Original Article

Triple Antibiotic Paste –Roles And Applications In Pediatric Dentistry

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Abstract

Triple Antibiotic Paste(TAP) is a combination of 3 antibiotics, ciprofloxacin, metronidazole, and minocycline. Despite the problems and pitfalls research pertaining to this paste has unveiled, it has been vastly used in endodontic treatments. The paste's applications vary, from vital pulp therapy to the recently introduced regeneration and revascularisation protocol. Studies have shown that the paste can eliminate the root canal microorganisms and prepare an appropriate matrix for further treatments. This combination is able to remove diverse groups of obligate and facultative gram-positive and gram-negative bacteria, providing an environment for healing. In regeneration protocol cases, this allows the development, disinfection, and possible sterilization of the root canal system, so that new tissue can infiltrate and grow into the radicular area. Moreover, TAP is capable of creating a discipline in which other wanted and needed treatments can be successfully performed. In conclusion, TAP, as an antibacterial intracanal medication, has diverse uses.

Key words-Antibiotics,Endodontics,Pediatric endodontics,Triple antibiotic paste

INTRODUCTION

Endodontic treatments are one of the most important and premiere therapies in the world of dentistry; they permit proper tooth function and maintain the dental structure in the oral cavity. Gradually, and as an adjunct to clinical approaches, root canal medicaments, particularly antibiotics, started to reveal their indispensable significance and pivotal rule in achieving successful outcomes .[1] Odontogenic infections originate from the dental structure, and like any other infections in our body they engage a huge number of different microbes and microorganisms .[2] Therefore, to confront an odontogenic derived infection, combinations of drugs particularly antibiotics are needed to combat the microbiota responsible for creating the lesion. That is why many antibiotics have been investigated, studied, and used to control and defeat dental infections .[3] The very first use of an antibiotic in endodontics dates back to 1951, when Grossman used a poly-antibiotic formula known as PBSC, a paste in a silicone vehicle and a combination of penicillin, bacitracin, streptomycin, and caprylate sodium . PBSC contained penicillin to affect gram-positive organisms, bacitracin to target penicillin-resistant strains, streptomycin for gram-negative organisms, and sodium caprylate for yeasts.[4] The clinical assessment of PBSC showed therapeutic effects; nevertheless, the formula was not very effective against anaerobic microorganisms that play a pivotal role in endodontic diseases. As a consequence, and in addition to the risk of sensitization and allergy to penicillin, the USA Food and Drug Administration banned PBSC for endodontic use in 1975 .[5] In 2006, the American Association of Endodontists introduced an article regarding several antibiotics for endodontic infections to control root canal microbiota which appear to have a key role in the pathogenesis and progression of the pulp and periapical pathosis.[6]

REVIEW

The very first aim of endodontic treatments is to eliminate as many bacteria as possible from the root canal system and create an environment in which no remaining microorganisms can survive. Ideally, this can only be obtained through the use of a combination of aseptic treatment techniques, chemo-mechanical preparation of the root canal, antimicrobial irrigation, and intracanal medicaments.[7] Approximately 50 percent of root canal peripherals and ramifications may remain uninstrumented during preparation of the root canal. In this condition, the remaining necrotic tissues may act as a nutrition source for the surviving bacteria .[8] Thorough and systemic mechanical instrumentation, irrigation, and use of inter-

appointment medication can perhaps reduce this phenomenon. Medicaments can play an important role in the preparation of the root canal for further therapies, for example in necrotic pulps and active exudation. Calcium hydroxide has long been used as an inseparable part of root canal treatment in necrotic cases, resulting in less signs and symptoms.[9] Traditionally, calcium hydroxide has been used in open-apex teeth with necrotic pulp tissues for inducing a bridge and preparing the root canal space for forthcoming therapies. Without the use of inter-appointment intracanal medications, such successful results are far-fetched .[10]

