A Systematic Review of the Preventive Effect of Oral Hygiene on Pneumonia and Respiratory Tract Infection in Elderly People in Hospitals and Nursing Homes: Effect Estimates and Methodological Quality of Randomized Controlled Trials

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The objective of this study was to investigate the preventive effect of oral hygiene on pneumonia and respiratory tract infection, focusing on elderly people in hospitals and nursing homes, by systematically reviewing effect estimates and methodological quality of randomized controlled trials (RCTs) and to provide an overview of additional clinical studies in this area. Literature searches were conducted in the Medline database, the Cochrane library databases, and by hand-searching reference lists. Included publications were analyzed for intervention (or topic) studied, main conclusions, strength of evidence, and study design. RCTs were further analyzed for effect magnitudes and methodological details. Absolute risk reductions (ARRs) and numbers needed to treat (NNTs) were calculated. Fifteen publications fulfilled the inclusion criteria. There was a wide variation in the design and quality of the studies included. The RCTs revealed positive preventive effects of oral hygiene on pneumonia and respiratory tract infection in hospitalized elderly people and elderly nursing home residents, with ARRs from 6.6% to 11.7% and NNTs from 8.6 to 15.3 individuals. The non-RCT studies contributed to inconclusive evidence on the association and correlation between oral hygiene and pneumonia or respiratory tract infection in elderly people. Mechanical oral hygiene has a preventive effect on mortality from pneumonia, and non-fatal pneumonia in hospitalized elderly people and elderly nursing home residents. Approximately one in 10 cases of death from pneumonia in elderly nursing home residents may be prevented by improving oral hygiene. Future research in this area should be focused on high-quality RCTs with appropriate sample size calculations. **J Am Geriatr Soc 56:2124–2130, 2008.**

Key words: dentistry; elderly; nursing home; pneumonia; randomized controlled trial

Health-care associated (hospital-acquired, or nosocomial) pneumonia occurs in patients in intensive care units and institutionalized individuals, such as nursing home residents.[1] Pneumonia is a common infection in elderly people and the most common cause of mortality from nosocomial infection in elderly patients, with a mortality rate of up to 25%.[1,2] Bacterial species that normally do not colonize the oropharynx frequently cause health care–associated pneumonia, and the oral cavity has been suggested as an important reservoir for these respiratory pathogens.[1] Elderly patients in nursing homes often have poor oral health due to difficulties in maintaining a sufficient level of personal oral hygiene and difficulties in accessing professional dental care.[3] Hence, a relationship between poor oral hygiene and bacterial pneumonia or lower respiratory tract infections has been suggested in the literature.[4–6] A plausible mechanism of health care–associated pneumonia could be aspiration of oral pathogens into the lungs.[7] Clinical trials have sought to determine whether oral care reduces the incidence of pneumonia, respiratory tract infections, and mortality in pneumonia in elderly people, and a relatively recent systematic review concluded that better oral hygiene and frequent professional oral care reduce the progression or occurrence of respiratory tract diseases in high-risk elderly people living in nursing homes and intensive care units.[8] This study was initiated to further elucidate and systematically summarize the effect estimates and the methodological quality of available randomized controlled trials (RCTs) linking oral hygiene status to pneumonia and respiratory tract infections in elderly people and to provide an overview of additional clinical studies in this area.

