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JULY- DEC 2017 • VOL 7 • ISSUE 2

Indian Journal of Comprehensive Dental Care

UNFINISHED ROOT CANAL AND RISK OF CARDIOVASCULAR DISEASES : A REVIEW AUTHOR SEQUENCE

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ABSTRACT:

Root canal treatments (RCTs) aim to eradicate pulpal diseases and save the infected teeth by eliminating microorganisms from the root canal system. Starting but not finishing an RCT can perpetuate a dead space for bacterial growth, which can spread to other sites in the body and develop systemic symptoms. Cardiovascular diseases (CVD) have a complex etiology determined by risk factors, which are in turn associated to a strong genetic component and to environmental factors. In the biological background for the development of CVD, low-grade chronic inflammation plays a role as a pathogenetic determinant of atherosclerosis.

Bacterial etiology has been confirmed for common oral diseases such as caries and periodontal and endodontic infections. Bacteria causing these diseases are organized in biofilm structures, which are complex microbial communities, composed of a great variety of bacteria with different ecological requirements and pathogenic potential. The biofilm community not only gives bacteria effective protection against the host's defense system but also makes them more resistant to a variety of disinfecting agents used as oral hygiene products or in the treatment of infections. Successful treatment of these diseases depends on biofilm removal as well as effective killing of biofilm bacteria.

Keywords: Root canal treatment, biofilm, endodontic infections, cardiovascular diseases

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Date of Submission : 1/11/16 Date of Acceptance : 12/12/16

INTRODUCTION

Cardiovascular disease (CVD) is one of the leading causes of mortality worldwide, approximately 30% of all deaths[1] and have a complex etiology determined by risk factors, which are in turn associated to a strong genetic component and to environmental factors.[2]

Atherosclerosis is the main cause of coronary heart and cerebrovascular disease which, in turn, are the most common causes of death in the industrialized world.[3] In recent years, low-grade chronic inflammation and bacterial or viral organisms involved in chronic inflammation have been proposed as strong factors associated with atherosclerosis and CVD events.[4]

Inflammatory and immune responses are initiated in the pulp tissue or periapical area when antigens are introduced into the root canal. Exudate is often found in it.[5]

Periodontal and pulpal diseases are 2 major low-grade chronic inflammatory infectious diseases of the oral cavity.[1] Periodontal disease is a chronic gram-negative anaerobic infection of the tooth-supporting structures with an estimated prevalence of as high as 75% in adults in the US.[6]

Apical periodontitis is caused by bacteria residing inside the root canals of the diseased teeth, and organized in a bio film, as a consequence of pulpal infection, which is usually the

ultimate result of a deep carious lesion.[2] Clinically, it is diagnosed from patient symptoms, clinical signs, and radiographic images; chronic apical periodontitis, and is confirmed through observation of periradicular radiolucencies on affected teeth.[7]

Additionally, acute endodontic inflammation also plays a role in CHD risk.[8] Links between endodontic inflammation and cardiovascular outcomes are biologically plausible, considering the predominance of Gram-negative anaerobes associated with endodontic infections (Baumgartner, 1991), evidence of cytokine production in inflamed pulp and periapical granulomatous tissues (Miller et al, 1996) , and observations of elevated systemic levels of inflammatory mediators (Marton et al, 1988).

Bacterial infection of the dental pulp ultimately results in the formation of dental periapical lesions consisting of granulomas and cysts, which represent two different stages of development of the same inflammatory lesion.[9]

Cytokines are produced in inflamed pulp and periapical granulomatous tissues, and systemic levels of inflammatory mediators have been observed in patients undergoing RCT. A plausible mechanism is that infectious processes associated with the root canal system may not only cause local manifestations of oral cavities but also extend to nearby and distant body compartments along anatomic pathways or systemic circulation.[1]

Ischemic heart disease, Dysrhythmias, and Infective Endocarditis are some of the cardiovascular conditions most commonly seen among the population.[10]

A comprehensive treatment plan should be constructed keeping in view all the pros and cons related to patient's medical condition.

