CHAPTER 1

INTRODUCTION

1.1 Background

Bacteria that are commonly found to cause persistent infections are: Enterococcus faecalis, Streptococcus sp, Psudoramibacter alactolyticus, Streptococcus windosus, Bacteroides gracilis, Filifactor alocis, and Fusobacterium nucleatum (Kanumuru, & Subbaiah, 2014). Enterococcus faecalis bacteria are responsible for 80-90% of infections of RCS. The integrated approach of using mechanical debridement and antimicrobial PDT significantly suppressed the bacterial population in the root canal (Gomes, Martinho, & Vianna, 2009). The enduring success of this treatment is reliant on the bacterial resistance and anatomy of the root canal (Estrela, et al., 2014). The presence of persistent infections in the RCS by microorganisms causes root canal failure. Generally, the persistent nature of the microbial population in the RCS leads to the failure of aPDT. These types of bacteria are commonly associated with many infections of RCS(Stuart, Schwartz, Beeson, & Owatz, 2006, Davis, Maki, & Bahcall, 2007).

Microorganisms have been shown their survival in root canals as solitary organisms having resistance to commonly used antimicrobial ingredients. Based on these survival habits, their complete elimination from the RCS fails root canal treatment (Lins, et al., 2015, Kunarti, Tjandra, & Prasetyo, 2019). The failure of Endodontic treatment is mainly due to the occurrence of facultative and gram-positive aerobic microorganisms. Several research studies reported that these microorganisms are resistant to the application of many antimicrobial treatments including chlorhexidine and sodium hypochlorite (Buck, Eleazer, Staat, & Scheetz, 2001, Dunavant, Regan, Glickman, Solomon, & Honeyman, 2006), calcium hydroxide, and several antibiotics

(Dahlen, Samuelsson, Molander, & Reit, 2000). Moreover, these bacterial species can make biofilms in the RCS and preserved their existence in severe conditions (Distel, Hatton, & Gillespie, 2002, Stuart, Schwartz, Beeson, & Owatz, 2006). Resistance development to PDT is dubious in free radicals, microbial cells, and singlet oxygen for interaction with many kinds of cellular structures and several pathways of metabolism (Wainwright & Crossley 2004). Furthermore, the disruption of biofilms and antimicrobial activity of photosensitizers has an uninterrupted influence on molecules of extracellular nature, due to its mediation with the high chemical activity of singlet oxygen. The twofold activity of PDT exemplifies an advantage over conventional antibiotics (Konopka & Goslinski 2007). This dual mechanism of action has been reported by many researchers.

Antimicrobial photodynamic therapy has gained the emphasis of researchers in recent years as a modern treatment approach to enhance the disinfection of root canal. The results of the PDT revealed important satisfactory results with substantial elimination of infectious bacteria in RCS (Seal, Ng, Spratt, Bhatti, & Gulabivala, 2002, Williams, Pearson, & Colles, 2006). Photodynamic 405 nm laser therapy is very effective against Enterococcus faecalis. This therapy is effective with and without photosensitizer, but the combined application of photosensitizer and laser is more effective (Kunarti, Tjandra & Prasetyo, 2019). Photodynamic therapy under different conditions is highly fruitful against Enterococcus faecalis (Nunes, et al., 2011). Furthermore, aPDT has shown its strong disinfection role in diverse environments for the treatment of RCS infections(Masuda, et al., 2018).

Antimicrobial PDT is also the substitute for the treatment of several local infections of microbial nature in endodontics and post-extraction pain. Similarly, alveolar osteitis and periimplantitis can be cured by the application of PDT (Hayek et al. 2005). During the past few years, vast research was done on the utilization of PDT in microbial disinfection (Fontana et al. 2009). PDT significantly reduced the bacterial infection, however total purging of bacteria from the target cells was not attained (Schneider et al. 2012 The success of complete removal of bacteria was rarely reported (Dortbudak et al. 2001). Similarly, the findings of other studies are in agreement with the above results that complete eradication of microbial load was achieved (Shibli et al. 2003). Adequate pieces of evidence from in vitro to in vivo studies have been reported for the reduction in total bacterial counts (Komerik et al. 2003 and Wood et al. 2006).