METHODS

Literature Searches

Literature searches were conducted in the MEDLINE database (April 2007–November 2007), focusing on combinations of search terms: "dental health"[All Fields], "muscle strength"[All Fields], "respiratory capacity"[All Fields], "survival"[All Fields], "pneumonia"[All Fields], "all cause mortality"[All Fields], "periodontitis"[All Fields], and "periodontium"[All Fields]). Additional literature searches were conducted in the Cochrane Central Register of Controlled Trials and the National Health Service Economic Evaluation Database (November 2007) using the Medical Subject Headings descriptor "Dental Care for Aged," search function: "explode all trees." A list of names of known authors in this research area was also used in the searches (kindly provided by Dr. P. Hämäläinen, Jyväskylä University, Jyväskylä, Finland). The literature searches were limited to publication years 1996 to 2007 and to studies conducted in humans only. Additional studies were located by scrutinizing the reference lists of obtained publications and the doctoral thesis by Hämäläinen.[9] The predetermined inclusion criteria were clinical studies, focusing on RCTs, linking oral hygiene to health care–associated pneumonia or respiratory tract infection in elderly people ($\geq$65, although not an absolute limit). Publications in Dutch, English, German, and any of the Nordic languages (Danish, Finnish, Icelandic, Norwegian, Swedish) were included. Publications about authority opinions and reports of expert committees were excluded, as were studies on subjects with mechanical ventilation or tube feeding. After the literature searches were completed, no additional publications were included.

Strength of Evidence

All publications were scrutinized for study design and ordered according to the hierarchical strength of evidence, from the strongest level (type-1 evidence) to the weakest (type-5) evidence, in accordance with the principles of evidence-based medicine (EBM).[10] Systematic reviews of RCTs were considered to be type-1 evidence; RCTs, type-2; and studies with a nonrandomized design, type-3. Type-4 evidence, as presented previously,[10] was not used in this study, because it is intended for well-designed nonrandomized studies from different research groups on a specific topic. Thus, all nonrandomized studies were grouped together on the type-3 level, with the exception of descriptive studies that were assigned the lowest (type-5) level of evidence.[10]

Methodological Assessments

All studies fulfilling the predetermined inclusion criteria were scrutinized for country of origin, intervention (or topic) studied, journal of publication, main conclusions, publication year, strength of evidence, and study design. The quality of RCTs was assessed using a validated scale that includes three items directly related to the validity of an RCT, described in detail elsewhere.[11] Briefly, the adequacy of reporting random allocation, double-blinding, and withdrawals and dropouts were rated, giving a total score of 0 to 5 points (0–2 points = poorer quality, 3–5 points = higher

quality).[11] Also, for RCTs a definition of pneumonia or respiratory tract infection, as well as the presence of a power calculation were assessed. Although, one of the authors (PS) was experienced in conducting quality assessments of RCTs, two of the authors (EN, PS) completed all assessments.

Data Extraction and Analyses

Data extraction from RCTs was focused on the outcome frequency in the control group (control event rate, CER%) and in the experiment group (experiment event rate, EER%)[1] and sample size in the control group and in the test group(s). For parallel group RCTs, the frequency of pneumonia, or lower respiratory tract infection, in the control group (CER%) and in the experiment group (EER%), were used to calculate the absolute risk reductions (ARRs; ARR = CER% − EER%), and numbers needed to treat (NNTs) were calculated with 95% confidence intervals (CIs) using standard formulas (95% CI = ARR ± 1.96 × standard error).[12,13] The NNT values (95% CIs for NNTs) were obtained as reciprocals of ARR (NNT = 100/ARR), as previously described.[12] To ensure the consistency of the assessments throughout the study, two authors (EN, PS) performed the data extraction independently, and any disagreements were solved in consensus meetings. Pooling data from individual studies (meta-analysis) was not deemed suitable because of heterogeneous study designs, quality of reporting methodological aspects, and trial conduct.

To provide an overview of additional clinical studies in this research area, the non-RCT studies that were identified in the literature were scrutinized for the authors' main conclusion(s).

RESULTS

Literature Searches

The Medline literature searches resulted in 191 eligible publications that were scrutinized for predetermined inclusion and exclusion criteria of this study. In addition, 137 studies were identified by hand-searching reference lists of the publications obtained. Fifteen publications fulfilled the inclusion criteria and remained throughout the assessments (Table 1). The studies included were published during 1996 to 2006, in 10 scientific journals and originated from six countries (Table 1).