DIFFERENT MICROBES FOUND IN ENDODONTIC INFECTION

The rationale for endodontic treatment is to eradicate the infection, to prevent microorganisms from re-infecting the root or periradicular tissues. Thus, a thorough understanding of the endodontic microbiota is the basis for the success of endodontic treatment.[11]

Intraradicular infections

The endodontic pathogens that cause primary intraradicular infections are:

1) Black pigmented Gram negative anaerobic rods (Bacteroides melaninogenicus).

(a) saccharolytic – Prevotella intermedia

(b) asaccharolytic – Porphyromonas gingivalis.[7]

2) Tannerella forsythia [12]

3) Fusobacterium nucleatum

4) Spirochetes are highly motile, gram negative bacteria. All

Procedure	***Prevelance of Bacteraemia***
Extraction	
• Single	51%
• Multiple	68-100%
Periodontal surgery	
• Flap procedure	36-88%
• Gingivectomy	83%
Endodontics	
• Intracanal instrumentation	0-31%
• Extracanal instrumentation	0-54%
Endodontic surgery	
• Flap reflection	83%
• Periapical curettage	33%

Table No: 1 prevelance of bacteraemia arising after various types of dental procedures and oral cavity.[29]

Regimen	Drugs
Standard regimen	Adults: 2.0 gm Amoxicillin Children: 50 mg Amoxicillin
Patients allergic to penicillin or already taking penicillin class of medication	Adults: 2.0 cephelexin Or 600 mg Clindamycin Or 500 mg Azithromycin or Clarithromycin Children: 50 mg Cephlexin Or 20 mg/kg Clindamycin or 50 mg Azithromycin
Alternative im/iv regime for patients allergic to penicillin and unable to take oral medications	Adults: 1.0 gm im or iv Cefazolin or Ceftriazone Or 600 mg im/iv Clindamycin Children: 50 mg im/iv Cefazolin/ Ceftriazone Or 20mg im/iv Clindamycin within 30 minutes before the procedure

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Table No: 2 Describes recommended antibiotic regimens for antibiotic prophylaxis.[35]

oral spirochetes fall into the genus Treponema.[13]

- Treponema denticola
- Treponema socranskii

6) Gram positive anaerobic rods:

- Actinomyces spp.
- Eubacterium spp.

7) Gram positive cocci that are present in endodontic infection:

- Streptococcus mitis
- Enterococcus faecalis.

Bacteria persisting intracanal disinfection procedures and after root canal treatment

The most common Gram negative anaerobic rods are:

- Fusobacterium nucleatum
- Prevotella spp.

The most common Gram positive bacteria are:

- Lactobacilli
- Staphylococci
- E. faecalis
- Eubacterium

Extraradicular infections

Intraradicular microorganisms usually constrain themselves in the root canal and can overcome the defense barrier and establish an extraradicular infection. This may lead to development of acute apical abscess in periapical tissue. The dominant microorganisms present are anaerobic bacteria[14]:

- Actinomyces spp.
- Porphyromonas gingivalis
- Prevotella spp.

PATHWAYS OF INFECTION

Kakehashi et al stated that there are so many ways by which

-Consultation: Type of heart disease, time elapsed from the cardiological event, clinical complications, treatment received.

- Take the prescribed medication as usual
- If nitrates are used, the patient should bring them
  - Take as a preventive measure before local anesthesia
  - Take in case chest pain develops

-Before 4-6 weeks after infarction: only emergency procedures.

-Very anxious patients: premedication (5-10mg of diazepam the night before and after 1-2 hours before treatment.

-Anesthesia: not to inject into a blood vessel and a maximum of two carpules with vaso-constrictor.

