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Triple Antibiotic Paste as an Intracanal Medicament in Root Canal Treatment

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Abstract: *Intracanal medicaments in the fields of endodontics are important for the disinfection of the root canal after cleaning and shaping. Since irrigation from chemicals such as sodium hypochlorite may not disinfect the root canal fully, medicaments can be used. The mixture of ciprofloxacin, metronidazole, and minocycline into Triple Antibiotic Paste (TAP) in a 1:1:1 ratio has been used as an alternative to the most common intracanal medicament, calcium hydroxide. This article aims to explore how TAP contributes to the success of root canal treatment, and the mechanisms of action of each antibiotic included. By inhibiting DNA replication through the inhibition of DNA topoisomerase and DNA-gyrase of bacteria by ciprofloxacin, inhibiting protein synthesis by metronidazole, and inhibition of protein synthesis and the stimulation of osteoblastic cells by minocycline, TAP fulfills the roles of an intracanal medicament. It is a healthy alternative as a root disinfectant and is effective through its antibacterial properties.*

Keywords: *Endodontics, Root Canal Treatment, Dentistry, Intracanal Medicament, Triple Antibiotic Paste, Oral Health, Ciprofloxacin, Minocycline, Metronidazole*

I. INTRODUCTION

Endodontic treatment involves the elimination of bacteria and the preservation of the tooth. One of the most effective methods of sterilizing the root canal system is using an intracanal medicament during endodontic therapy, also known as root canal treatment (RCT). After accessing the root canal and commonly using sodium hypochlorite as irrigation, intracanal medicaments such as calcium hydroxide can be used. This will in turn eliminate substances and bacteria through their antibacterial properties. Alternatives such as triple antibiotic paste (TAP) can be used based on the environment and if other medicaments do not fulfill their purpose. Additionally, these compounds have standards in order to be used during endodontic procedures. Malu et al. described the conditions of an intracanal medicament, which included being effective and biocompatible, non irritating when applied, and able to treat damaged tissue while bringing a positive, lasting effect over periods of time [1]. These standards can be seen when using all usable intracanal medicaments like TAP, which is especially effective for weeping canals, dressing leakages, and aiding with tissue debris.

II. TRIPLE ANTIBIOTIC PASTE

A. Components

TAP is composed of the antibiotics metronidazole, ciprofloxacin, and minocycline. It can be made by combining the three antibiotics in a 1:1:1 ratio, along with a Macrogol and Propylene Glycol Paste (MP) [1]. It would include 33% of metronidazole, 33% of ciprofloxacin, and 34% of minocycline. MP, when combined with different pastes, serves to increase penetration into the dentinal tubules [2]. However, there are many methods to create TAP, including mixing it with a 1:3:3 ratio of ciprofloxacin, metronidazole, and minocycline, and also replacing MP with a different substance. The different concentrations and materials used may have an effect on restorative endodontic success. Dengre et al. compared TAP mixed with MP, aloe vera, and distilled water, and determined that aloe vera had achieved the highest clinical success compared to the other methods [3]. Nevertheless, all three solutions presented high success rates. It was suggested that aloe vera had anti-inflammatory, antifungal, and antibacterial properties which gave it an edge. Saline can also be mixed with the three antibiotics, showing that TAP is versatile through different combinations.

B. Mechanism of Action of Metronidazole

The presence of both aerobic and anaerobic bacteria prompts the use of a combination of antibiotics. This suggested that not one single drug could eliminate all bacteria, but it did prompt metronidazole to be the first antibiotic used [4]. It is a nitroimidazole compound seen to have a strong effect on protozoa, which are parasitic eukaryotes, and anaerobic bacteria, which survive and grow without the presence of oxygen.

Metronidazole is commonly used for anaerobic bacterial infections and protozoal infections. Connor B. Weir and Jacqueline K. Le determined that metronidazole first diffuses through the cell membrane of both anaerobic and aerobic bacteria, but only has antibacterial effects towards anaerobes [5]. From there, intracellular transport proteins alter the chemical structure of pyruvate-ferredoxin oxidoreductase through reductive activation. Pyruvate-ferredoxin oxidoreductase is an enzyme used in anaerobic bacterial metabolism [6]. Then, cytotoxic particles affect the host cell DNA, causing strand breakages and destroying the DNA helix [5]. Lastly, the cytotoxic particles are broken down.

Metronidazole can also disinfect lesions and is effective in the deep layers of lesions [7]. Since the root canal can be filled with many types of bacterial flora, other drugs can be used to be more effective or to completely disinfect it, working together to fulfill the purpose of an intracanal medicament.

C. Mechanism of Action of Ciprofloxacin

Ciprofloxacin alone is commonly used to treat pneumonia, prostatitis, and many infections including urinary tract infection [8]. It is part of the fluoroquinolone class of drugs and is most effective towards gram-negative bacteria. However, it still has effectiveness towards gram-positive bacteria. By inhibiting the enzymes DNA topoisomerase and DNA-gyrase, DNA replication inside bacteria is inhibited. TAP has both bactericidal and bacteriostatic properties [4]. With the combination of two other antibiotics, ciprofloxacin gives TAP more versatile functions. Metronidazole and ciprofloxacin are the bactericidal agents, while minocycline is the bacteriostatic agent. This allows for successful pulp revascularization. Metronidazole and ciprofloxacin also generate fibroblasts, which is important for repair and connection of the different parts of the tooth

D. Mechanism of Action of Minocycline

The last antibiotic, minocycline, is in the tetracycline class of antibiotics [9]. Many antibiotics in this class, including minocycline, contain anti-infectious properties. They have anti-inflammatory as well as immunomodulatory effects. Minocycline's bacteriostatic process includes preventing protein synthesis. By binding to the 30S subunit, it stops the elongation of the amino acid chain [9]. The tRNA which brings in the amino acids cannot function. Another positive benefit of minocycline is the improvement of revascularization of immature teeth [4]. However, minocycline may cause tooth discoloration. Using other medicaments such as amoxicillin and cefaclor may fix this limitation [1].

III. PULP REVASCULARIZATION AND REGENERATION

When TAP disinfects the pulp using its many functions through the three antibiotics, chances for pulp revascularization and regeneration may occur. Maria do Couto et al. investigated pulp revascularization using TAP, and concluded that pulp revascularization was effective for incomplete root formations, through asymptomatic results and efficient periapical integrity [10]. Factors such as the absence of different symptoms, periapical healing, apical closure, reduction of apical diameter, and an increase of root length were evaluated.

For most studies, patients were asymptomatic through a one, twelve, and eighteen month follow up period using pulp revascularization procedures and TAP.

TAP has also shown to increase dentin thickness, increasing it the most compared to calcium hydroxide and formocresol [11]. By inducing stem cells, TAP benefits the regeneration procedures, making them more effective. Additionally, using TAP and sodium hypochlorite lessened the chances for a periapical lesion, while increasing root length.

IV. CONCLUSION

Triple antibiotic paste is a proper intracanal medicament that uses the functions of metronidazole, ciprofloxacin, and minocycline in root canal treatment. By inhibiting different processes and enzymes through the three antibiotics, TAP disinfects the affected regions and helps root canal treatment and other procedures such as the regeneration procedures to work effectively. One disadvantage of using TAP is the tooth discoloration by minocycline. Other compounds may also be used, such as calcium hydroxide. Nevertheless, triple antibiotic paste is a satisfactory intracanal medicament that may be used as an alternative to other medicaments based on the specific situation.

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