Methodological Assessments of RCTs

One systematic review (type-1 evidence) and five RCT publications (type-2 evidence) were identified (Table 1), although two of the RCT reports covered the same trial (i.e., duplicate publication) (Table 1). Methodological quality assessment of the RCTs revealed that one of the RCTs contained an appropriate methodology of double-blinding, and an adequate method of random allocation was given in three RCT publications (Table 2). Moreover, three of five RCT reports gave a complete reporting of withdrawals and dropouts (Table 2). High-quality scores (3 to 5 points on the Jadad scale) were assigned for three RCT reports (Table 2). A power calculation was not reported in any of the RCTs, whereas a definition of the studied endpoint

Table 1. Included Publications About the Association Between Oral Hygiene and Pneumonia or Respiratory Tract Infection in Elderly People (n = 15) Listed According to the Year of Publication

Reference (Objective Studied)	Year of Publication	Country of Origin	Study Design	Intervention Studied	n	Strength of Evidence
[14] (Prevention of respiratory tract infection)	1996	United States	Randomized controlled trial	Chlorhexidine gluconate rinse	353	Type 2
[15] (Prevention of respiratory tract infection)	1996	Japan	Randomized controlled trial	Oral care	46	Type 2
[16] (Relationship between respiratory tract infection history and oral hygiene)	1997	Switzerland	Retrospective longitudinal	None	302	Type 3
[17] (Predictors of aspiration pneumonia)	1998	United States	Prospective, case-control	None	189	Type 3
[18] (Chronic obstructive pulmonary disease and history of periodontal disease)	1998	United States	Prospective, case-control	None	1,118	Type 3
[5] (Association between oral microflora and existing medical factors)	1999	United Kingdom	Cross-sectional	None	28	Type 3
[19]* (Prevention of pneumonia)	1999	Japan	Randomized controlled trial	Oral care	366	Type 2
[20] (Prevalence of oral colonization by potential respiratory pathogens)	1999	United States	Cross-sectional	None	58	Type 3
[21] (Risk factors for aspiration pneumonia)	2001	United States	Prospective, case-control	None	358	Type 3
[22] (Correlation between microbial findings in pneumonia and oral status)	2002	Switzerland	Cross-sectional	None	20	Type 3
[23]*(Prevention of fatal pneumonia)	2002	Japan	Randomized controlled trial	Oral care	366	Type 2
[24] (Prevention of fatal pneumonia)	2002	Japan	Randomized controlled trial	Oral care	88	Type 2
[25] (Correlation between dentures and pharyngeal microflora)	2003	Japan	Cross-sectional	None	50	Type 3
[26] (Dental status and pulmonary function)	2004	Finland	Cross-sectional, prospective cohort	None	203/88	Type 3
[8] (Association between oral health and pneumonia or other respiratory diseases)	2006	Canada	Systematic review	None	None	Type 1

* Duplicate publications, analyzed here from different endpoints.

(pneumonia or respiratory tract infection) was given in four of five trial reports (Table 2). In total, three of the RCTs (one duplicate publication) were parallel group trials, and one had a cross-over design (Table 2).

Effect Estimates in RCTs

In the parallel-group RCT publications (n = 4), two of which covered the same trial (i.e., duplicate publications), sufficient primary data were given for secondary analyses. Four different endpoints were analyzed (Table 3). All of these RCTs revealed positive preventive effects of oral care on pneumonia or respiratory tract infection in nursing home residents[15,19,23,24] or hospitalized elderly patients.[14] The ARRs ranged from 6.6% to 11.7%, and the NNTs ranged from 8.6 to 15.3 individuals (Table 3). One of the RCTs studying the preventive effect for death from pneumonia on nursing home residents, with tooth brushing after every meal, alone or in combination with daily 1% povi-

done iodine scrubbing of the pharynx, had 95% CIs for ARR and NNT values that were solely positive, indicating strong evidence of a clinically relevant effect (Table 3). Moreover, data from one RCT indicated that preoperative 0.12% chlorhexidine gluconate oral rinse may reduce the incidence of respiratory tract infection in hospitalized elderly patients undergoing heart surgery (Table 3).