The type of intracanal medication depends upon the precise diagnosis of the tooth condition, a thorough knowledge of the type of microorganisms involved, and finally, their mechanisms of growth and survival. The presence of bacteria within the root canal is the main factor of endodontic disease, and therefore the use of an antimicrobial agent is essential. Many forms of intracanal medicaments, apart from antibiotics and calcium hydroxide have been used in an attempt to accomplish the above aim. These mainly include chlorhexidine and ethylenediaminetetraacetic acid. [11]Currently, the common antibiotic-containing commercial pastes are Ledermix (Lederle Pharmaceuticals, Wolfratshausen, Germany) and Septomixine Forte (Septodont, Saint-Maur, France). Both preparations have corticosteroids as anti-inflammatory agents. However, neither of these pastes can be considered suitable for use against endodontic microbiota owing to their inappropriate spectrum of activity.[12] Recently, another combination of antibiotics, called 'triple antibiotic paste' (TAP) was introduced especially for the regeneration and revascularization protocol and the treatment of open apex teeth with necrotic pulp. This material has also shown other applications in endodontics. Initially, TAP was largely developed by Hoshino and colleagues, who investigated the effectiveness of the paste on the removal of microorganisms from the root canals. [13]Researchers have also used TAP *in vitro* to disinfect *Escherichia coli*-infected dentine. Later, particular attention was given to the antibiotic paste and its effect against microorganisms present in carious dentine and infected pulp. The outcome showed excellent results in the eradication of the bacteria from the radicular system.[14]

TAP is a combination of ciprofloxacin, metronidazole and minocycline. Metronidazole, as a nitroimidazole compound, is particularly toxic to anaerobes and is considered an antimicrobial agent against protozoa and anaerobic bacteria. Minocycline is bacteriostatic and shows activity against gram-positive and gram-negative bacteria. It also causes an increase in the amount of interleukin-10, which is an inflammatory cytokine. Moreover, ciprofloxacin — as a synthetic fluoroquinolone — possesses fast bactericidal action and exhibits high antimicrobial activity against gram-negative bacteria, whilst limited activity against gram-positive ones. Many anaerobic bacteria are resistant to ciprofloxacin. Hence, it is often used with metronidazole in treating mixed infections to compensate for its limited scope. Therefore, TAP can affect gram-negative, gram-positive, and anaerobic bacteria, and this combination can be effective against odontogenic microorganisms .[15,16]

If the TAP is to be used, ciprofloxacin, metronidazole, and minocycline should be mixed equally (1:1:1) to a final concentration of 0.1–1.0 mg/mL

Applications of TAP in endodontics[17]

The applications of TAP in endodontics can be considered as follows:

1. In the regeneration and revascularization protocol of the pulp
2. As an intracanal medicament for the treatment of
   1) Periapical lesions
   2) External inflammatory root resorption
   3) Root fracture
   4) Primary teeth
3. As an intracanal agent to control flare-ups
4. As a medicated sealer (to prevent possible re-infection)
5. As an additive to gutta-percha points in root canal obturation (known as medicated gutta-percha points)
6. As an intracanal medicament loaded on a scaffold

Use in Pediatric Dentistry

Previous research in pediatric dentistry has illustrated that TAP can be used in a very effective way with good clinical success in primary teeth .[18] However, intracanal medication should not replace the instrumentation phase since the antibiotic agents alone cannot eradicate canal infection in long term. In these studies, non-instrumentation endodontic treatment 'Lesion Sterilization and Tissue Repair' and the triple antibiotic the paste were used .Few authors have utilised the Triple antibiotics paste and have got good results.[19]

Sato *et al*. experimented with these drug combination *in vitro* to show its effectiveness in the deep caries, necrosed pulp, and infected root canals of primary teeth and found to be very effective.[20]

Few years later, Hoshino *et al*. found that a combination of ciprofloxacin, metronidazole, and minocycline with a dilution 25 gm/ml of paste has ability to decontaminate infected root canal *in vitro*. Proceeding further, Banchs and Trope suggested that this method may not be suitable for determining whether combinations of drugs can kill all the bacteria in

a flora.[21] On the other hand, Ozan and Er reported endodontic treatment of a large cyst like periradicular lesion using a combination of antimicrobial drugs.

