Triple Antibiotic Paste Pulpectomy- A review article

[1]Dr. Arnab Mondal, MDS, [2]Dr. Swapnaneel Pradhan, MDS, [3]Dr. Soumik Chakrabarty, BDS

[1]Consultant Pedodontist, [2]Consultant Prosthodontist, [3]Consultant Dental Surgeon
[1]Department of Pediatric and Preventive Dentistry,
[1]Dr. Mondal's Dental Clinic, Kolkata, India.

***Abstract*— Pulpectomy is the most common and only choice most of the time to preserve primary dentition and the challenges are many when treating the same. The most challenging situation being the presence of abscess and the effective use of medications to treat the same. A newly developed concept of non-instrumentation is lesion sterilization and tissue repair (LSTR), which involves a topical application of triple antibiotic paste containing metronidazole, minocycline, and ciprofloxacin. TAP can sterilize non-vital and infected pulp in both permanent and primary dentitions by being placed near the orifices after debriding the pulp chamber only and without preparing the radicular procedure and can be used as a substitute for pulpectomy in the management of non-vital primary molars with a simpler, clinical, radiographic success rate.**

Index Terms*— *triple antibiotic paste, LSTR, pulp regeneration and revascularization

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I. INTRODUCTION

The role of micro-organisms in progression and development of periapical pathologies has been proved by a number of animal and human studies.

Earlier techniques involved removal of bacteria residing in root canals using methods like filing or by chemical irrigation using conventional root canal procedures. However, in recent days more efficient ways have emerged which will be able to remove bacteria residing in deeper layers with the use of number of root canal medicaments, particularly antibiotics which help in achieving successful outcomes. [1,2]

The root canal infection occurs as a result of multiple microorganisms, of which, E. faecalis dominates along with polymicrobial anaerobic species which requires certain advanced methods. [3]

The advanced method for sterilization of deep rooted bacteria was named as LSTR which is a acronym for lesion sterilization and tissue repair. This process allowed the clinician to use a combination of antibiotics (metronidazole, ciprofloxacin, and minocycline) for controlling of oral infections such as dentinal, pulpal, and periapical lesions and aimed to eliminate causative bacteria from the diseases by sterilizing the lesions and promoting tissue regeneration using the host's natural tissue recovering process. A number of antibiotic combinations where tested and used in different ratios by different authors in history to accomplish the complete removal of all pathogenic microorganisms in pulpal and periapical lesions. [4]

II. HISTORY

- In the year 1951, Grossman first used antibiotics in endodontic therapy using a poly-antibiotic formula known as PBSC, a combination of penicillin, bacitracin, streptomycin and caprylate sodium in a silicon vehicle. However, since the formula was not efficient against anaerobic bacteria, it failed to gain popularity.
- In the year 1993, Sato *et al* experimented with combinations of ciprofloxacin, metronidazole plus a third antibiotic amoxycillin/cefaclor to clarify the antibacterial efficacy.
- In the year 1996, Hoshino *et al* found that a combination of ciprofloxacin, metronidazole and minocycline with a dilution 25gm/ml of paste has the ability to decontaminate infected root canal. [2,5,6]

III. RATIONALE FOR THE USE OF TAP

- Endodontic therapy is efficient in removing bacteria and their by-products by destroying the microbial ecosystem using chemical and mechanical methods. Several drugs and medicaments have been suggested to accompany these techniques for greater efficacy.
- Bacteria residing mainly in the root canals and superficial layer of infected root canal wall can be removed by conventional root canal procedures. However, in spite of following proper protocols and good obturation techniques, there have been many failures and are attributed to bacteria which reside in the deep layers of root canal dentine.
- Application of antibacterial drugs to such endodontic lesions can be done to eradicate the bacteria residing in deep layers. For sterilization of such lesions, a single antibacterial drug may be ineffective because of different types of bacteria. Also bacteria may be smeared along the root canal during endodontic treatment. For sterilization of the deep layers of infected root dentin, root canal medicaments should be able to penetrate the root canal dentin. The penetrative ability of these drugs can be improved by mixing them with propylene glycol and macrogol to form an ointment base. [7]

IV. COMPOSITION

There are number of studies done by several authors in search for the perfect combinations for Triple Antibiotic Paste:

- Sato *et al*. performed a number of experiments using the 3-Mix with and without Rifampicin.
- In another study, Ciprofloxacin and Metronidazole was combined along with a third antibiotic, namely Amoxicillin, Cefaclor, Cefroxadine, Fosfomycin or Rokitamycin.
- Ruparel et al. in his study, used Minocycline instead of Cefaclor and referred to it as the modified Triple Antibiotic Paste (TAP) and tried another combination referred to as the Double Antibiotic Paste (DAP).
- The Double Antibiotic Paste (DAB) is referred to as the 2-Mix, because it consists of only Ciprofloxacin and Metronidazole.
- Pinky *et al*. and Nanda *et al*., in their study removed Metronidazole from the 3-Mix and tried Ornidazole instead.
- Minocycline was no longer used because of its ability to cause discolouration during revascularization procedures in young permanent tooth and affecting the developing successor when used in an deciduous tooth.
- Algarni *et al*. in his study used antibiotic gels containing Clindamycin modified 3-Mix and compared it with the 2-Mix.[7]

However the most accepted combination was the one given by Hoshino et al.:
It consists of An Antibiotic 3mix and a carrier which is incorporated in nitric oxide:

3mix in the Ratio- 1:1:1
Metronidazole- 400mg- Nitroimidazole group- for anaerobic bacteria and protozoa
Minocycline- 100mg- Tetracycline derivative- inhibit collagenase and matrix metalloproteinases
Ciprofloxacin- 200mg- Fluoroquinolone derivative, generates fibroblasts and acts against gram positive and gram negative bacteria

Carrier(MP) in the Ratio- 1:1
Macrogol ointment and **propylene glycol**

3mix is incorporated in NO using
1:5 (MP: 3mix)

V. Preparation of Triple Antibiotic Paste

- The traditional Triple antibiotic paste consists of 33% metronidazole, 34% minocycline and 33% ciprofloxacin with macrogol and propylene glycol paste.
- However, the traditional composition had certain drawbacks which were:
  - Minocycline lacked required efficacy for eradication of deep rooted bacteria and caused discolouration of tooth when used .
  - Another major drawback was its radiolucency which did not allow proper tracking of flow of the paste inside the tooth when viewed radiographically.
- To overcome these drawbacks, MTAP was introduced.
- Modified Triple Antibiotic Paste consists of 30% Metronidazole, 30% Clindamycin, 30% Ciprofloxacin, 10% Iodoform with Macrogol and propylene glycol.
- In MTAP, Minocycline was eliminated and substituted with Ciprofloxacin and Iodoform was added for its ability to show radio-opacity.[8]

VI. Lesion Sterilisation and Tissue Repair

- The process which allows the use of a combination of antibiotics (metronidazole, ciprofloxacin, and minocycline) for controlling of oral infections such as dentinal, pulpal, and periapical lesions is known as LSTR.
- It aims to eliminate the bacteria from the diseases by disinfecting the lesions and promoting tissue regeneration by the host's natural tissue recovering process.
- Presence of Three types of antibiotics ensure complete removal of all pathogenic microorganisms in pulpal and periapical lesions.

VII. Clinical Indications for LSTR

- For primary teeth which are affected with pain and are tender on percussion
- Teeth presenting with Grade I and II mobility
- Presence of an abscess and sinus tract
- Presence of radiolucency in furcation area
- Pulpless primary teeth in hemophilic patient
- Immature primary teeth with necrotic pulp and incompletely formed roots.

VIII. Contraindication of LSTR

- Patient sensitive or allergic to ciprofloxacin, minocycline, or metronidazole
- Radiographic evidence of excessive internal or external root resorption
- Primary tooth nearing exfoliation
- Perforated pulpal floor
- Excessive bone loss in furcation area involving underlying tooth germ
- Non restorable crown of permanent tooth where postplacement and core buildup are not possible. [9]

IX. Clinical Procedure

According to Nanda *et al*.,

- Isolation with rubber dam
- Administration of Local anesthetic (optional)
- Removal of caries
- Preparation of access cavity
- Extirpation of necrotic coronal pulp
- Irrigation with normal saline (0.9%) and drying with cotton pellet
- Enlargement of canal orifices. It should be 1 mm in diameter and a depth of 2 mm to receive medication
- The cavity is then filled with 3 antibiotic mix and teeth restored with glass ionomer cement, and stainless steel crown is given. [10]

X. Merits of Triple Antibiotic Paste

(1) Disinfection of Root canals

- The bacteria residing in root canals is poly-microbial in nature and is generally resistant to a single antibiotic.
- To overcome this resistance, Triple antibiotic paste is used till date as the most effective combined drug.
- Kaur *et al*. in his study, compared the antimicrobial effects of Triple Antibiotic Paste with different combinations against Enterococcus Faecalis which is considered as the most prevalent bacteria present in infected root canal
    - Amoxycillin + Metronidazole
    - Amoxycillin + Clavulanic acid + Metronidazole
    - Amoxycillin + Cloxacillin+ Metronidazole
- It was found that the combination of Triple Antibiotic Paste stood most efficient among the other combinations. [3,11]