Non-RCT Publications

A majority of the studies had a non-RCT study design (n = 10), contributing to type-3 level of evidence (Table 1). These studies were of heterogeneous designs and studied various aspects regarding the association and correlation between oral hygiene or oral microflora and pneumonia or respiratory tract infection (Table 1). Nevertheless, the main conclusions from non-RCT clinical studies are similar to those from the RCTs and indicate a correlation between poor oral hygiene or deficient denture hygiene and

Table 2. Quality of Randomized Controlled Trial Reports About the Preventive Effect of Oral Hygiene Interventions on Pneumonia or Respiratory Tract Infection in Elderly People (n = 5)

Reference	Randomization Method	Double-Blinding	Withdrawals and Dropouts	Jadad Score[*]	Power Calculation	Definition Present[†]	Trial Design
14	Adequately reported	Adequately reported	Incompletely reported	4	Not reported	Yes	Parallel
15	Incompletely reported	Incompletely reported	Incompletely reported	1	Not reported	Yes	Cross-over
19[‡]	Adequately reported	Incompletely reported	Adequately reported	3	Not reported	Yes[‡]	Parallel
23[‡]	Adequately reported	Incompletely reported	Adequately reported	3	Not reported	Yes[‡]	Parallel
24	Incompletely reported	Incompletely reported	Adequately reported	2	Not reported	No	Parallel

[*] Quality score 0–5 points, according to Jadad et al.[11]
[†] Definition of respiratory tract infection of pneumonia given in the report.
[‡] Duplicate publications, analyzed here from different endpoints.

pneumonia or respiratory tract infection in dependent or frail elderly people (Table 4).

DISCUSSION

The aim of this study was to investigate the preventive effect of oral hygiene on health care–associated pneumonia and respiratory tract infection in elderly people by systematically summarizing the scientific evidence derived from RCTs and to provide an overview of additional clinical studies on this subject, published during the last decade. To locate as many relevant publications as possible, a database literature search strategy with low specificity was chosen. The MEDLINE and Cochrane library databases were searched for clinical studies, focusing on RCTs, of the effects of oral hygiene on pneumonia and respiratory tract infections in elderly people. Additional studies were located by scrutinizing the reference lists of the obtained publications, although because the chosen database search filters did not automatically include relevant publications about

general effects of oral hygiene on pneumonia or respiratory tract infection, it is possible that some relevant studies may have been falsely excluded from the literature searches.[27] Moreover, no attempts were made to locate unpublished studies, but to reduce the extent of language bias, RCTs written in eight different languages were allowed for inclusion. Despite the limitations of the current literature search strategy, the included sample is highly representative, containing a majority of the published RCTs available about the preventive effect of oral hygiene on pneumonia and respiratory tract infections in elderly people. Data from the included RCTs were not considered a suitable meta-analytical approach because of the heterogeneity in primary endpoints, methodological quality, study conducts, and study design. Therefore, the RCTs were analyzed separately. The included RCTs were also heterogeneous in the study populations, with four of the located RCTs conducted in nursing homes[15,19,23,24] and one in a hospital.[14]

The quality of the included trials was assessed using the Jadad scale, a validated 5-point quality scale that includes

Table 3. Effect Estimates in Parallel Group Randomized Controlled Trials (n = 4) About the Preventive Effect of Oral Hygiene Interventions on Pneumonia and Respiratory Tract Infection in Elderly People

Reference (Intervention)	Experiment Group Event Rate %[*]	n	Control Group Event Rate %[*]	n	Absolute Risk Reduction % (95% CI)	Number Needed to Treat (95% CI)	Outcome Measure	Follow-Up Period
[14] (Preoperative and postoperatively chlorhexidine 0.12% oral rinse versus saline solution rinse)	2.9	173	9.4	180	6.6 (1.6–11.5)	15.3 (8.7–62.3)	Respiratory tract infection	Until discharge
[19][†] (Tooth-brushing after every meal and/or 1% povidone iodine scrubbing of pharynx)	11.4	184	18.7	182	7.3 (0.0–14.6)	13.8 (6.9 to − 4,200.7)	Pneumonia	2 years
[23][†] (Tooth-brushing after every meal and/or daily 1% povidone iodine scrubbing of pharynx)	7.6	184	16.5	182	8.9 (2.3–15.5)	11.3 (6.5–44.2)	Death from pneumonia	2 years
[24] (Professional mechanical oral health care weekly)	5.0	40	16.7	48	11.7 (− 0.9–24.2)	8.6 (4.1 to − 117.0)	Death from pneumonia	2 years

[*] Frequency of pneumonia or respiratory tract infection.
[†] Duplicate publications, analyzed here from different endpoints.
CI = confidence interval.

