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Lokale en eventuele systemische gevolgen van endodontische infecties

Samenvatting

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Bij infectie van de pulpaholte zijn bacteriën zowel in plankton als in biofilm aanwezig. Parodontitis apicalis, die röntgenologisch onopgemerkt kan zijn, kan ontstaan of persisteren ter verdediging om systemische verspreiding van bacteriën en hun producten naar elders in het lichaam te voorkomen. Er bestaat niettemin het gevaar dat micro-organismen zich verspreiden en septische emboli ontstaan, in het bijzonder in een medisch gecompromitteerde patiënt; bovendien kan een lang bestaande ontsteking systemische effecten hebben en de algemene gezondheid beïnvloeden. Het is van belang om effectieve procedures te ontwikkelen om de belasting van een infectie van de pulpaholte tot een minimum terug te brengen.

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Introduction

Apical periodontitis, a local consequence of endodontic root infection, has been defined as 'the inflammatory processes of the periodontal tissues that are initiated and maintained by an endodontic source of irritants' (Happonen and Bergenholtz, 2003). Apical periodontitis is radiographically diagnosed in 5.2% of non-endodontically treated teeth in an adult Dutch population (De Cleen *et al*, 1993). As shown by recent epidemiological studies in several countries (De Moor *et al*, 2000; Kirkevang *et al*, 2001; Dugas *et al*, 2003), endodontic post-treatment apical periodontitis (PTAP) was radiographically verified in 40-50% of the root-filled teeth. The apical periodontitis is regarded as an important protective, inflammatory buffer zone, preventing the spread of bacteria and bacterial elements to other body compartments (Stashenko, 1990). The purpose of this report is to review and discuss the local and systemic consequences of the root infection.

Root infection and apical periodontitis

The microflora in infected root canals have been studied by direct microscopy, cultivation methods and molecular techniques. A mixture of several species is cultured from samples taken from root canals in primary endodontic infections and many studies have shown that apical periodontitis is associated with their presence (Sundqvist, 1976; Weiger *et al*, 1995). For example, the material of Sundqvist (1976) comprised 32 incisors with pulpal necrosis that had remained completely intact after trauma. Nineteen of these teeth demonstrated apical periodontitis radiographically, of which 18 teeth presented with positive cultures for bacteria. The other 13 teeth did not demonstrate apical periodontitis and none of them presented with a positive culture. Baumgartner and Falkler (1991) cultured the apical region of canals in carious exposed teeth with apical radiolucency. They found that all canals were infected in the apical 5 mm, overall 50 strains of bacteria were identified, 34 of which were strict anaerobes.

It has been reported recently that a biofilm is a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adhere to an inert or living surface (Costerton *et al*, 1999). Bacteria organized in biofilms are more resistant than planktonic bacteria to the host defense mechanisms and disinfectants (Costerton *et al*, 1999). Because biofilms are the preferred method of growth on a surface for most species of bacteria, it is likely that bacteria are present in biofilms on the dentinal wall or at the external surface of the root tip (Tronstad and Sunde, 2003; Nair *et al*, 2005). Bacterial biofilms are said to be the common cause for persistent inflammation (Costerton *et al*, 1999).

Acute apical periodontitis is characterized by vascular dilatation, an exudate of neutrophil leucocytes, and edema in the apical periodontal ligament. Clinically, severe symptoms such as pain, tenderness and swellings may be present. Recordings from two clinics in Scandinavia indicate that about 40% of the diagnoses of all patients coming for emergency treatment were pulpitis and acute apical periodontitis (Widström *et al*, 1990; Eriksen, 1991).

Chronic apical periodontitis is characterized by an inflammatory cell infiltrate rich in lymphocytes, plasma cells, and macrophages, and the production of granulation tissue. Most teeth with chronic apical periodontitis stay asymptomatic and in function. They are revealed mostly by routine radiographic examination. It must be realized that the tissue reaction to irritation is a dynamic response, often fluctuating with time between acute and chronic inflammation. Although a granuloma is principally a chronic inflammatory lesion, acute exacerbations are common.

