

SPECIAL REVIEW IN PERIODONTAL MEDICINE

Oral biofilms, periodontitis, and pulmonary infections

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Bacteria from the oral biofilms may be aspirated into the respiratory tract to influence the initiation and progression of systemic infectious conditions such as pneumonia. Oral bacteria, poor oral hygiene, and periodontitis seem to influence the incidence of pulmonary infections, especially nosocomial pneumonia episodes in high-risk subjects. Improved oral hygiene has been shown to reduce the occurrence of nosocomial pneumonia, both in mechanically-ventilated hospital patients and non-ventilated nursing home residents. It appears that oral colonization by potential respiratory pathogens, possibly fostered by periodontitis, and possibly by bacteria specific to the oral cavity or to periodontal diseases contribute to pulmonary infections. Thus, oral hygiene will assume an even more important role in the care of high-risk subjects – patients in the hospital intensive care and the elderly. The present paper critically reviews the recent literature on the effect of oral biofilms and periodontitis on pneumonia.

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Pneumonia is an infection of the lungs caused by bacteria, mycoplasma, viruses, fungi, or parasites. Bacterial pneumonia is a common and significant cause of mortality and morbidity in human populations. Pneumonia together with influenza is a top ten cause of death in the world, and in elderly nursing home residents the leading cause of death. Pneumonia also results in morbidity and considerable decline in the individual quality of life as well as in increased medical care costs for the healthcare system. Bacterial pneumonia includes community-acquired pneumonia and hospital-acquired (nosocomial) pneumonia. Nosocomial pneumonia, occurring >48–72 h after admission to a hospital or

nursing home, can be divided into two subtypes: ventilator-associated pneumonia (VAP) and non-VAP. Pneumonia accounts for 10% of infections in intensive care units (ICU) being the most common infection in this hospital setting (Vincent *et al*, 1995). The onset of pneumonia can easily double the length of the patient's hospital stay, and the cost of VAP treatment has been estimated to average as high as \$40 000 per patient (Rello *et al*, 2002). Pneumonia is also prevalent in nursing homes, comprising 13–48% of all infections (Crossley and Thurn, 1989). The mortality rate of nosocomial pneumonia can be as high as 25%.

The oral cavity may be an important source of bacteria that cause infections of the lungs. Dental plaque, a tooth-borne biofilm that initiates periodontal disease and dental caries may also influence the initiation and progression of pneumonia because of relocation of the bacteria from the biofilm into the respiratory tract. Bacteria causing community-acquired pneumonia are typically species that normally colonize the oropharynx such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Mycoplasma pneumoniae*. Nosocomial pneumonia is, in contrast, often caused by bacteria that are not common members of the oropharyngeal flora such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and enteric Gram-negative bacteria. These organisms populate the oral cavity in certain settings, for example in institutionalized subjects and in people living in areas served by unsanitary water supplies (Scannapieco, 1999). Respiratory pathogens, such as *S. aureus*, *P. aeruginosa*, and *Escherichia coli*, have been found to be present in substantial numbers on the teeth in both institutionalized elders (Russell *et al*, 1999) and intensive care patients (Scannapieco *et al*, 1992). In this review we concentrate on the possible effect of oral biofilms and periodontitis on pneumonia.

Mechanisms behind the association between oral bacteria/periodontitis and pneumonia

One cubic millimeter of dental plaque contains about 100 million bacteria (Thoden van Velzen *et al*, 1984) and may serve as a persistent reservoir for potential

pathogens, both oral and respiratory bacteria. It is likely that oral and respiratory bacteria in the dental plaque are shed into the saliva and are then aspirated into the lower respiratory tract and the lungs to cause infection (Scannapieco, 1999; Scannapieco *et al*, 2001). Cytokines and enzymes induced from the periodontally inflamed tissues by the oral biofilm may also be transferred into the lungs where they may stimulate local inflammatory processes preceding colonization of pathogens and the actual lung infection (Scannapieco, 1999; Scannapieco *et al*, 2001). Other possible mechanisms of pulmonary infection are inhalation of airborne pathogens or translocation of bacteria from local infections via bacteremia.