Table 4. Main Conclusions in the Nonrandomized Clinical Studies About the Association Between Oral Hygiene and Pneumonia or Respiratory Tract Infection in Elderly People (n = 10)

Reference	Main Conclusion(s)
16	Poor oral hygiene and potential dental emergency could be major risk factors for respiratory tract infection in frail elderly people.
17	Dependency upon others for feeding or oral care and number of decayed teeth were best predictors for aspiration pneumonia.
18	Alveolar bone loss is associated with risk for chronic obstructive pulmonary disease.
5	Oropharyngeal gram-negative bacilli colonization can be associated with aspiration pneumonia, and there is a correlation between Gram-negative bacilli and denture use.
20	Deficient dental plaque control and chronic obstructive pulmonary disease may be related to respiratory pathogen colonization of dental plaque in chronic care facility residents.
21	Oral and dental factors are significant risk factors for aspiration pneumonia.
22	Microorganisms of dental plaque or associated with periodontal disease may give rise to aspiration pneumonia in susceptible individuals.
25	Dentures should be considered an important reservoir of organisms that could colonize the pharynx, and it is important to control denture plaque for prevention of aspiration pneumonia.
26	Periodontal infections and complete prostheses may be reservoirs for pathogens that may be harmful and partly explain the observed reduction in forced expiratory volume during the first second.
8	Fair evidence of an association between pneumonia and oral health. Poor evidence of a weak association between chronic obstructive pulmonary disease and oral health. Good evidence that oral hygiene and frequent professional oral care reduce the progression or occurrence of respiratory diseases among high-risk elderly people living in nursing homes.

three items to assess the methodology used for random allocation, double-blinding, and a description of withdrawals and dropouts for each intervention or control group.[11] The Jadad scale has been widely used in medical and dental research and has been shown to incorporate components that are directly related to the control of bias.[11,28,29]

If an intervention is intended for clinical use, it is important to use clinically relevant outcome measures to monitor the effect magnitude.[12] Therefore, it was decided to present the preventive effects of different interventions with ARRs and NNTs, as recommended in evidence-based medicine.[12] ARR describes the absolute reduction in the event rate (e.g., frequency of pneumonia), whereas the NNT values give the number of patients needed to treat with the studied intervention to prevent one outcome of interest (e.g., pneumonia) during the follow-up period.[12]

Of the RCTs on prevention of pneumonia or respiratory tract infection in elderly people with oral hygiene interventions, the most convincing effects were seen for weekly provided professional oral care and for tooth brushing after every meal (in combination with 1% povidone iodine scrubbing of pharynx when necessary). These RCTs showed ARRs between 7% and 12%, and the highest NNT value was 14 individuals.[19,23,24] Moreover, in one RCT, solely positive 95% CIs strengthened the evidence of the preventive effect.[23]

One additional RCT studied the effect of preoperative 0.12% chlorhexidine gluconate oral rinse for prevention of nosocomial respiratory tract infection in patients undergoing heart surgery.[12] This RCT revealed an overall positive effect, with a NNT of approximately 15 individuals and solely positive CIs.[12] Curiously, in the same trial, although beyond the scope of this study, a reduction in mortality after surgery was also seen in the chlorhexidine group.[12] However, these are data from one RCT, and additional trials from independent research groups would be necessary to confirm the findings.

The findings of the current study are largely consistent with a previous systematic review that concluded that there is good evidence that oral care reduces the progression or occurrence of respiratory diseases in high-risk elderly people living in nursing homes and intensive care units.[8] Moreover, the current study demonstrates that conclusive data are available from RCTs of a clinically relevant preventive effect of oral care on mortality from pneumonia and on pneumonia as such.