1.2 Characteristics of bacteria causing endodontic diseases

The microorganisms responsible for resistant infections and post-treatment diseases are mainly gram-positive facultative coccoid, dominated by enterococcus (Love 2001). Gram-negative bacteria and Gram-positive bacteria have dissimilar membrane structures (Konopka & Goslinski 2007; Maisch et al. 2004). As the majority of the endodontic infections are caused by both Gram (+ve) and Gram (-ve) bacteria, hence use of amphiphilic PSs in the photodynamic therapy has proved significant output in the eradication of microbial cells (Giusti et al. 2008 and Liu et al. 2012).

The most common bacteria causing endodontic diseases are Fusobacterium nucleatum, Actinomyces naeslundii, Prevotella nigrescens, Porphyromonas gingivalis, Bacteroides fragilis, Porphyromonas gingivalis Actinomyces naeslundii, Pepto streptococcus (Liu et al. 2012

Basic endodontic infection is a result of bacteria that enter and reside in the necrotic pulp tissue. It is mainly described by anaerobic bacteria which is the most dominant form of bacterial (Siqueira et al. 2005). The bacterial profiles of the endodontic microbiota vary from one individual to another (Siqueira et al. 2004). The oral microbiome is related to the development of some oral diseases like endodontic infection, dental caries, and periodontal disease (Struzycka, 2014, Liu et al. 2012). The bacteria that colonize and invade the pulp at the start can cause initial endodontic infection and this endodontic infection is called a polymicrobial infection ruled by anaerobic bacteria (Munson et al. 2002, SiqueiraJr. I.N.Rˆoc, 2009). Alternatively, the secondary (chronic) infection was because of microorganisms that had been contributors of secondary and primary infection and in some ways, they resisted intercanal antimicrobial treatments and had been able to exist in treated canals in nutrient-deficient periods. Gram-negative microorganisms and spirochetes are mainly responsible for the early development of peri-implantitis (Hultin et al.2002).

Enterococci are a common type of bacteria that inhabit the human and animal gastrointestinal region, oral cavity, and vagina. While initially considered non-virulent enterococci are now documented as major sources of common microbial infections globally (Kayaoglu, & Orstavik, 2004). In dentistry, it has been found that Enterococcus species, particularly Enterococcus faecalis, are associated with chronic periodontitis (Souto, & Colombo, 2008) and unsuccessful treatment of root canal concerning chronic apical periodontitis (Love 2001). Persistent microbial infections were successfully eliminated from periapical lesions in endodontic treatment (Sunde, 2002).

Endodontic infection-causing microorganisms are optional anaerobic types, proficient of growing in the presence of oxygen or anaerobic conditions (Courvalin, Dunny, Murray, & Rice, 2002, Rôças, Siqueira, & Santos, 2004). Microbial species live in large amounts in the lumen of the human intestine and, in most cases, without causing harm to them. They also exist in smaller numbers in the oral cavity and in the female genital tract (Koch, Hufnagel, Theilacker, &

Huebner, 2004). They used several food sources including, glycerol, glucose, lactate, malate, citrate, arginine, agmatine, and α-keto-acids (Courvalin, Dunny, Murray, & Rice, 2002). These bacteria subsist in very severe situations including alkaline high PH (9.6) and salt absorptions (Courvalin, Dunny, Murray, & Rice, 2002, Tendolkar, Baghdayan, & Shankar, 2003). They can survive in Bile salts, under high heavy metals contaminated conditions, and resistant to detergents, ammonia, azide, and desiccation (Courvalin, Dunny, Murray, & Rice 2002). They can grow between 10 and 45 ° C and survive 30 minutes at a temperature even above 60 ° C (Tendolkar, Baghdayan, & Shankar, 2003).