In a healthy subject, the respiratory tract is able to defend against aspirated bacteria. Patients with diminished salivary flow, decreased cough reflex, swallowing disorders, poor ability to perform good oral hygiene, or other physical disabilities have a high risk for pulmonary infections. Mechanically ventilated patients in ICUs with no ability to clear oral secretions by swallowing or by coughing, are at risk for VAP especially if the ventilation lasts for more than 48 h (Estes and Meduri, 1995). Oral bacterial load increases during intubation and higher dental plaque scores predict risk of pneumonia (Munro *et al*, 2006). Anaerobic bacteria are frequently found to colonize the lower respiratory tract in mechanically-ventilated patients (Estes and Meduri, 1995; Robert *et al*, 2003). Colonization of bacteria in the digestive tract has been suggested to be a source for nosocomial pneumonia, but recently oral and dental bacterial colonization has been proposed to be the major source of bacteria implicated in the etiology of VAP (Garcia, 2005).

In the institutionalized elderly the aspiration of saliva seems to be the main route of bacteria into the lungs causing aspiration pneumonia. Dysphagia seems to be an important risk factor, even a predictor, for aspiration pneumonia (Langmore *et al*, 1998). The major oral and dental risk factors for aspiration pneumonia in veteran residents of nursing homes were number of decayed teeth, periodontitis, oral *S. aureus* colonization, and requirement of help feeding (Terpenning *et al*, 2001). Inadequate oral care and swallowing difficulties were associated with pneumonia in 613 elderly nursing home patients (Quagliarello *et al*, 2005).

Studies on the relationship between the oral microflora/periodontitis and pneumonia

Very little data on the relationship of oral microflora to community-acquired pneumonia are available. Most of the studies have been conducted in populations with a high prevalence of pneumonia, such as hospitalized patients and the elderly in nursing homes. An epidemiologic study found no association between periodontal state or poor oral hygiene and acute respiratory disease in the community-dwelling population (Scannapieco *et al*, 1998), but ample evidence exists to support a role for oral bacteria and/or poor oral health in the pathogenesis of nosocomial pneumonia. Poor oral

health, dental plaque, or oropharyngeal bacterial colonization have been associated with the occurrence of pneumonia in hospitalized or ICU patients (Scannapieco *et al*, 1992; Bonten *et al*, 1996; Garrouste-Orgeas *et al*, 1997; Fourrier *et al*, 1998; Preston *et al*, 1999; El-Solh *et al*, 2004), but a clear relationship between periodontitis and pneumonia has not always been found (Chabrand *et al*, 1986; Treloar and Stechmiller, 1995). Higher plaque scores, bacterial presence in saliva, or colonization in the oropharynx seem to be associated with pneumonia in elderly nursing home patients (Mojon *et al*, 1997; Langmore *et al*, 1998; Russell *et al*, 1999; Terpenning *et al*, 2001).

Recent systematic reviews of the literature substantiate the link between poor oral health and pneumonia (Scannapieco *et al*, 2003; Azarpazhooh and Leake, 2006), but more studies on the possible role of periodontitis are needed. Dentate status may be a risk for pneumonia and respiratory tract infections – patients with natural teeth developed aspiration pneumonia more often than edentulous subjects (Terpenning *et al*, 1993; Mojon *et al*, 1997). Cariogenic bacteria and periodontal pathogens in saliva or dental plaque are found to be risk factors for aspiration pneumonia in nursing home patients (Langmore *et al*, 1998; Terpenning *et al*, 2001). It is well known that the teeth and gingival margin are places that favour bacterial colonization, and periodontal pockets may serve as reservoirs for potential pathogens for pneumonia. Previous studies have shown that enteric bacteria colonize periodontal pockets (Slots *et al*, 1988; Rams *et al*, 1990). Periodontitis together with poor oral hygiene or by facilitating colonization of dental plaque may promote pneumonia.

Intervention studies on the role of improved oral cleaning in reducing pneumonia

Oral interventions to reduce pulmonary infections have been examined in both mechanically ventilated ICU patients and non-ventilated elderly patients. These studies included chemical intervention using topical antimicrobial agents and traditional oral mechanical hygiene performed by a professional.

Hospitalized ICU patients seem to benefit from daily oral cleansing. Studies have shown that the use of oral topical chlorhexidine (CHX) reduces pneumonia in mechanically ventilated patients and may even decrease the need of systemic IV antibiotics or shorten the duration of mechanical ventilation in the ICU (DeRiso *et al*, 1996; Fourrier *et al*, 2000; Genuit *et al*, 2001; Koeman *et al*, 2006). Moreover, oral application of CHX in the early post-intubation period lowers the numbers of cultivable oral bacteria and may delay the development of VAP (Grap *et al*, 2004). Studies validating the effectiveness of oral CHX on reducing pneumonia are not unanimous. For example, Fourrier *et al* found that gingival decontamination with CHX gel significantly decreased the oropharyngeal colonization by bacteria in ventilated patients, but was not sufficient to reduce the incidence of respiratory infections

