

REVIEW ARTICLE

Role of Triple Antibiotic Paste In Revascularization And Endodontics- A Review

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ABSTRACT

Antibiotics are most important for the management of bacterial infections. During root canal treatment, antibiotics may be used systemically or locally. Because of the possibility of systemic side effects, Local use of antibiotics in root canal therapy in the form of intracanal medicaments and irrigants is more desirable. The aim of this article was to review the applications of antibiotic-containing medicaments in endodontics. The search was performed from 1990 to 2015 research papers. The keywords searched on Medline were 'Antibiotics in endodontics', 'Antibiotics and revascularization', 'Antibiotics and TAP'. Suitable sources of information are studied after reviewing the reference section. After reviewing various articles, local administration of antibiotics seems more effective mode than systemic application. Antibiotics plays significant role in endodontic treatment, out of which a combination of three antibiotics (metronidazole, ciprofloxacin and minocycline) seems to be effective at reducing bacterial numbers in the root canal systems of infected teeth.

Keywords: Triple antibiotic paste (TAP), ciprofloxacin, metronidazole, minocycline, root canal treatment, revascularization

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INTRODUCTION

The success of the endodontic treatment depends on microbial suppression in the root canal and periapical region. Endodontic instrumentation alone cannot achieve a sterile condition. With the advent of non-instrumentation endodontic treatment, lesion sterilization and tissue repair, local application of antibiotics has been investigated. Triple antibiotic paste (TAP) containing metronidazole, ciprofloxacin, and minocycline have been reported to be a successful regimen in controlling the root canal pathogen and in managing non-vital young permanent tooth. This paper reviews the existing literature on biocompatibility, efficiency, drawbacks of TAP in endodontic therapy and pulp revascularization.

Antibiotics were first discovered in 1928 but were not used regularly until 1940 (Abbott 2000).¹ Grossman (1951) was first reported to use as polyantibiotic paste in endodontics.² The significant role of microorganisms in development of pulpal - periradicular diseases have been demonstrated by various studies.³ To reduce this microbial count within the root canal system, various instrumentation techniques, irrigation protocols, and intracanal medicaments have been used by clinicians and researchers. There is no definitive evidence in the literature which shows mechanical instrumentation alone results in bacteria free root canal system. On the contrary; there are studies which show a significant portion of root canal walls remains untouched and therefore mechanical instrumentation alone cannot eliminate the bacteria completely from the root canal system.^{4,5} Hence, additional measures such as use of chemical agents are required in order to disinfect and kill microorganisms in root canal system. Since the root canal infection is polymicrobial in nature, significance is given to the role of triple antibiotic paste in endodontics, therefore the purpose of this paper was to review the

studies related to the use of antibiotics in endodontics.

MATERIALS AND METHODS

An electronic search was undertaken based on keywords: 'Antibiotics and endodontics', 'Antibiotics and revascularization', 'Antibiotics and triple antibiotic paste', in the PubMed database. The research publications selected for the review were up to 2015 and were limited to English language papers only.

Most of the articles searched were from Pubmed journals. Among these articles, case study articles, original research articles were mostly selected and few references were taken from D.C.N.A and one of the articles was selected from google scholar. All the aspects of triple antibiotic paste (TAP) have been covered in endodontics like its role as antibacterial agents, its role in healing of periapical lesions, its use in revascularization procedure, its effectiveness against *E. faecalis*, its biocompatibility and deleterious effect, effect on the dentinal wall thickness and finally discoloration caused by TAP paste.

DISCUSSION

Proper cleaning and shaping is the most important aspect in success of root canal treatment.^{4,5} Abbott et al. (1990) discouraged the indiscriminate use of antibiotics. He insisted on the importance of antibiotics in the form of intracanal medicaments in endodontics, and concluded that the systemic antibiotics should be restricted to patients who have local signs of infection, malaise and elevated body temperature.⁶ Due to the polymicrobial nature of root canal infections, combination of drugs will be more effective mode to treat these infections. After reviewing various studies in literature, the recommended protocol is the combination of metronidazole, ciprofloxacin, minocycline in an appropriate delivery system (TAP).

Hoshino et al. (1996) studied the antibacterial effect of ciprofloxacin, metronidazole and minocycline mixture, on microorganism from infected root canal walls. The result of this study shows the significance of drug combination and its role to eradicate bacteria from the infected dentine of

root canals.⁷

The use of triple antibiotic paste (TAP) during root canal treatment has been found to be effective in non surgical management of teeth with non vital pulp and persistent sinus tract. This promotes the healing and repair of the periodontal tissues. Several researchers have investigated this action. Windley et al. (2005) also demonstrated that TAP in dog teeth, lowered bacterial count to lowest.⁸ Takushige et al. (2004) concluded that the clinical symptoms of all the cases disappeared in primary teeth associated with periapical lesion, after treatment with antibiotic paste (Lesion sterilisation and tissue repair (LSTR) therapy).⁹ Even Kusgoz et al. (2009), successfully used clinically MTA and TAP in teeth with large periradicular lesion.¹⁰

Enterococcus faecalis is the most common microorganism responsible for endodontic failure. Adl et al. (2012) studied the in vitro antimicrobial ability of TAP and its components as well as calcium hydroxide mixtures against *Enterococcus faecalis*. They concluded that the triple antibiotic paste with 2% chlorhexidine would be the preferred medicament against *E. faecalis* and among its components; minocycline has the greatest antibacterial efficacy.¹¹ Sabrah et al. (2013), also concluded that TAP and double antibiotic paste (DAP) were more effective against *E. faecalis* and *P. gingivalis* as compared to Ca(OH)₂ paste.¹²