Table No: 3 Dental management in patients with Ischemic heart disease.

the microorganisms reach the pulp.[11] The various routes are:

1. Dentinal tubules: After a carious lesion or during dental procedures, microorganisms may use the pathway in a centripetal direction to reach the pulp. Bacteria gain access to the pulp when the dentin distance between the border of carious lesion and the pulp is 0.2 mm.[15]

2. Periodontal membrane: Microorganisms from gingival sulcus may reach the pulp chamber through the periodontal membrane, using a lateral channel or the apical foramen as a pathway. This pathway becomes available to microorganisms during a dental prophylaxis, due to dental luxation, as a result of the migration of epithelial insertion to the establishment of periodontal pockets.[11]

3. Faulty restoration: Studies have proven that salivary contamination from the occlusal aspect can reach the periapical area in less than 6 weeks in canals obturated with guttapercha and sealer.[16] Three possible metastatic pathways can be responsible for the consequences of oral infections on systemic diseases such as CVD.[2]

1. Metastatic spread of infection from the oral cavity
2. Metastatic injury by circulating oral microbial toxins
3. Metastatic inflammation arising from an immune response to oral microorganisms.

Cardiovascular diseases are one of the main causes of mortality in the developed world. The two cardiovascular conditions that cause most deaths are ischemic heart disease and cerebrovascular disease.[17]

Dental professionals may be the first line of defense in the detection and referral of a patient suspected of having cardiovascular disease, an uncontrolled disease status, or oral adverse drug reactions, and they have a key role to play in oral and systemic disease prevention and treatment.[10]

The Focal Infection Theory

A focal infection is a localized or generalized infection caused by the dissemination of microorganisms or toxic products from a focus of infection.[18]

Rosenow[19] (1917) reinforced the concept of a focus of infection from which microorganisms could enter the blood stream causing systemic illness. He insisted that enclosed lesions that could only drain into the circulation, such as a necrotic pulp, were the most dangerous foci of infection.

Fish Theory

In 1939, Fish theorized that the zones of infection are not an infection by themselves but the reaction of the body to infection. He concluded that this response occurred regardless of the virulence of the organisms.[20] Zones of Fish theory are:

Zone of Infection: This is the nidus of infection at the foramen where the bacteria are confined; characterized by PMN's and microorganisms along with the necrotic cells.[20]

Zone of contamination: This zone is characterized by death of normal tissue cells, due to high concentration of toxins and lymphocytes.[20]

Zone of irritation: This zone consists of some normal tissue cells that have survived due to lower concentration of toxins. Osteocytes and histiocytes resorb bone and isolate the infection at its center. No bacteria are present in this zone.[20]

Zone of stimulation: This zone has a severe dilution of bacterial toxins; this stimulates fibroblasts and osteoblasts to produce an irregular bone matrix.[20]

Bacteraemia in nonsurgical root canal treatment:

Bender et al. (1963) showed that endodontic procedures with instrumentation beyond the apex produce bacteraemia in 31% of cases, but, when instrumentation was confined within the tooth, blood cultures were negative.[14]

ENDODONTIC BIOFILMS

Biofilm is defined as aggregate of microorganisms in which cells that are frequently embedded within a self produced

matrix of extracellular polymeric substance (EPS) adhere to each other or to a surface.[21]

BIOFILMS IN ENDODONTIC INFECTION:

Endodontic bacterial biofilms can be categorized as[22]:

- intracanal biofilms,
- extraradicular biofilms,
- periapical biofilms and
- biomaterial-centered infections.

Intracanal microbial biofilms

They are microbial biofilms formed on the root canal dentin of an endodontically infected tooth.[23] Major bulk of the organisms existed as loose collections of filaments, spirochetes.[21]

Extraradicular microbial biofilms

They are also termed as root surface biofilms which are formed on the root surface adjacent to the root apex of endodontically infected teeth.[24] Extraradicular biofilms are reported with asymptomatic periapical periodontitis and in chronic apical abscesses.[25]

Periapical microbial biofilms

They are isolated biofilms found in the periapical region of endodontically infected teeth. These microorganisms have the ability to overcome host defense mechanisms.[26]

Biomaterial-centered infection

Biomaterial centered infection is caused when bacteria adhere to an artificial biomaterial surface and form biofilm structures.[27] In endodontics, biomaterial-centered biofilms form on root canal obturating materials.