Akgun advocated the use of TAP for a traumatized immature tooth with a periapical lesion. Literature also reveals that non vital teeth with immature roots were treated with antibiotic pastes. [22]

Jaya *et al*. evaluated and compared the clinical and radiographic effectiveness of metronidazole and tinidazole in two groups of patients with primary teeth and found to be very effective with no significant difference between the two groups.[23]

Tinidazole is a second-generation synthetic nitroimidazole group of drug and is more effective than metronidazole in anaerobic infections and produces fewer and milder side effects Divya and Retnakumari conducted a study of 3 cases to determine the capability of the TAP to eliminate causative bacteria from lesions and to augment the host's natural recovery process to repair the damaged tissue. In the treatment process, both softened dentin and carious dentin can be intentionally left so that an inflamed pulp with spontaneous pain will recover after LSTR treatment.[24]

Nanda *et al*. selected forty necrosed primary molars from healthy children and divided them into two groups. The first group was treated with metronidazole paste and the second group with ornidazole paste. The result showed that both the antibacterial pastes can be used effectively in endodontic treatment of necrosed primary teeth.[25]

Method of Preparation

The antibiotic paste should be freshly prepared before use. A clean mortar pestle is used for mixing. The three antibiotics ciprofloxacin, metronidazole, and minocycline powder are dispensed and mixed with a ratio of 1:3:3. Then, equal amount of propylene glycol is added to form a creamy paste. Extra paste can be stored in air-tight container for future use. However, the loss of translucency of the paste indicates contamination and it should be discarded.[26,27]

Drawback and modifications

The most important drawback is the tooth discoloration after treatment studies, which indicated that TAP was associated with the highest amount of discoloration as compared to other medicaments and control group, which was related to of minocycline. Different medicament replacements, such as amoxicillin and Cefaclor (a member of the second-generation cephalosporins), have been used to prevent the problem.[28] In addition to avoid the discoloration dentin bonding agent (resin) is used to avoid penetration of minocycline and to avoid discoloration, tooth bleaching procedure is used to reverse the discoloration. An investigation carried to find the antibacterial efficacy and discoloration activity of TAP, Augmentin, and tigecycline. It concluded that the TAP, augmentin, and tigecycline reduced bacterial growth significantly with minimal discoloratio. Evaluation of the discoloration induced by two TAPs (TAP 1 [metronidazole + ciprofloxacin + cefaclor] and TAP 2 [metronidazole + ciprofloxacin + minocycline]) when used at different depth levels. TAP 1 and TAP 2 both showed an increased discoloration, whereas greater discoloration was seen with TAP 2, containing minocycline. At greater depths, where the more thick temporary restoration was used, had shown less discoloration.[29,30]

CONCLUSION

If endodontics is to succeed, root canal microbiota should be properly reduced. Endodontic treatments rely mainly upon the elimination and possible eradication of the involved microbiota and their various virulent features from the root canal system. Biomechanical instrumentation, though an essential step, does not always provide such an environment in the root canal system. Non-instrumentation methods such as tooth repair and strategies towards maintaining a situation for regeneration and revascularization of the pulp should be considered, in which local use of drugs, particularly antibiotics, has shown their significance.

Amongst the combination of antibiotics, TAP, owing to its effectiveness on different microorganisms and its diverse applications and triumphs, is of particular interest in endodontics. However, development of resistant bacterial strains and tooth discoloration are some of its pitfalls. Nonetheless, TAP seems to be a successful combination of drugs in root canal disinfection/sterilization and pulp regeneration and revascularization protocol.

REFERENCES

1. Bhanderi S. The importance of endodontics - continuing education at the FGDP (UK) Prim Dent J. 2014;3:14.
2. Hargreaves KM, Cohen S. Cohen's pathways of the pulp. 10th ed. St. Louis (MO): Mosby; 2011
3. Mohammadi Z. Antibiotics as intracanal medicaments: a review. J Calif Dent Assoc. 2009;37:98–108.
4. Mouton Y. The antibiotics. Role of antibiotics in the prevention of infectious diseases. Lille Med. 1975;20:914–915.
5. Enzler MJ, Berbari E, Osmon DR. Antimicrobial prophylaxis in adults. Mayo Clin Proc. 2011;86:686–701
6. Grossman LI. The use of disinfectants and antibiotics in endodontic practice. J Am Dent Assoc. 1956;53:411–415.
7. Busse HJ, Denner EB, Lubitz W. Classification and identification of bacteria: current approaches to an old problem. Overview of methods used in bacterial systematics. J Biotechnol. 1996;47:3–38
8. Busse HJ, Denner EB, Lubitz W. Classification and identification of bacteria: current approaches to an old problem. Overview of methods used in bacterial systematics. J Biotechnol. 1996;47:3–38
9. Wynn RL, Bergman SA, Meiller TF, Crossley HL. Antibiotics in treating oral-facial infections of odontogenic origin: an update. Gen Dent. 2001;49:238–244