On the other hand, the periapical vascular network has a rich collateral circulation greatly enhancing the ability of the tissue to heal if the cause of the inflammation is removed. It has been reported that one month after extraction of teeth with periapical inflammation, no inflammatory cells were present in the surrounding tissues (Holland, 1992; Mason and Holland, 1993), indicating that the source of irritation had been removed. However, in many cases apical periodontitis may occur or

persist following endodontic treatment, indicating the presence of a source of irritation (Caplan, 2004).

Residual post-treatment endodontic root infection

Molander et al (1998) examined the microbiological status of 120 root filled teeth with or without radiographically verified apical periodontitis. Using a sampling technique they discovered bacteria in 68% of filled canals associated with radiographic apical periodontitis and 45% of filled canals without radiographic apical periodontitis. Because 'sampling' in the apical ramification, isthmuses and other canal irregularities was not possible, negative cultures could not assure absence of bacteria. Furthermore, planktonic cells are more likely to be collected by sampling whereas bacterial cells enclosed deeply in biofilms may not be collected. And furthermore, since it was impossible to collect samples from much of the root canal system, the accurate analysis of the quantity and type of bacteria remaining in each root canal was impossible. Therefore, it is not reliable to diagnose absence of bacteria using sampling techniques and the authors concluded: 'All root-filled teeth should be regarded as potentially infected' (Molander et al, 1998).

In a recent histological study by Nair et al, (2005), bacteria, mostly in biofilms, were found in inaccessible intercanal isthmus and accessory canals in 14 (88%) out of 16 teeth that were root filled in a single visit. Microbial sampling would have been impossible in these inaccessible areas. Thus, it could be argued that many filled roots act as implants with low-grade infection embedded within connective tissue (Haapasalo et al, 2003). The residual post-treatment endodontic root infection may cause persistent apical periodontitis (Nair et al, 1990). At the same time, over-instrumentation, and/or over-filling with resultant extrusion of debris and material during root canal treatment may also lead to persistence of inflammation (Yusuf, 1982).

Post treatment apical periodontitis

As root infection has not been eliminated by the treatment procedures, post treatment apical periodontitis (PTAP) may be present in many cases. It has been reported that in a Lithuanian population, the frequency of radiographically verified PTAP was 35% (Sidaravicius et al, 1999). In a study in Belgium radiographically verified PTAP was observed in 40% of the root-filled teeth (De Moor et al, 2000). In a study in Denmark the periapical status of nearly 600 root-filled teeth was compared in 1974-1975 and 1997-1998 (Kirkevang et al, 2001). Radiographically verified PTAP was observed in approximately 50% of the root-filled teeth in both groups, and in molars the prevalence of PTAP was as high as 65% in both groups. In two samples of Canadian populations the prevalence of radiographically verified PTAP was 44% and 51% (Dugas et al, 2003).

In an *in vivo* histological study by Ricucci and Langeland (1998), the apical and periapical tissues were examined histologically following root canal treatment. A

strict aseptic technique was applied. Each canal was irrigated with copious amounts of 1% NaOCl using a syringe and filled with laterally condensed gutta-percha points and Pulp Canal Sealer (Kerr Manufacturing Co., Romulus, MI, USA). Twenty-two treated roots including 13 with a vital pulp and 9 with a necrotic pulp were followed up for at least 3 years after completion of treatment. The average observation period was 5 years and 4 months (ranging from 3 years to 10 years 8 months). In 18 (82%) of the 22 roots the canal was filled to 0-2 mm from the apex. However: "Despite careful preparation of optimal access and meticulous root canal cleaning and shaping, in all cases remnants of pulp tissue and dentine chips were found at different levels of the root canals" (Ricucci and Langeland, 1998). At the end of the observation period, despite the fact that 18 (82%) of the 22 roots were free of an apical radiolucency, the root apices with surrounding bone or fragments of periodontal ligament attached to the extracted roots were free of inflammatory cell in only three (14%) of the 22 roots (Ricucci and Langeland, 1998).