BACTEREMIA

Bacteria were first demonstrated scientifically in the diseased dental pulp by Miller (1894). William Hunter (1900) theorized that microorganisms present in the oral cavity could disseminate throughout the body, resulting in systemic disease.[22]

Dissemination of oral microorganisms into the bloodstream is common, in less than 1 min after an oral procedure, organisms from the infected site may have reached the heart, lungs, and peripheral blood capillary system.[28]

There are more than 10^{13} microbes on all surfaces of the body. In the oral cavity there are several barriers to bacterial penetration from dental plaque into the tissue: a physical barrier composed of the surface epithelium; defensins, which are host-derived peptide antibiotics.[28]

In many instances the occurrence of endocarditis does not relate to the so-called dental-induced bacteraemia. It may well transpire that random bacteraemia may be more causative in IE than dental surgeons carrying out treatment.[29]

Antibiotic prophylaxis (AP) may be defined as the use of an antimicrobial agent before any infection has occurred for the purpose of preventing a subsequent infection (Gerding 1996, Titsas & Ferguson 2001).

Bacteraemia is usually eradicated by the reticulo-endothelial system within a few minutes and poses no threat to the healthy patient. However, some medically compromized patients may be at risk from this transient blood-borne infection, mostly infective endocarditis (IE) (Dajani et al.1997).

Thus, implementation of antibiotic prophylaxis (AP) has been advocated widely in an attempt to provide some degree of protection for 'at-risk' patients.[17]

EFFET OF PULP ON PERIODONTAL TISSUES

Tissues of dental pulp and periodontium are interlinked from the embryonic stage.[30]

Pulp communicates with periodontal ligament via the apical foramen, auxiliary canals and dentinal tubules. The first indication of periodontal involvement as a sequelae to pulp involved is the thickening of periodontal ligament space at the apical end. Root canal system" is a complex anatomical space within the root of the tooth. Main canals terminate in the PDL at an exit point close to the end of the root. [31] When the pulp begins to break down, the bacterial by-products of cellular necrosis egress from within the root canal system through the POE's into the surrounding PDL and bone. These toxins in turn will destroy the healthy peri-radicular tissues and create bone loss.[31]

Relationship of cardiovascular disease and periodontitis

Periodontitis has been proposed as having an etiological or modulating role in cardiovascular diseases[10]. Aerobic and anaerobic bacteria are the microorganisms found in periodontal disease. The chronic activity of bacteria, their toxins, followed by a host immune response, lead to a progressive failure of periodontal attachment. The pro-inflammatory cytokines TNF-alpha, IL-1beta, and gamma interferon as well as prostaglandins reach high tissue concentrations in periodontitis. The periodontium can therefore serve as a renewing reservoir, which can enter the circulation and induce systemic effects. Periodontal disease is believed to provide inflammatory cytokines, which promote atherosclerosis and thrombotic events.[2]

Relationship of cardiovascular diseases with apical periodontitis

Apical periodontitis is a sequel to endodontic infection and develops as the host response to microbial infection that

comes from the root canal system of the affected tooth.[32] Endodontic infection that leads to apical periodontitis is caused by a mixture of oral bacterial species also found in dental plaque, dominated by obligate anaerobes.

