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Review Article

Components and outcome of triple antibiotic paste and its application in endodontic infections

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ABSTRACT

In the field of endodontic therapies, the use of antibiotics, especially in the form of root canal medications, plays a pivotal role in ensuring successful treatment outcomes. This review examines the role of triple antibiotic paste (TAP) in such therapies, delving into its composition, application, and effects on endodontic infections. TAP, a combination of metronidazole, ciprofloxacin, and minocycline, targets the diverse microbial flora in odontogenic infections. Its local application within the root canal space proves more effective than systemic administration, significantly reducing microbial count and aiding in tissue regeneration and disinfection. However, the use of TAP is not without challenges, as it can cause tooth discoloration, particularly due to minocycline, and raise concerns about antibiotic resistance and long-term biocompatibility. This study, conducted through a comprehensive literature search, evaluates the efficacy of TAP, its impact on tooth structure, and its role in maintaining the vitality of diseased pulp. The findings highlight TAP's significant role in endodontic treatments, emphasizing its benefits in achieving therapeutic goals while acknowledging the need for careful consideration of its drawbacks.

Keywords: Triple antibiotic paste, TAP, Disinfection, Minocycline, Metronidazole, Ciprofloxacin

INTRODUCTION

Endodontic therapies hold a key position in dental care, enabling the preservation and functionality of teeth within the mouth.[1] Various techniques, ranging from the classical step-back method to modern practices, have demonstrated mixed levels of effectiveness and setbacks in treating different pulp-periapical states.[2]

Over time, the use of root canal medications, especially antibiotics, has become increasingly crucial and central in ensuring positive treatment results.[3] Antibiotics,

discovered in 1928, did not become a regular part of medical treatment until 1940, as noted by Abbott in 2000.[4]

In 1951, Grossman was the first to document the employment of a polyantibiotic paste in the field of endodontics.[5]Antibiotic therapy is now integral to a wide range of medical treatments, serving as a primary defense against various microorganisms.[6] Many different formulations of antibiotics are used for the treatment and prevention of active infections.[7]

Antibiotics are classified in multiple ways, some are grouped into subclasses like cillins, mycins, and porines. Alternatively, they can be categorized based on the types of bacteria they target, such as those effective against gram-positive and gram-negative bacteria, or those aimed at strict and facultative aerobes and anaerobes.[6] Each antibiotic, including derivatives of penicillin, has unique characteristics and effects, like amoxicillin differing from ampicillin and penicillin V in its bacterial range and prescription method. Similarly, clindamycin, although in the same class, differs from erythromycin in its microbial targets. Cillins typically target gram-positive bacteria, whereas antibiotics like metronidazole are effective against gram-negative bacteria.

When dealing with various types of bacteria, it is common to use a mix of antibiotics, a method also frequently employed in dentistry.[8] Odontogenic infections, originating from tooth structures, require multiple antibiotics to address the diverse organisms responsible for these lesions.[9] Hence, antibiotics have become indispensable in dental care, used for treating various diseases and for prophylaxis.[10] Successful treatment of odontogenic lesions, especially those related to endodontic issues, relies heavily on effective decontamination. While endodontic instruments and irritants are primary tools for decontamination and disinfection, in cases with a high concentration of microorganisms, intracanal medications become crucial. These medications, placed temporarily in the root canals, aim to establish a sterile environment by eliminating pathogenic microbes.[11]

In cases of chronic infection, the complex anatomy of root canals protects pathogens from irrigation and instrumentation. This complexity necessitates a combination of drugs, commonly known as the triple antibiotic paste (TAP).

TAP is effective against a broad spectrum of bacteria, including obligatory or facultative, gram-positive or gram-negative types. It disinfects and sterilizes the root canal system, clearing microbial colonization and facilitating tissue regeneration in young, immature teeth.[11]

Intracanal medicaments should meet several ideal requirements, such as not being irritating, not causing staining, being biocompatible, effective for extended periods, and being adept at repairing peri-radicular tissue. TAP excels in these areas, particularly in treating weeping canals, neutralizing tissue debris, eradicating residual microorganisms, and preventing dressing leaks.

METHODS

This study was based on a comprehensive literature search conducted on 29 November 2023, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the components and outcomes of triple antibiotic paste and its application in endodontic infections. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

TAP is an intracanal medicament comprising a combination of three antibiotics: metronidazole, ciprofloxacin, and minocycline, mixed in an equal ratio of 1:1:1. This formulation is used in endodontics due to the inadequacy of a single antibiotic to eliminate all types of polymicrobial flora. TAP effectively disinfects the area, ensuring thorough cleansing. In endodontic regenerative procedures, TAP demonstrates remarkable antibacterial properties. Its combination of three distinct antibiotics significantly reduces the likelihood of microbial resistance. Moreover, TAP not only serves as an antimicrobial agent but also promotes regeneration. It facilitates the growth of stem cells in the apical region of the tooth, aiding in the formation of an apical barrier.[11] This dual action of disinfection and regeneration enhancement makes TAP a valuable tool in endodontic treatments.