Some variation was seen in the quality of reporting the RCTs, and the Jadad quality scores varied from 1 to 4 points. In general, trials with 0 to 2 points are considered to be of poorer quality, and trials with 3 to 5 points are considered to be of higher quality.[11] Because the only information that a reader can obtain about the trial conduct is from its written report, it is possible that the trial conduct has not been thoroughly described in the actual trial report.[11,26] This is evident in the current study, in which differences in the two RCT reports covering the same trial were found.[19,23] Therefore, recommendations for reporting parallel-group randomized trials (e.g., the Consolidated Standards Of Reporting Trials statement) should be followed.[30] Beyond the random allocation process, methodology of double-blinding, and reporting of withdrawals and drop-outs, a high-quality RCT needs to fulfill a number of methodological requirements to eliminate the risk of incorporation of bias into the trial results.[11] For example, in the context of power calculation, the primary statistical endpoints need to be predefined and analyzed separately, or if combined endpoints are chosen, they must be compensated for in the statistical analyses and sample size calculations.[31] Similarly, larger sample sizes are required for multicenter studies to compensate for cluster effects.[32] For clinical application of trial reports, the trial had to have been conducted in a homogenous study population similar to the population in which the trial results are intended for in clinical practice.[12] As for the trials included in the current study, it is important to keep in mind that three of the trials were conducted in nursing home,[15,19,23,24] and one RCT in a hospital;[14] thus, the trial results may only be applicable in these selected populations.

Statisticians have expressed a serious concern regarding underpowered trials, because a trial with inadequate statistical power may falsely reject a true effect of an intervention.[33] It was somewhat troubling to find that none of the RCTs included reported a sample size or power calculation. Hence, insufficient sample size may have caused the CIs to cross 0 in some of these trials.[30] Therefore, it is important to remember that absence of statistical significance is not evidence of absence of a difference between the studied groups.[33] Although the results presented in the RCTs

included point to the same direction, the methodological compromises in the RCTs included raise a concern as to whether the association between the improvement in oral hygiene and reduction in pneumonia or respiratory tract infections may be associated with an unknown risk factor. Further clinical research in this area should focus on adequately powered, preferably double-blinded, RCTs, studying the preventive effect of different oral hygiene regimens on pneumonia and respiratory tract infections.

A number of non-RCT studies with cross-sectional and longitudinal design were also located in the literature searches. These studies mainly provided microbiological associations between health care–associated pneumonia and respiratory tract infection, in addition to data on the incidence of and the association between oral hygiene and pneumonia or respiratory tract infection. The strength of evidence from these studies was moderate to weak (type-3) and inconclusive, although data from these non-RCT studies aid in understanding how oral care is handled and how it can affect health status and may therefore prove useful for etiological discussions or hypothesis generation for future research.

It was beyond the scope of this study to analyze magnitudes of different risk factors for pneumonia or respiratory tract infection (e.g., smoking, other diseases), all of which should be balanced in an adequately allocated RCT but should be reviewed from a sample of case-control studies. Although this systematic review was focused on RCTs, rigorously conducted observational studies have been shown to be powerful in identifying unbiased risk estimates for different outcomes.[34] Nevertheless, in evidence-based medicine, the RCT is considered a criterion standard for studying preventive and therapeutic interventions, and systematic reviews of RCTs are considered the highest level of evidence.[10] The present study was not intended as a clinical guideline but as a systematic review of the current evidence from RCTs and as an overview of clinical studies in this area.

Within the limitations of this study, it can be concluded that available results from RCTs provide strong evidence that mechanical oral hygiene decreases mortality risk from pneumonia and seems to have a clinically relevant preventive effect on nonfatal pneumonia in dependent elderly individuals. These data show that providing mechanical oral hygiene may prevent approximately one in 10 cases of death from pneumonia in dependent elderly people and indicate a largely similar effect for prevention of pneumonia.

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