(Fourrier *et al*, 2005). Another study by Houston *et al* (2002) reported that a significant reduction in pneumonia using CHX rinse in ICU patients was achieved only after 24 h of intubation. However, the efficacy of oral CHX decontamination to reduce VAP needs further investigation as no clear reduction in mortality rate has been shown. In addition to CHX, other antiplaque agents have been investigated. The use of antimicrobial gels including polymyxin B sulfate, neomycin sulfate, and vancomycin hydrochloride (Pugin *et al*, 1991) or gentamicin/colistin/vancomycin (Bergmans *et al*, 2001) have also been shown to reduce VAP. Recently, the first study showing that mechanical oral care in combination with povidone iodine significantly decreases pneumonia in ventilated ICU patients was published (Mori *et al*, 2006). This suggests that tooth brushing combined with a topical antimicrobial agent is a promising method for oral cleansing of mechanically ventilated patients.

Institutionalized but non-ventilated patients, mainly elders living in nursing homes, appear to benefit from improved oral care by showing lower levels of oral bacteria and fewer pneumonia episodes and febrile days. Daily tooth brushing and topical oral swabbing with povidone iodine significantly decreased pneumonia in residents in long-term care facilities (Yoneyama *et al*, 1999, 2002; Yoshida *et al*, 2001). However, in an earlier study by the same research group, oral care with both brushing and antimicrobial gargling had an effect only on febrile days but not on the incidence of pneumonia (Yoneyama *et al*, 1996). Interestingly, professional cleaning by a dental hygienist once a week significantly reduced the prevalence of fever and fatal pneumonia in 141 elderly patients in nursing homes (Adachi *et al*, 2002). Similar once-a-week professional oral cleaning significantly reduced influenza infections in an elderly population (Abe *et al*, 2006). Dental plaque is known to form clearly visible masses in the teeth in a few days, but these studies suggest that improved oral care even without chemical agents and even if not performed daily not only reduces the oral bacterial, viral, and fungal load, but may have an effect on reducing the risk of pneumonia. Therefore, more studies are needed to find the easiest oral decontamination methods to reduce pulmonary infections in elderly nursing home patients.

Our previously published systematic literature review revealed that interventions improving oral hygiene by mechanical and/or topical chemical disinfection or antibiotics reduce the incidence of hospital-acquired pneumonia by an average of 40% (Scannapieco *et al*, 2003). Oral cleansing reduces pneumonia in both edentulous and dentate subjects, suggesting that oral colonization of bacteria contributes to nosocomial pneumonia to a greater extent than periodontitis. However, intervention studies on the treatment of periodontitis on the incidence of pneumonia have not been performed due to the complexities required in investigating ICU or bed-bound nursing home patients. In edentulous people, dentures may easily serve as a similar reservoir as

teeth for oral and respiratory bacteria if not cleaned properly and daily.

Conclusions and future visions

Poor oral health, dependence on help conducting daily oral hygiene, oral colonization of periodontal and respiratory pathogens, all possibly influenced by periodontitis, are associated with nosocomial pneumonia. A direct causal relationship between periodontitis and pneumonia has not been established, however. Based on the studies reviewed here it seems that oral colonization by potential respiratory pathogens contributes to pulmonary infections. The specific contribution of periodontitis *per se* to pneumonia risk is presently unknown. It will be difficult to determine whether periodontitis is related to pneumonia in ICU subjects, for example, due to the limited access to these patients' oral cavity, and the rapid turnover of patients in the hospital that presents logistical challenges to such research. Thus, oral hygiene of both dentate and edentulous subjects will assume an even more important role in elder care.

Chronic periodontal infections are common – the prevalence of severe periodontitis in Western countries has been estimated to be 5–15%. Pneumonia and other respiratory infections are common in community-dwelling populations but especially in high-risk subjects such as mechanically-ventilated ICU patients and residents in long-term care facilities. With improved oral hygiene and preventative approaches to dental care, people are able to keep their natural teeth longer, even for life. Edentulousness will someday be a rare phenomenon; in the future there will be more elderly dentate people, having more teeth than ever, but who will also have impaired ability to perform oral hygiene, and hence more cases of periodontal diseases. To assure that improved knowledge and methods to save people's natural teeth are not taking us from one problem to another, emphasis on the importance of good oral hygiene and periodontal treatment, especially in subjects who are in high risk for pulmonary infections, is crucial.

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