Seltzer et al (1969; 1973) performed vital pulpectomies in 53 normal human maxillary central incisors. Four days to 1 year after treatment, all root apices with surrounding bone were block resected for histologic examination. Of the 53 teeth only eight were observed for 6-12 months and they were all prepared slightly short of or beyond the apex with their root fillings being confined within the root. PTAP of varying degrees was present in 7 of the 8 teeth at the end of the observation period. When the root was instrumented noticeably short of or at least 2 mm beyond the apex or apically over-filled, severe periapical inflammation was observed. Since these teeth contained healthy, non-infected pulp tissue it seems likely that the canals were infected either by procedural contamination or by coronal leakage.

In experiments with dogs, ferrets and monkeys, teeth were root filled and histologically examined after 5-12 months. The authors reported that chronic inflammation persisted in the periapical tissues at the end of the observation period (Holland, 1992; Leonardo et al, 1997).

Insensitive clinical diagnosis of apical periodontitis

It should not be forgotten that many bony lesions limited to cancellous bone are not detected with conventional radiographic techniques (Huomonen and Ørstavik, 2002). Clinically, a large bony lesion of up to 8 mm diameter may be present without symptoms or radiolucency (Stabholz et al, 1994; Ricucci and Bergenholtz, 2003). Therefore, the prevalence of periapical radiolucencies in above studies must be thereby an underestimation of the real situation. Histologic observation of root apices with surrounding bone removed from either patients or human cadavers has demonstrated that the tissue around 50-90% of root filled human teeth is inflamed (Brynolf, 1967; Ricucci and Langeland, 1998; Barthel et al, 2004).

Some investigators have used the periapical index (PAI) to assess the outcome of root canal treatment (Ørstavik et al, 1987; Waltimo et al, 2001; Ørstavik et al, 2004). These investigators agree that many bone lesions within the can-

cellous bone are not visible radiographically (Huomonen and Ørstavik, 2002), but also believe in a fixed relationship between radiographic findings and histological diagnoses of apical periodontitis of different extent and severity (Brynolf, 1967). With the PAI system, score 1 denotes a radiographically healthy periapex; scores 2 to 5 represent increasing extent and severity of apical periodontitis (Ørstavik *et al.*, 1987). However, a relationship between the radiographic findings and histological diagnoses found in one study does not prove existence of a fixed relationship between the radiographic findings and histological diagnoses (Brynolf, 1967). PAI score 2 has been categorized into 'success' that should be free of apical periodontitis ((Ørstavik *et al.*, 1987; European Society of Endodontology, 1994; Ørstavik *et al.*, 2004). Score 2 might, however, also be considered as unsuccessful. Then, considering that cases with score 2 comprised 30% of all cases at the end of the study, it can be assumed that many cases with apical periodontitis were wrongly diagnosed (Ørstavik *et al.*, 1987).

Spreading microorganisms and septic emboli

Through acute periapical abscess pus, microorganisms and their products may spread. Acute manifestations of endodontic lesions involve the formation of abscesses in the periapical tissues. Although these lesions most often confined to the oral region, they may extend to both nearby and distant body compartments along the anatomical pathways. Hence, a periapical abscess may spread and reach the brain, the cavernous sinus, the eye or the mediastinum. In addition to the direct spread of pus and bacterial elements, brain and lung abscesses may also be caused by septic emboli. Furthermore, oral bacteria involved in endodontic infections may be aspirated into the lung and cause serious infections (Skaug, 2003). However, complications of this nature are now rare in the industrialized world.