(2) Use in regeneration and revascularization techniques

- Revascularization is the process of inducing bleeding from periapical area of the root canal which harbours the stem cells and thereby revascularizing the apical pulp.
- Reyhani *et al*, conducted a study to evaluate the antimicrobial effects of different concentrations of TAP at 1-, 2-, 3-, and 4-week intervals on mature Enterococcus faecalis biofilm.
- The results revealed that TAP completely eliminated E. faecalis biofilms at all the intervals at concentrations of 1000, 100, and 10 mg/mL, whereas 1-, 0.1-, and 0.01-mg/mL TAP resulted in significant reduction of CFU means compared with the control group.
- It was concluded that Use of lower concentrations of TAP at short term could eradicate E. faecalis biofilm and decrease high- concentration side effects.
- TAP is considered the least toxic compared to other root canal medicaments and can be used at very less concentrations to successfully eradicate E Faecalis. [8,12]
    - 1 mg/dL
    - 0.1 mg/dL
    - 0.01 mg/dL

(3) Lesion Healing

- Triple antibiotic paste is highly efficient in treating periapical lesions.
- Reddy *et al*., conducted a study to evaluate the clinical and radiographic success of pulpectomies primary teeth with chronic infection using a mixture of metronidazole, ciprofloxacin, and minocycline (3MIX)-MP as an intracanal medicament before the obturation.
- It was concluded from the study that all the primary teeth with chronic infection which were treated using 3MIX-MP, followed by the instrumentation and obturation provided excellent clinical and radiographic success when compared to conventional pulpectomy and non-instrumentational lesion sterilization tissue repair therapy. [13]

XI. Demerits of Triple Antibiotic Paste

Triple antibiotic paste is considered as one of the most successful intra canal medicament but possess some drawbacks-

(1) Effect on dentinal structures

- Prather et al, investigated the effects of triple antibiotic paste (TAP) and modified triple antibiotic paste (MTAP) concentrations on the microhardness and chemical structure of radicular dentine using conventional TAP or MTAP and methylcellulose-based TAP or MTAP.
- All treatment groups showed significant reductions in microhardness of roots when compared to untreated control roots.
- However, methylcellulose-based antibiotics caused significantly less reduction in microhardness when compared to antibiotics.
- In addition, 1 g/mL TAP and DAP caused significantly lower phosphate/amide I ratios when compared to other groups.
- The use of 1 mg/mL methylcellulose-based TAP and MTAP may minimize the reduction in microhardness of roots compared with the currently used 1 g/mL concentration of these antibiotics.
- It was caused due to demineralizing effect of antibiotic mixture on dentin which not only caused mild erosion but also decreased the mechanical properties of dentin leading to tooth brittleness.[14]

(2) Effect on Stem Cells

- Triple Antibiotic paste is considered very less toxic when compared to other root canal medicaments but may still prove little toxicity when administered at higher doses.
- TAP should be administered at concentrations which will show effective bactericidal action and also maintain the vitality of stem cells.
- The recommended dosage of TAP should be in the range of 0.1 to 2mg/ml. [15]

(3) Discolouration of TAP

- Discolouration caused due to TAP on tooth is one of the biggest drawbacks of TAP.
- The discolouration caused by TAP was because of the antibiotic minocycline present in the composition which lead to the reduction in its acceptance.
- Later, MTAP or Modified Triple antibiotic paste was introduced with change in its composition by substituting Minocycline with Ciprofloxacin to prevent the discolouration.
- Kim *et al*, found out in their study that incorporation of dentin bonding agent can reduce the amount of discolouration caused by TAP. [8,16]
- Venkataraman *et al.* conducted a study to evaluate the crown discoloration produced by different modifications of TAP using TAP with minocycline, TAP with amoxyclav, and TAP with clindamycin in 40 freshly extracted tooth.
- Results revealed that Modified TAP with clindamycin did not induce clinically visible discoloration up to 3 weeks after placement