Mozayeni et al. (2014) studied the antimicrobial activity of four intracanal medicaments on *Enterococcus Faecalis*, concluded that antibacterial efficacy of the TAP and chlorhexidine gel CHX gel was better than CHX alone.¹³ Sabrah et al. (2015) investigated the antibacterial effect of various concentrations of antibiotics on biofilm of *E faecalis*, and its action on the survival of human dental pulp stem cells (DPSCs), concluded that the different concentration of intracanal medicaments has a critical role in the disinfection of the canal and to reduce the adverse effect on stem cells during the endodontic regeneration procedure.¹⁴

Traditionally, necrotic immature permanent teeth are treated with calcium hydroxide or MTA apexification. But this treatment protocol does not increase in root length or thickening of dentinal walls. These types of therapy is of longer

duration, with multiple appointments, which in turn lead to contamination of the root canal system and increased brittleness of root dentin and risk of root fracture.¹⁵ recently, various studies in the literature show the role of revascularization therapy for such type of cases. In revascularization therapy, vital pulp cells and blood clot remaining at the apical end of the root canal is utilised.¹⁶ Petrino et al. (2010) while applying revascularization protocol using a triple antibiotic paste and a coronal seal of mineral trioxide aggregate on six immature teeth with apical periodontitis discovered that all six teeth showed resolution of periapical radiolucencies and three showed root development. They further concluded that clinicians should consider the use of an anesthetic without a vasoconstrictor when trying to induce bleeding for revascularization and a collagen matrix is useful for the controlled placement of MTA.¹⁷

Gelman et al. (2012) reported successful revascularization of a necrotic immature upper left central incisor wherein the periapical lesion was healed and the apexogenesis was complete with use of TAP.¹⁸

Noy et al. (2013) reported the regenerative endodontic treatment of an immature permanent canine following infant oral mutilation. By regenerative endodontics, treatment was initiated by irrigating the root canal, followed by three weeks application of TAP dressing and creating a blood clot scaffold covered with mineral trioxide aggregate (MTA). 4 years of followup demonstrated healing of the periapical lesion.¹⁹

Tawfik et al. (2013) assesses the regenerative potential of immature teeth with necrotic pulps following revascularization in dog teeth. Except control subgroups, disinfection of root canal was done prior to revascularization using TAP. This procedure allowed the continued development of roots in teeth with necrotic pulps.²⁰ Metronidazole and ciprofloxacin can generate fibroblasts, which shows the biocompatible nature of TAP.²¹ However a study by Pereira et al. (2014) showed persistent inflammatory responses and no repair with an associated high gene expression of biomarkers and angiogenesis to the mouse subcutaneous tissue when TAP was used.²²

A study by Yadlapati et al. (2014) also showed the deleterious effect of the triple antibiotic paste

on human periodontal ligament fibroblasts and minimal effect of $\text{Ca}(\text{OH})_2$ on cell viability and production of cytokine. The TAP showed deleterious effects on HPDL viability and increased expression of the pro-inflammatory cytokine IL6.²³

TAP caused aesthetic problems leading to tooth discoloration.²⁴ A study by Nagata JY. (2014) evaluated pulp revascularization using 2 different protocols on traumatized immature teeth. They found significant discoloration of the crown in TAP group.²⁵

Kirchhoff et al. (2014) observed the discolouration of teeth with closed and open apices after placement of TAP in the pulp chamber. TAP discoloured the tooth structure, but discolouration could be reversed with sodium perborate paste.²⁶ For the removal of TAP paste, a study by Arslan et al. (2014) concluded that passive ultrasonic irrigation (PUI) with 1% NaOCl effectively removes TAP from artificial grooves in the root canal.²⁷

Regarding the effect of TAP on dentinal wall thickness, Yassen et al. (2013) studied the use of medicaments in endodontic regeneration on root fracture and microhardness of radicular dentin. He found the significance of duration and resistance to fracture. He concluded that three week application of TAP, double antibiotic paste DAP OR $\text{Ca}(\text{OH})_2$ significantly reduced the resistance to fracture of extracted teeth as compared to 1 week application.¹⁵

Prather et al. (2014) studied the role of concentration of TAP and modified MTAP on microhardness and the chemical structure of radicular dentin and found that 1 mg/mL methylcellulose-based TAP and MTAP is sufficient concentration to minimize the reduction in microhardness as compared to 1 g/ mL concentration currently used.²⁸ But a study by Yassen et al. (2014) found a reduction in hardness of dentin and increase in indentation properties of immature radicular dentin when treated with antibiotic paste followed by ethylenediaminetetraacetic acid (EDTA).²⁹

While Nerness et al. (2015) concluded that the 1g/ mL concentration of TAP used with or without ethylenediaminetetraacetic acid caused significant higher surface loss and surface roughness of radicular dentin as compared to 1mg/ mL

concentration of TAP.³⁰

Akçay et al. (2014) studied the effect of calcium hydroxide, double antibiotic paste and triple antibiotic paste on the bond strength of epoxy resin-based sealer to root canal dentin. TAP improves the bond strength of the epoxy resin-based sealer in the middle and apical thirds.³¹

Finally, there are studies which concern the bacterial resistance caused due to the use of antibiotic paste. The microorganisms from endodontically failed canals were different from that of untreated necrotic dental pulps. It was concluded that the microbial flora in the canals after endodontic failure comprised predominantly facultative anaerobes and gram-positive species. Most frequently isolated species were *E. faecalis* and showed resistance.³²

CONCLUSION

Application of Antibiotics locally within the root canal space is more effective than systemic mode of administration in endodontic procedures.

TAP has been reported to be a highly effective in reducing the microbial count of the root canal space during endodontic procedures. A Minocycline, a constituent of TAP is known to produce discoloration of the teeth when used within the root canal space during endodontic procedures.

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