Components of TAP

The components of TAP each have distinct properties and functions.

Minocycline

As a broad-spectrum antibiotic, minocycline is effective against a wide variety of bacteria. It is bacteriostatic, meaning it inhibits bacterial growth without necessarily killing the bacteria directly. This action prevents the release of antigenic products in the infected area. Minocycline is not only an effective antibacterial agent but also promotes regeneration. It inhibits clastic cells and collagenase activity, facilitating the growth of healthy cells and aiding in the regenerative process.[12,13]

Metronidazole

This chemical, part of the nitroimidazole class, shows a broad spectrum of activity against anaerobic bacteria and protozoa. Metronidazole is particularly effective against

anaerobic bacteria, including anaerobic cocci, and is used in both local and systemic forms. It works by penetrating bacterial membranes and binding to their DNA, disrupting the helical structure and quickly causing cell death. It outperforms calcium hydroxide against certain strains and is effective in inhibiting the growth of all obligatory anaerobes tested.[11,14]

Ciprofloxacin

A second-generation fluoroquinolone antibiotic, ciprofloxacin is used to treat various bacterial infections, including those causing stomach pain, diarrhea, and urinary tract infections. Its high tissue penetration makes it effective in both oral and intravenous forms. Ciprofloxacin, like other fluoroquinolones, is chosen for its ability to reach high concentrations in tissues.[15] Each of these components contributes to TAP's effectiveness in endodontic treatments, offering a broad spectrum of antibacterial activity and aiding in tissue regeneration.

The objective behind combining antibiotics in endodontic treatments, such as in the TAP, arises from the limitations of conventional antibiotics when used alone. Single antibiotics often fail to create a completely bacteria-free zone within the canal due to the complex and diverse nature of the microbiota involved in tooth infections.

Additionally, using a single antibiotic can disrupt the native bacterial flora in the canal, potentially leading to more aggressive infections. Therefore, to combat microbial resistance and effectively treat endodontic illnesses, a mixture of antibiotics is employed. This approach increases the spectrum of antimicrobial activity, ensuring a more comprehensive treatment of the diverse microbial population in tooth infections.[4,19,20]

Table 1: Comparison of two preparation methods for TAP including concentrations and additional components.[16-18]

Preparation method	Ciprofloxacin	Metronidazole	Minocycline	Additional components	Concentration
Method 1	33%	33%	34%	Macrogol and propylene glycol paste	0.1-1.0 mg/ml
Method 2	1 part	3 parts	3 parts	Not specified in original text	Not specified

Mechanism of action

The efficacy of TAP in endodontic therapy lies in its broad-spectrum antimicrobial activity. By combining three antibiotics with different targets and modes of action, TAP effectively disrupts the microbial ecosystem within the root canal, thereby reducing the bacterial load and aiding in the resolution of infection. This is particularly important in cases where a single antibiotic might not be effective due to the presence of bacteria with varying sensitivities and resistance patterns.[11]

Clinical efficacy of TAP

The use of TAP has been reported to be successful in controlling root canal pathogens. Studies have shown that TAP can significantly reduce bacterial counts in infected root canals, leading to improved treatment outcomes. Its use has been particularly noted in the management of non-vital young permanent teeth, where it helps in disinfection and subsequent healing and regeneration of the tooth structure.[21]

Effect of TAP on tooth structure

TAP has several impacts on tooth structure, notably on dentin, tooth color, and stem cells.

Impact on dentin

Research has shown that TAP can lead to demineralization in dentin, resulting in alterations in its mechanical characteristics. This change often manifests as increased brittleness in the tooth structure. A notable observation is the significant reduction in dentin microhardness, especially at 500 µm from the pulp-dentin interface, when TAP is applied at a higher concentration of 1 g/ml. This effect is primarily attributed to minocycline, a component of TAP, which induces calcium chelation from the dentin.[22]

Influence on tooth color

A notable disadvantage of using TAP is tooth discoloration, largely due to the presence of minocycline. This issue, however, can be mitigated through alternative medicaments such as amoxicillin and cefaclor. Additionally, the application of dentin bonding agents has been found to effectively limit tooth discoloration to a considerable extent.[23]

Effect on stem cells

TAP plays a pivotal role in regenerative endodontic procedures. It is important to maintain the health of apical stem cells, thereby creating a microbial-free environment conducive to the proliferation and regeneration of these cells.

Although materials like calcium hydroxide have been used for similar purposes, their toxic effects on the apical papilla often discourage their use. TAP, in contrast, successfully addresses this concern. It is recognized as an optimal intracanal disinfecting material, given its superior properties and its ability to facilitate a conducive environment for stem cell regeneration and health.[24]

Applications

TAP, with its potent antimicrobial properties, has a wide range of applications in endodontics. It is primarily utilized to maintain the vitality of the pulp, aiding in its regeneration and revascularization. This makes TAP not just a disinfectant but also a key player in the process of revitalizing diseased pulp tissue.[25] The application of TAP, often in conjunction with calcium hydroxide, has been observed to result in increased root length more frequently than non-surgical root canal treatments or mineral trioxide aggregate (MTA) apexification.