(4) Removal of TAP

- Complete removal of TAP using conventional irrigation and instrumentation is often challenging and inefficient.
- Arsalan et al. in his study evaluated the efficacy of needle irrigation, the EndoActivator System (Dentsply Tulsa Dental Specialties, Tulsa, OK), and PIPS on the removal of antibiotic pastes from an artificial groove created in a root canal
- Results revealed that PIPS removed significantly more antibiotic pastes than the EndoActivator and needle irrigation.
- The EndoActivator was superior to needle irrigation in removing antibiotic pastes.
- It was concluded that is difficult to completely remove antibiotic pastes from root canals. [17]

XII. Conclusion

As the antibiotic resistance has become an emerging global problem these days, the development of multidrug resistance strains may decrease the success of this treatment modality. Triple Antibiotic Paste can be considered as an efficient weapon to combat against bacteria residing in root canal. Although TAP have some of the drawbacks which cannot be left out but still it has been considered as a superior intracanal medicated when compared to the ones used currently.

Further research regarding the material will provide deep insight on its negative and positive properties and will allow to create a better material with suitable alterations.

References

[1] Vijayaraghavan R, Mathian V, Sundaram A, Karunakaran R, Vinodh S. Triple antibiotic paste in root canal therapy. Journal of Pharmacy and Bioallied Sciences 2012;4(6):230.

[2] Parhizkar A, Nojehdehian H, Asgary S. Triple antibiotic paste: momentous roles and applications in endodontics: a review. Restorative Dentistry & Endodontics 2018;43(3).

[3] Makandar SD, Noorani TY. Triple antibiotic paste - Challenging intracanal medicament: A systematic review. Journal of International Oral Health2020;12(3):189–96.

[4] Goswami S. Lesion sterilization and tissue repair in pediatric dentistry. SRM Journal of Research in Dental Sciences 2018;9(2):79.

[5] Hoshino E, Kurihara-Ando N, Sato I, Uematsim H, Sato M, Kota K, et al. In-vitro antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. 1996.

[6] Hoshino E, Kurihara-Ando N, Sato I, Uematsim H, Sato M, Kota K, et al. In-vitro antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. 1996.
[7] Nalawade TM, Parikh D, Mallikarjuna RM. Annals and Essences of Dentistry Lesion Sterilization and Tissue Repair (LSTR) Technique and its Clinical Application in Primary and Permanent Teeth: A Review. 2019.
[8] Makandar SD, Noorani TY. Triple antibiotic paste - Challenging intracanal medicament: A systematic review. Journal of International Oral Health2020;12(3):189–96.
[9] Goswami S. Lesion sterilization and tissue repair in pediatric dentistry. SRM Journal of Research in Dental Sciences 2018;9(2):79.
[10] 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. Journal of Oral Biology and Craniofacial Research 2014;4(2):114–9.
[11] Kaur M, Kendre S, Gupta P, Singh N, Sethi H, Gupta N, et al. Comparative evaluation of anti microbial effects of triple antibiotic paste and Amox and its derivatives against E. faecalis: An in vitro study. Journal of Clinical and Experimental Dentistry 2017;9(6):e799–804.
[12] Frough Reyhani M, Rahimi S, Fathi Z, Shakouie S, Salem Milani A, Soroush Barhaghi MH, et al. Evaluation of Antimicrobial Effects of Different Concentrations of Triple Antibiotic Paste on Mature Biofilm of Enterococcus faecalis. Journal of Dental Research, Dental Clinics, Dental Prospects 2015;9(3):138–43.
[13] Reddy G, Sridevi E, Sai Sankar A, Pranitha K, Pratap Gowd M, Vinay C. Endodontic treatment of chronically infected primary teeth using triple antibiotic paste: An in vivo study. Journal of Conservative Dentistry 2017;20(6):405–10.
[14] Prather BT, Ehrlich Y, Spolnik K, Platt JA, Yassen GH. Effects of two combinations of triple antibiotic paste used in endodontic regeneration on root microhardness and chemical structure of radicular dentine. Journal of Oral Science 2014;56(4):245–51.
[15] Ruparel NB, Teixeira FB, Ferraz CCR, Diogenes A. Direct effect of intracanal medicaments on survival of stem cells of the apical papilla. Journal of Endodontics 2012;38(10):1372–5.
[16] Kim B, Song M-J, Shin S-J, Park J-W. Prevention of tooth discoloration associated with triple antibiotics. Restorative Dentistry & Endodontics 2012;37(2):119.
[17] Arslan H, Akcay M, Capar ID, Ertas H, Ok E, Uysal B. Efficacy of needle irrigation, EndoActivator, and photon-initiated photoacoustic streaming technique on removal of double and triple antibiotic pastes. Journal of Endodontics 2014;40(9):1439–42.