficacy of oral CHX in reducing LRTI.

Methods

Data sources

A computerized PubMed literature search of articles published before 15 January 2007, was performed using the key words 'chlorhexidine', 'oropharyngeal', 'decontamination', 'respiratory' and 'pneumonia' iteratively in different combinations. Truncation was used to identify a range of similar terms. The reference lists of the retrieved articles were reviewed for additional studies, as were review articles on the subject. The search strategy was repeated using MEDLINE and the Cochrane Central Register of Controlled Trials databases.

Study selection

Inclusion criteria for the meta-analysis were the following: (i) randomized, controlled trials; (ii) use of oral chlorhexidine as the sole intervention; (iii) reporting of LRTI definitions and of the incidence of LRTI as a study outcome.

Data extraction

Each study was reviewed for patient population, study design, sample size, LRTI definitions and the incidence of LRTI in treatment and control groups, respectively. In addition, the mean duration of ventilation, disease severity and length of stay of study patients were extracted. Data extraction was performed independently by both authors with a structured form and checked for accuracy. Differences were resolved by consensus.

Data analysis

Pooled effect sizes of relative risk (RR) were estimated using the DerSimonian and Laird random effects model (RR_{random}) and the Mantel–Haenszel fixed effect model (RR_{fixed}); 95% confidence intervals (CI) were presented. Heterogeneity was calculated using $I^2 = [(Q - df)/Q] \times 100$, where Q is the chi-squared statistic and df is the number of degrees of freedom. This describes the percentage of the variability in effect estimates that is due to heterogeneity rather than chance. A value $>50\%$ may be considered substantial heterogeneity. To assess publication bias, a funnel plot was performed. For all statistical analyses, the RevMan 4.2 software (Cochrane Collaboration) was used. Sensitivity analysis was performed by different subanalyses.

Results

Study selection and characteristics

The initial PubMed search yielded 161 articles. Of these, eight studies were considered for inclusion in the meta-analysis.[8–10,12–16] Four of the studies[8,10,12,13] had already been included in the meta-analysis published by Pineda *et al.* in 2006,[11] and six of the studies[8–10,12,13,15] in a recent meta-analysis by Chlebicki *et al.* performed before 15 April 2006.[17] Subsequently, two additional studies were published.[14,16] Reviewing of the reference lists of the retrieved studies or of review articles on the topic generated an additional study.[18]