Surgical and non-surgical endodontic treatment procedures are likely to result in transient bacteremias. In healthy individuals transient bacteremias are usually of no clinical significance and asymptomatic because the number of bacterial cells in the blood usually is less than 10 colony-forming units per ml and the humoral immune response readily eliminates the organisms. However, in compromised hosts with cancer, unregulated diabetes or immunodeficiency who lack normal protection against infections, the bacteria may start to multiply in the blood resulting in a serious bacteremic infection (Skaug, 2003). Bacteremia is considered a risk factor for the development of endocarditis.

Potential systemic effects

Whether a long-standing root infection and apical periodontitis will influence general health has been discussed for nearly a century, but no definite conclusion has been agreed (Caplan, 2004).

Recently, long-standing inflammation has been related to the risk of cardiovascular diseases. In a study where

plasma C-reactive protein, a marker for systemic inflammation, was measured in 1,068 male adults, half of them developed coronary heart disease over the course of a 14-year-study (Ridker *et al.*, 1997). It was found that those with very low levels of C-reactive protein, less than 0,5 mg/L, rarely had coronary heart disease; however, when C-reactive protein was higher than 1,0 mg/L, the risk of coronary heart disease was increased (Ridker *et al.*, 1997, Loos *et al.*, 2000). Risks were stable over long periods, were not modified by smoking, and were independent of other lipid-related and non-lipid-related risk factors (Ridker *et al.*, 1997). In a study by Loos *et al.* (2000), localized and generalized periodontitis resulted in significantly higher systemic level of C-reactive protein; importantly, the possible confounding factors including smoking, hypertension, cholesterol etcetera had been controlled. It is of concern to study whether long-standing apical periodontitis of endodontic origin also elevates the systemic level of C-reactive protein.

It is now assumed that long-standing, low-grade infection may activate immune cells; certain parts of the body are mistakenly selected by immune cells for attack, macrophages begin attacking cholesterol deposits in the coronary arteries, causing the plaque to burst, provoking coronary heart disease (Ridker *et al.*, 1997). These assumptions remain to be evaluated further.

In a recently published epidemiologic study (Caplan *et al.*, 2004), during a maximum follow-up of 32 years with 708 male adults, lesions of endodontic origin among those younger than 40 years old were statistically significantly associated with risk of coronary heart disease after controlling for baseline values of education, income, total cholesterol, triglycerides, diabetes, hypertension and smoking. After root canal treatment, the lesion is reduced to a level not detectable by radiographs, whether the reduced inflammation still influences the occurrence of coronary heart disease or other systemic diseases is unknown.

On the other hand, a significant link between apical periodontitis and systemic diseases was not proven (Thoden van Velzen *et al.*, 1984; Caplan, 2004). Importantly, studies that failed to reveal the link between apical periodontitis and systemic diseases do not prove absence of the link partly because of the insensitive diagnosis of apical periodontitis (Huomonen and Ørstavik, 2002). The apical periodontitis-absent group, which served as matched control in these studies, may have contained many individuals with radiographically undetectable apical periodontitis.

It has been recommended that a root-filled tooth without symptoms should be examined radiographically during a follow-up period of up to four years before a final diagnosis of post-treatment situation can be made (European Society of Endodontology, 1994). As a result, post-treatment root infection and PTAP may be present for years before a decision is made either to retreat the root, undertake apical surgery or monitor the case further (see also Siers in the second part of this special issue, december 2005).

From the above, it is concluded that long-standing inflammation may have systemic effects and influence

general health. It seems preferable to develop procedures that reduce root infection to a level that eliminates periapical inflammation.

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Local and potential systemic consequences of endodontic root infection

In root infections, bacteria are present not only in planktonic cells but also in biofilms, which are more resistant to host defence mechanisms and disinfectants. Apical periodontitis, which may be radiographically undetectable, may develop or persist as a host defence mechanism to prevent the systemic spread of bacteria and their by-products to other sites of the body. The risk of spreading microorganisms and septic emboli is present especially in compromised hosts; furthermore, long-standing inflammation may have systemic effects and affect general health. Effective procedures should be developed to minimize the burden of root infection.

Summary

Key words:

- Endodontology
- Systemic diseases
- Periodontitis