Revascularization, a crucial process in endodontic treatment, involves inducing bleeding in the root canal to transport stem cells from the periapical region. This aids in elongating the root. TAP's antimicrobial action is particularly effective against *Enterococcus faecalis*, a prevalent microbe in root canal infections. Its dual effect - combating microbial infection and facilitating stem cell proliferation- contributes significantly to root lengthening.[26,27] Another important application of TAP is as an intracanal medicament in various clinical scenarios. It is effectively used in the treatment of periapical lesions, external inflammatory root resorption, root fractures, and treatment flare-ups. Flare-ups, a common complication in endodontic therapy, are characterized by severe pain and swelling following a treatment session, often leading to an unplanned additional appointment for acute management.[28]

TAP's role in the regeneration and revascularization of the pulp is particularly noteworthy. By preserving pulp vitality, TAP helps in regenerating and revascularizing diseased pulp tissues, thereby contributing to the overall success of endodontic treatments. This regenerative capability is crucial, especially in cases where root development is incomplete or has been compromised due to infection or other factors. In the case of root fractures and external inflammatory root resorption, TAP's antimicrobial action plays a vital role in managing infections and preventing further deterioration of the condition. Its ability to effectively eradicate a range of microbes, including the stubborn *Enterococcus faecalis*, makes it a reliable choice in these complex clinical situations.

Furthermore, TAP's application extends to managing treatment flare-ups, a relatively frequent occurrence in endodontic procedures. These flare-ups, marked by sudden and intense pain and swelling, can significantly impact the patient's comfort and the treatment's progress. TAP's efficacy in quickly managing microbial infections helps in controlling these symptoms and preventing further complications.

Use of TAP in the treatment of primary teeth

The application of TAP in the treatment of primary teeth has shown significant results, as highlighted in various studies. Nakornchai et al. reported that TAP, along with Vitapex® (J. Morita Corporation, Kyoto City, Japan), achieved a high success rate in the root canal treatment of infected primary teeth, with TAP specifically showing a success rate of 96%.[29]

In a study that examined the effectiveness of TAP throughout 24-27 months post-surgery, researchers focused on both clinical and radiographic outcomes in non-instrumentation endodontic treatment of primary mandibular molars. While the success rate based on a two-year radiographic study was low, the overall findings indicated a high success rate for this approach.[30] Further research conducted by Takushige et al explored the impact of TAP on the clinical outcomes of lesion sterilization and tissue repair treatment in primary teeth with peri-radicular lesions.

After the treatment, clinical symptoms such as sinus tracts, gingival swelling, and dull soreness were notably alleviated. Additionally, the teeth that underwent successful treatment with TAP not only appeared normal on radiographs but also erupted normally.[31,32] These studies underscore the effectiveness of TAP in treating infections in primary teeth, particularly in non-instrumentation endodontic procedures. The high success rates and positive clinical and radiographic outcomes demonstrate TAP's potential as a valuable treatment option in pediatric dentistry. The ability of TAP to effectively sterilize lesions and promote tissue repair, as well as its high success rate in clinical applications, make it a noteworthy choice for endodontic treatment in primary teeth.

Advantages of TAP

TAP offers significant benefits in endodontic therapy. Its primary advantage lies in its ability to concentrate high levels of antibiotics directly at the infection site, enhancing antimicrobial effectiveness while reducing systemic impact.[21] This targeted application is vital for achieving therapeutic goals without the side effects typically associated with systemic antibiotics. Additionally, TAP effectively creates a conducive environment for tissue regeneration and disinfection, further underlining its importance in endodontic treatments.[33]

Limitations and challenges

Despite its benefits, the use of TAP is not without challenges. There are concerns about potential tooth discoloration, particularly due to the presence of minocycline. Additionally, the risk of developing antibiotic resistance cannot be overlooked. The long-term effects of TAP on the surrounding tissues and its biocompatibility are also areas of ongoing research and debate.[6]

Another limitation related to dentin demineralization and tooth discoloration. The choice of TAP, therefore, involves

a careful consideration of its effects on the mechanical properties of dentin, the aesthetic aspects of tooth color, and the biological implications on stem cell health and regeneration.

Future directions in research

Future research on TAP and its alternatives in endodontic therapy is crucial. This includes studying the long-term effects of TAP on tooth structure and surrounding tissues, exploring ways to mitigate its potential drawbacks, and developing new formulations that can provide similar or superior efficacy without the associated risks.

CONCLUSION

Local application of antibiotics in the root canal area is more efficient than systemic administration for endodontic treatments. TAP is notably effective in decreasing the microbial load in the root canal during these procedures and increasing the success rate of endodontic treatments. However, minocycline, one of the components of TAP, can cause tooth discoloration when applied within the root canal space in endodontic processes.

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