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Triple Antibiotic Paste: A Review of Literature

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Abstract

'Triple antibiotic paste' (TAP) and its uses in dentistry, specifically endodontics, were the subject of this study, which examined the most recent research and ideas in these areas. The three antibiotics ciprofloxacin, metronidazole, and minocycline make up TAP. Despite the difficulties and drawbacks that research on this paste has revealed, endodontic treatments frequently use it. Applications for the paste range from essential pulp therapy to the recently proposed regimen for regeneration and revascularization. According to studies, the paste can get rid of the germs in the root canals and create the right environment for additional treatments. By eliminating several classes of obligatory and facultative gram-positive and gram-negative bacteria, this combination creates a favorable environment for healing. In situations when a regeneration protocol is used, this permits the growth, cleaning, and maybe sterilization of the root canal system, allowing for the infiltration and growth of new tissue into the radicular area. TAP can also establish a discipline in which other desired and necessary treatments can be successfully carried out. As an antibacterial intracanal drug, TAP has a variety of applications. However, the paste has shown drawbacks despite its beneficial effects.

Keywords: *TAP, Antibiotics, Endodontics.*

Introduction

Mechanical instrumentation cannot alone create a bacterial-free environment in root canals since the root canal system exhibits various and complex anatomies. On the other hand, residual necrotic tissue can hinder the effectiveness of root canal irrigants and medications as well as the ability of root canal fillings to adapt to dentin. In order to properly remove the leftover tissues from the root canal area and be able to eradicate the microbes, specific disinfection and irrigation techniques are needed.**[**1**]**

Microorganisms found in the root canal system are clearly linked to the onset and course of an endodontically generated periapical lesion.**[**2**]** Bacteria can invade and live deeply within dentin and in cementum surrounding the periapex when they are present in diseased root canals and periradicular tissues. Endodontic treatment is to get rid of the bacteria in the affected root canal and stop infection.**[**3**]** The root canal infection is regarded as a polymicrobial infection that includes both aerobic and

anaerobic microorganisms. It is doubtful that a single antibiotic could effectively sterilize the canal due to the complexity of the root canal infection. More likely, a combination would be needed to address the diverse flora encountered. The combination that appears to be most promising consists of metronidazole, ciprofloxacin, and minocycline.**[**4**]** TAP is an antibiotic combination that was created specifically to aid in the process of rejuvenation. After doing studies on its efficiency in clearing out the bacteria from the root canal, Hoshino and colleagues introduced it. As a powerful anti-microbial agent, this mixture is utilized to treat necrotic pulp in open apex teeth and has numerous other uses in the field of endodontics. **[**5,6**]** This review of literature aims to discuss properties of TAP, its composition, its various applications and indications.

Rationale of using antibiotics:

Systemic antibiotic therapy has shown to be helpful in both surgical and non-surgical dental procedures, but it also has significant drawbacks, including a variety of side effects (allergic reactions or toxicities) and the emergence of resistant strains of microorganisms. Additionally, undergoing a systemic antibiotic therapy depends on a variety of variables, such as the patient's compliance with following a specific dosage regimen, the gastrointestinal system's absorption of these medications, and their transportation through the blood circulatory system to the infected area, which implies that the area needsing the medication has a proper blood supply, which is no longer present in teeth with necrotic pulp, a pulpless and infected canal, or a root-canal infection.**[**7,8**]**

Single empirical antibiotics cannot provide a bacterial-free environment in the canal due to the polymicrobial nature of tooth infection. Additionally, non-specific antibiotic therapy may cause the normal bacterial flora to be destroyed, which would then allow any remaining virulent microorganisms to repopulate the canal. To stop the development of microbial resistance, it is crucial to utilize a combination of antibiotics against all endodontic infections.**[**9**]**

Antimicrobial Used in TAP:

In 1990, Hoshino et al. combined antibiotics in a 1:1:1 ratio, including metronidazole 500 mg, ciprofloxacin 200 mg, and minocycline 100 mg.6 In 1998, Takushige et al. utilised a 1:3:3 ratio of the aforementioned antibiotics.**[**6**]** The nitroimidazole group compound metronidazole binds to DNA and inhibits the growth of both gram positive and gram-negative anaerobes. The fluoroquinolone group of drugs includes ciprofloxacin, which inhibits DNA gyrase and aids in the eradication of gram-negative bacteria. The broad range antibiotic minocycline works by preventing the production of new proteins,

collagenases, and matrix metalloproteinases. It eliminates Spirochetes as well as gram-positive and gram-negative microbes. Since minocycline has the drawback of causing tooth discoloration, antibiotics like amoxicillin, cefaclor, cefroxadine, fosfomycin, or rokitamycin can be used as substitutes. The photo-induced response is what causes discoloration. Minocycline chelates with calcium ions to produce insoluble complexes. **[**10-12**]**

Application of TAP

Lesion Sterilization and Tissue Repair (LSTR): The LSTR is an endodontic treatment method that includes no or minimal instrumentation, followed by the administration of an antibiotic solution in a propylene glycol vehicle to clean root canal systems and peri-apical lesions. The fundamental principle of LSTR is "do not remove or touch and leave it." Caries, pulpitis, and infection of the root canal are all treated and medicated by it. LSTR's guiding principle is that the host's natural defences can restore the damage. Bacterial burden can be reduced by medicating the pulp chamber and canals to sterilize them. A 20–40% cleaning activity and debridement result from medication-assisted sterilization. Most commonly a combination of three antibiotics along with solvent macrogol and propylene glycol are used, so it is also known as three mix MP pastes. If the procedure is successful tissue repair can be expected.**[**13**]**