The proximity to the bloodstream of micro flora present in the root canal and periapical tissues can cause a transient bacteremia during clinical dental procedures. Normally, microorganisms penetrated into the blood stream are eliminated by the host within minutes. However, it is known that in patients with valvular heart disease, a transient bacteremia may lead to infective endocarditis and myocardial infarction.[2]

Endo-perio lesions

The pulp-periodontal interrelationship is a single or biologic unit in which there are so many paths of communication. They can get affected individually or combined. Endodontic-periodontal problems are responsible for more than 50% of tooth mortality today.[33]

There are various pathways for the exchange of infectious elements and irritants from the pulp to periodontium or vice versa, leading to the development of endodontic periodontal lesions.

1. Pathways of developmental origin: *Apical foramen, accessory /lateral canals *Congenital absence of cementum

2. Pathways of pathological origin: *Empty spaces created by Sharpey's fibers *Root fracture following trauma *Idiopathic root resorption - internal and external

3. Pathways of iatrogenic origin: *Exposure of dentinal tubules * Accidental lateral root perforation *Root fractures during endodontic procedures.

It is easier to determine the origin of the lesion when a pulp vitality test is positive because this will rule out an endodontic etiology. However, pulp tests may not be always reliable. If pulpal necrosis is associated with inflammatory involvement of the periodontal tissue, it presents a greater diagnostic problem. In this situation, the location of these pulpal lesions is most often at the apex of the tooth, but they may also occur at any site where lateral canals exit into the periodontium.[33]

ANTIBIOTIC PROPHYLAXIS

Prophylaxis is recommended in all the dental procedures involving the manipulation of gingival tissue, periapical region or the perforation of the oral mucosa such as extractions, endodontic treatment.

Prophylaxis in turn is not recommended in the routine injection of anesthetic solutions in non-infected tissues, dental X-rays or bleeding secondary to lip or oral mucosa traumatism.[34]

Guidelines

Various guidelines have been proposed for AP, although it has not been possible to perform controlled clinical trials in human beings to establish their effectiveness, because of ethical issues of withholding AP from patients. Current guidelines from the British Cardiac Society (BCS) (Ramsdale et al. 2004), the AHA (Dajani et al. 1997) and the BSAC (Gould et al, 2006) differ with regard to which antibiotic regimens should be prescribed and for which dental procedures.[14]

BSAC guidelines for antibiotic prophylaxis:

1. Conditions predisposing to risk of infective endocarditis
   - History of infective endocarditis
   - Ventricular septal defect
   - Patent ductus arteriosus
2. Patients not at risk from infective endocarditis
   - After coronary by-pass surgery
   - Six months after surgery for-
   - Ø Ligated ductus arteriosus
   - Ø Surgically closed atriolar ventricular septal defects
3. Special risk patients

Ø Those who require a general anaesthetic and have a prosthetic heart valve or are allergic to penicillin or who had penicillin more than once in the previous month.

American Heart Association Guidelines for antibiotic prophylaxis:

1. High risk category
   - Prosthetic heart valves
   - Previous bacterial endocarditis
2. Moderate risk category
   - Most other congenital cardiac malformations
   - Hypertrophic cardiomyopathy
3. Neglible risk category
   - Isolated secundum atrial septal defect
   - Previous coronary artery by-pass graft surgery

Dental procedures for which antibiotic prophylaxis is recommended to prevent infective endocarditis (AHA recommendations):[29]

Dental extractions

Periodontal procedures

Dental implant placement Endodontic instrumentation or surgery beyond the apex

Possible risks associated with antibiotic prophylaxis:

When antibiotics are given prophylactically to prevent

Infective Endocarditis (IE), the clinician needs to consider the risk and cost benefit of such treatment. The most significant adverse event associated with the penicillins is hypersensitivity reactions. These can range from a troublesome rash to a life threatening anaphylactic reactions.[29]

The chance of a penicillin reaction following administration of the drug is in the range of 0.7–5 %. However, high doses of oral amoxycillin can cause an allergic rate similar to intramuscular penicillin.[36] Patients receiving penicillin (amoxycillin) prophylaxis to prevent IE are 5 times more likely to die from an anaphylactic reaction to the drug than to die from contracting endocarditis.