10. Bansal R, Jain A. Overview on the current antibiotic containing agents used in endodontics. N Am J Med Sci. 2014;6:351–358
11. American Association of Endodontists. Antibiotics and the treatment of endodontic infections. Chicago (IL): American Association of Endodontists; 2006.
12. Mohammadi Z, Abbott PV. On the local applications of antibiotics and antibiotic-based agents in endodontics and dental traumatology. Int Endod J. 2009;42:555–567
13. Murvindran V, James DR. Antibiotics as an intracanal medicament in endodontics. J Pharm Sci Res. 2014;6:297–301
14. Love RM. Enterococcus faecalis--a mechanism for its role in endodontic failure. Int Endod J. 2001;34:399–405.
15. Peters OA. Current challenges and concepts in the preparation of root canal systems: a review. J Endod. 2004;30:559–567.
16. Park HB, Lee BN, Hwang YC, Hwang IN, Oh WM, Chang HS. Treatment of non-vital immature teeth with amoxicillin-containing triple antibiotic paste resulting in apexification. Restor Dent Endod. 2015;40:322–327.
17. Huang GT. Apexification: the beginning of its end. Int Endod J. 2009;42:855–866.
18. Longman LP, Preston AJ, Martin MV, Wilson NH. Endodontics in the adult patient: the role of antibiotics. J Dent. 2000;28:539–548
19. Chu FC, Leung WK, Tsang PC, Chow TW, Samaranayake LP. Identification of cultivable microorganisms from root canals with apical periodontitis following two-visit endodontic treatment with antibiotics/steroid or calcium hydroxide dressings. J Endod. 2006;32:17–23
20. Banchs F, Trope M. Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? J Endod. 2004;30:196–200
21. Sato T, Hoshino E, Uematsu H, Noda T.In vitro antimicrobial susceptibility to combinations of drugs on bacteria from carious and endodontic lesions of human deciduous teeth. Oral Microbiol Immunol 1993;8:172-6
22. Akgun OM, Altun C, Guven G. Use of triple antibiotic paste as a disinfectant for a traumatized immature tooth with a periapical lesion: A case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:e62-
23. Jaya AR, Praveen P, Anantharaj A, Venkataraghavan K, Rani PS.In vivo evaluation of lesion sterilization and tissue repair in primary teeth pulp therapy using two antibiotic drug combinations. J Clin Pediatr Dent 2012;37:189-91.
24. Divya S, Retnakumari N. Lesion sterilization and tissue repair in primary teeth with periapical pathosis – A case series. J Dent Med Sci 2014;3:7-11
25. Nanda R, Koul M, Srivastava S, Upadhyay V, Dwivedi R. Clinical evaluation of 3 mix and other mix in non-instrumental endodontic treatment of necrosed primary teeth. J Oral Biol Craniofac Res 2014;4:114-9
26. Thibodeau B, Teixeira F, Yamauchi M, Caplan DJ, Trope M. Pulp revascularization of immature dog teeth with apical periodontitis. J Endod. 2007;33:680–689.
27. Bose R, Nummikoski P, Hargreaves K. A retrospective evaluation of radiographic outcomes in immature teeth with necrotic root canal systems treated with regenerative endodontic procedures. J Endod. 2009;35:1343–1349.
28. Parasuraman VR, Muljibhai BS. 3Mix- MP in Endodontics – An overview. IOSR J Dent Med Sci. 2012;3:36–45.
29. Wigler R, Kaufman AY, Lin S, Steinbock N, Hazan-Molina H, Torneck CD. Revascularization: a treatment for permanent teeth with necrotic pulp and incomplete root development. J Endod. 2013;39:319–326
30. Nagata JY, Gomes BP, Rocha Lima TF, Murakami LS, de Faria DE, Campos GR, de Souza-Filho FJ, Soares Ade J. Traumatized immature teeth treated with 2 protocols of pulp revascularization. J Endod. 2014;40:606–612