Enterococcus faecalis is most abundant isolation sites are chronic root canal infections and post-treatment infections. One of the virulence aspects related to this recurrent presence of these microbial species. It was found during an in-vitro analysis that while the Enterococcus faecalis has the potential ability to form biofilm in the RCS, with the presence of intracanal medications. Biofilm is a highly organized structure where bacteria clumps form biofilms by joining together through a matrix of carbohydrates. Also, these bacteria have the potential for survival without being divided into the biofilm and have induced apatite reprecipitation, particularly in a mature biofilm (Ahmeduddin, Nagesh, Reddy, & Raj, 2012, Manikandan, Hegde, Shetty, & Geethashri, 2013).

Bacterial species have been observed regularly in root canals that were gone through the treatment of filling associated with insistent apical periodontitis (Hargreaves & Berman, 2011). Based on their unique genetic makeup and morphology, they can survive in a variety of severe environmental conditions and under the action of many antibiotics (Medeiros, et al., 2014). Consequently, these bacterial species are accountable for the most common causes of endodontic failure (Siddiqui, Awan, & Javed, 2013).

A high occurrence of numerous microbial species has been found in filled RCS related to tenacious apical periodontitis (Holliday, 2011). Due to unique characteristics (genetic & morphological); Enterococci can easily resist intracanal actions and application of many antibiotics, even in the conditions of ecological stress (Medeiros, et al., 2014). Therefore, the responsibility for the failure of endodontic treatment lies in the presence of persistent bacterial species (Siddiqui, Awan, & Javed, 2013). These microbes have proven their viability as single microorganisms and can survive in poor nutritional conditions (Zhang, Du, & Peng, 2015). These bacteria can infiltrate deep (1,250 μm) into the dentinal tubules and dentin collagen (Du, et al., 2014).

Regardless of the convenience of numerous traditional mechanical root canal procedures and other chemicals, root canals are not free of microorganisms (Vera, et al., 2012). The drawback of most commonly used irrigants such as sodium hypochlorite (130 μm) is their less penetration into the dentinal tubules Hence, more effective conveyance of irrigant and system of agitation are requisite for effective PDT. In this regard application of Lasers has been recommended as an effective method for disinfection. Earlier studies reported that lasers can play a vital role in the removal of bacteria and could increase post-endodontic treatment success. Several types of lasers have been examined to develop enhanced treatment methods. In this case use of high-power lasers for endodontic treatment is most common. Application of 810 nm diode resulted in the obstruction of the dentinal tubules and total counts of Escherichia coli and Enterococcus faecalis bacteria (Rios et al., 2011, Vatkar, Hegde, & Sathe, 2016, Bago, et al., 2013, Stojicic, Amorim, Shen, & Haapasalo, 2013).

Many proven studies showed that photodynamic therapy can decrease the population of Enterococcus faecalis in dental infection and several studies showed that doxycycline can be a good photosensitizer in the process of photodynamic therapy but there are not many authentic studies to check the effect of combined application of doxycycline as a photosensitizer and photodynamic therapy against Enterococcus faecalis. I chose to write this review to check the combined effect of photodynamic therapy and photosensitizer and the effectiveness of photodynamic therapy against endodontic disease caused by Enterococcus faecalis.

1.3 Research Question/problem

The following is the research question of this systematic review

"Is antimicrobial photodynamic therapy effective against endodontic disease"?

1.4 Aims

The following are the aims of this review

1) To analyze the different recent studies of antimicrobial photodynamic therapy against endodontic disease.
2) To see whether antimicrobial photodynamic therapy is highly effective or not against endodontic disease.

1.5 Limitations

The following are the limitations of this review article

1) Articles reviewed that were published between 2010 and 2020 only.
2) Articles published in the English language only were considered.
3) Experimental and clinical studies were included.