The World Health Organisation has recognised antimicrobial resistance as a global problem.[37] Approximately one third of all antibiotics are prescribed for prophylactic purposes and a high proportion of these are for prevention of IE.[38]

The continued and repeated use of prophylactic antibiotics has caused selection of antimicrobial resistance in oral streptococci.[39] Overprescribing of antimicrobials has made some antibiotic regimens less effective.[40]

DENTAL CONSIDERATIONS IN PATIENTS WITH HEART DISEASES

Patients suffering from cardiac diseases like ischemic heart disease, valvular disease are prone to angina or myocardial infarction.[35]

ISCHEMIC HEART DISEASE:

Ischemic heart disease is the main cause of death in the developed world.[41] This is characterized by a reduction in coronary blood flow followed by thrombus formation that occludes the arterial lumen. Angina is often precipitated by physical activity or stress and may radiate to the arm or jaw or may present as facial or dental pain. Fear and anxiety associated with a dental procedure may be a precipitating factor for angina in some patients.[42] Chest pain (angina) occurs when coronary occlusion is partial and no necrosis is produced, while acute myocardial infarction is observed when coronary occlusion is total and necrosis is produced as a result.[43]

Management: Treatment for patients with ischemic heart disease should include morning appointments, short appointments, oral premedication with an anxiolytic drug or nitrous oxide or oxygen sedation, limited use of vasocontrictors.[44]

ARRHYTHMIAS

Arrhythmias are variations in normal heart rate due to cardiac rhythm, frequency or contraction disorders .[45] Atrial fibrillation is the most common type of cardiac arrhythmia.[46]

Management: Consultation with the supervising physician is advised in order to know the current condition of the patient and the type of arrhythmia involved, as well as the medication prescribed.[46] Anxiolytics can be used to lessen stress and anxiety. It is very important to limit the use of a vasoconstrictor in local anesthesia. Sublingual nitrites are to be administered in the event of chest pain. The patient should be placed in the Trendelenburg position. The dental team should be prepared for basic cardiopulmonary resuscitation.[41]

HEART FAILURE

Heart failure (HF) is defined as the incapacity of the heart to function properly, pumping insufficient blood towards the tissues and leading to fluid accumulation within the lungs, liver and peripheral tissues.[41]

Management: Dental treatment is to be limited to patients who are in stable condition. Anxiety and stress are to be avoided during the visits. The patient should be placed in the semi-supine position in a chair. In patients administered digitalis, the vasoconstrictor dose is to be limited to two anesthetic carpules. Aspirin can lead to sodium and fluid retention, and therefore should not be prescribed in patients with heart failure.[41]

INFECTIVE ENDOCARDITIS

Infectious endocarditis (IE) is an infrequent condition resulting from the association of morphological alterations of the heart and bacteremia of different origins.[41] Infective endocarditis is a serious problem, with an estimated incidence of 1.5-3.3 per 1000 intravenous drug abusers and 5-10% mortality rate.[47]

Management: According to the European Society of Cardiology and American Heart Association, antibiotic therapy of IE relies on monotherapy or combination of bactericidal drugs active on the microorganism involved, administered intravenously, at high dosage and for up to 6 weeks.

CONCLUSION

Unfinished RCTs are associated with a higher risk of CVD hospitalization. An RCT can be left unfinished for several reasons, including symptomatic teeth infected with gram-negative anaerobic bacteria.[48] The root canal flora of teeth with clinically intact crowns and necrotic pulps is dominated by obligate anaerobes.[49] These microbes can indirectly elevate inflammatory mediator levels and cytokines.[50]

An unfinished RCT, involving a temporary restoration, can increase the risk of contamination of the oral cavity, leading to bacterial infection of the root canal system and apical periodontitis when the inflammation progresses to the

periapical tissues.[1]

Willershausen et al (2009)[51] reported that patients who have experienced myocardial infarction had a higher number of radiographic apical lesions compared with healthy patients.

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