The clinical and radiographic success of treating primary teeth with the triple antibiotic paste was investigated by Prabhakar et al. They treated 60 teeth in two groups, and after a year, both groups had great clinical success, but a statistically significant difference was found: the pulpectomy teeth had an 83% success rate compared to the pulpotomies' 37% success rate.**[**14**]**

In 58 children aged 24 to 27 months, Trairatvorakul assessed the clinical and radiographic success rates of three mixed antibiotics used in non-instrumentation endodontic treatment of primary mandibular molars. Based on radiographic examination during a 2-year follow-up, he draws the conclusion that non-instrumentation endodontic treatment with 3-mix-MP demonstrated good clinical success but had a low success rate. Consequently, 3 Mix antibiotic therapy cannot serve as a long-term alternative to a conventional root canal treatment agent.**[**15**]**

In order to assess the clinical and radiographic success of endodontic treatment employing combinations of antibacterial medications consisting of 3 mix (group A) and ciprofloxacin, ornidazole, and minocycline (group B), Pinky et al. studied 40 infected primary teeth in 4- to 10-year-old children. The outcome revealed no statistically significant differences between the groups, indicating that these combinations had a 100% success rate in treating primary teeth that were necrosed.**[**3**]**

Apexification:

Apexification involves temporarily filling the canal with tissue up until a firm tissue barrier form at the apex. The likelihood of revascularization is eliminated because the canal space is filled, leaving no room for important tissue to proliferate into the root canal. Studies have shown that applying topical doxycycline and minocycline to avulsed, developing permanent teeth can enhance the radiographic and histological signs of revascularization. Recent studies have shown the possibility of revascularization following infection if a sterile environment is created. To promote the formation of new tissue, the canal should be filled with a resorbable matrix following disinfection. To avoid re-infection, the coronal access must be sealed in the end. **[**16-18**]**

TAP's biocompatibility has been established. Tetracycline inhibits matrix metalloproteinases and collagenases, is noncytotoxic, and raises interleukin-10 levels, an anti-inflammatory cytokine. In addition, ciprofloxacin and metronidazole can stimulate fibroblasts. **[**19-22**]**

Intra-canal Medicament:

The root canal microbiome is multi-microbial and contains actinomyces, aerobic and anaerobic bacteria, as well as other bacteria that are antibiotic-resistant. Due to the prevalence of antibiotic resistance, various antibiotics were needed to treat the polymicrobes and overcome the resistance.**[**23**]** TAP is now the most successful pharmacological combination for overcoming bacterial strain resistance. $Ca(OH)_2$ and TAP's effects were investigated by Pai et al. (2014).**[**24**]** They discovered that 3 of 20 patients with 15% $Ca(OH)_2$ experienced flare-ups between appointments. However, none of them experienced flare-ups between appointments in relation to the TAP. In a different investigation, it was discovered that TAP demonstrated superior disinfection abilities in comparison to $Ca(OH)_2$. **[**25,26**]**

In a different trial, the effectiveness of TAP in combination with other antibiotics was assessed, including amoxicillin and metronidazole, amoxicillin and clavulanic acid and metronidazole, amoxicillin and clavulanic acid and metronodazole, and amoxicillin and cloxacillin and metronodazole. In comparison to other formulations, they discovered that the TAP displayed the largest bacterial inhibitory zone. **[**27**]** Researchers looked at the antibacterial effectiveness of TAP and $Ca(OH)_2$ in conjunction with 2% chlorhexidine against E. faecalis. They discovered that $Ca(OH)_2$ combined with 2% chlorhexidine is more effective against E. faecalis than TAP. TAP could remove germs from the dentin up to a depth of 400 µm, but $Ca(OH)_2$ could only do so up to a depth of 200 µm.**[**28**]**

Revascularization:

These days, regenerative endodontics is no longer a hypothetical approach but rather a practical alternative to conventional root apexification. The biology behind this procedure involves the apical tissue cells activated due to the induced blood clot into the disinfected pulpal cavity. Thus, these apical stem cells in turn activate and helps in the formation of hard tissue inside the dentinal walls. Therefore, root canal medicaments ideally should possess good antibacterial properties and should provide favorable environment for stem cells to regenerate.

In the past, calcium hydroxide (Ca(OH)2) was frequently employed to treat immature roots and create a calcified barrier during apexification. Triple antibiotic paste (TAP) was first introduced at this period, but due to its disadvantages, such as its high pH, it was initially not employed for revascularization treatment. Combining ciprofloxacin, metronidazole, and minocycline is a common TAP during revascularization treatments and has been shown to be quite effective in treating infected root canal systems. However, other intracanal drug mixtures have also been used in studies, including those containing metronidazole and ciprofloxacin (double antibiotic paste; DAP) and metronidazole, ciprofloxacin, and cefaclor (modified triple antibiotic paste; mTAP).**[**29**]**

Conclusion

The removal of microorganisms from the root canal is essential for the endodontic procedure to be successful. Re-infection and failure can be brought on by microbes in the periapical area. The literature that is currently available makes it very evident that TAP can be used to sterilise canals and treat periapical disease. The availability of viable stem cells is what determines how well TAP works to manage immature, non-vital permanent teeth. The potential downsides of this procedure include the emergence of bacterial strains that are resistant to treatment and tooth discolouration. TAP appears to be a potential drug for revascularization and sterilisation.

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