

Review on non- instrumentation endodontic treatment

Dr. Mukta Bihanga Pandey*, Dr. Supriya Banerjee**, Dr. Amitava Bora***

*Dental Surgeon, Department of Dentistry, Murshidabad Medical College and Hospital

** Dental Surgeon, Department of Dentistry, Chinchurah District Hospital

*** Assistant Professor, Department of Paediatric Dentistry, Burdwan Dental College

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Tripathi KD (1985) in his Essentials of Medical Pharmacology 5th edition, mentioned metronidazole is a nitroimidazole compound that exhibits broad spectrum of activity against protozoa and anaerobic bacteria. Metronidazole is selectively toxic to anaerobic microorganisms. Its nitro group is reduced by certain redox proteins to highly reactive nitro radical after entering the cell. It binds to the DNA, disrupts the helical structure and lead to rapid cell death. Tetracycline, which includes doxycycline and minocycline are primarily bacteriostatic, inhibiting protein synthesis by binding to 30S ribosomes in susceptible organism. They exhibit broad spectrum of activity against gram positive and gram negative microorganisms. Minocycline is a semisynthetic derivative of tetracycline with a similar spectrum of antibacterial activity. Ciprofloxacin is a synthetic fluoroquinolone with rapid bactericidal action. It inhibits the enzyme bacterial DNA gyrase, which nicks the double stranded DNA, introduces negative supercoil and then reseals the nicked end. The bactericidal action probably results from digestion of DNA by exonucleases whose production is signaled by the damaged DNA. It exhibits very potent activity against gram negative bacteria but very limited activity against gram positive bacteria. Most of the anaerobic bacteria are resistant to ciprofloxacin. Hence it is often combined with metronidazole in treating mixed infections.(1)

Sato, T. Hoshino, E et al. (1993) assessed the in vitro antibacterial efficiency of a mixture of ciprofloxacin, metronidazole and minocycline (3Mix), with and without the addition of rifampicin (100 µg each/ml) (4Mix), against oral bacteria. Review of Literature 36 of children. The antibiotic combinations were observed to be effective against both carious and endodontic lesions in vitro.(2)

Iwaku M, Hoshino E et. al.(1996) published a research from The Cariology Research Unit of the Niigata University that they developed the concept of 'Lesion sterilization and tissue repair LSTR' therapy which employs the use of a combination of antibacterial drugs for disinfection of oral infectious lesions, including dentinal, pulpal, and peri-radicular lesions. Repair of the damaged tissues can be expected if lesions are disinfected.(2)

Hoshino et al. (1996) formulated antibiotic (3Mix) – ratio 1:1:1 – Ciprofloxacin 200 mg, Metronidazole 500 mg, Minocycline 200mg – ratio 1:1 - Macrogol ointment, Propylene glycol 3Mix is incorporated into MP using the following - 1:5 (MP:3Mix) - 1:7 (standard mix). (2)

Sato et al. (1996) studied the ability of a mixture of ciprofloxacin, minocycline and metronidazole (0.5mg of each) in an in vitro study to eliminate experimental infection in deep layers of root dentin by E.coli. In other in vitro study the minimal inhibitory combination for ciprofloxacin and minocycline against E. faecalis and E. faecium were found to be 5 and 20 µg respectively and metronidazole was reported to have no inhibitory effect.(3)

Peters OA et al. (2001) informed that due to the complex anatomy of the root canal, mechanical instrumentation leaves significant portions of the root canal walls untouched [2] and there is no evidence that instrumentation alone can completely eliminate microorganisms from the root canal. Therefore additional irrigants and medicaments are required to disinfect the root canal system to reduce the bacterial load to promote healing.(2)

Cruz EV et al. (2002) investigated the penetration effect of propylene glycol into root dentine. The area and the depth of penetration of Safranin O dye in propylene glycol were reported to be significantly greater than dye with distilled water into root dentine. The presence of smear layer significantly delayed the penetration of the dye in this study indicating the need for their removal for better diffusion of medicament.(4)

Takushige T et al. (2004) suggested that the drugs are powdered and mixed in a ratio of 1:3:3 (3 Mix) and added either with macrogol -propylene glycol (3 MP) or a canal sealer (3 Mix-sealer).(5)

Alam T, Nakazawa F, et al.(2005) reported a combination of ciprofloxacin, metronidazole and minocycline (100µg each /ml) that inhibited the growth of every strain completely. Their study suggested 3mix may be effective in persistent endodontic infection. (3)

Windley et al. (2005) assessed the efficacy of triple antibiotic paste in disinfection of immature dog teeth with apical periodontitis. The samples were assessed before and after irrigation with 1.25% NaOCl and after dressing with triple antibiotic mixture. Of the 30 samples that were cultured before treatment, 90% remained positive following irrigation with 10ml of NaOCl. This level dropped to 30% following application of triple antibiotic paste for 2 week signifying the efficiency of triple antibiotic mixture.(6)

Pallotta RC et al.(2007) reported ciprofloxacin and metronidazole in combination with calcium hydroxide to be effective against four species (*S. aureus*, *Pseudomonas aeruginosa*, *Enterococcus faecalis* and *B. fragilis*) tested when compared with calcium hydroxide, iodine, potassium iodide and iodoform. They suggested that the drug combination can be effective in mixed bacterial flora as in infected root canal.(7)

Carreira Cde M et al.(2007) in their in vitro study the antimicrobial action of ciprofloxacin, metronidazole and polyethylene glycol and natrosol vehicles were assessed against 23 strains [14]. It was concluded that ciprofloxacin presented antimicrobial action against all tested bacterial strains, and its association with metronidazole was reported to be synergistic. The vehicle polyethylene glycol showed antimicrobial effect and the ciprofloxacin /polyethylene glycol association was the most effective combination for reducing the tested bacteria and yeasts. Thus delivery of the drug with ideal vehicle into root canal reduces the bacterial loads in the infected root canal.(8)

Baumgartner, J.C. et al.(2008) mentioned that in the root canal a polymicrobial ecosystem is produced that selects for anaerobic bacteria over time. This suggests that a symbiotic relationship may lead to an increase in virulence by the organisms in that ecosystem. Therefore the role of endodontic therapy is total disruption of the microbial ecosystem.(3)

Prabhakar, A. et al. (2008) conducted a study on 60 infected primary molar and divided them into two group. In one group they had removed only the coronal portion of pulp and in the other group both coronal and radicular pulp and applied tri-mix(ciprofloxacin,metronidazole,minocycline) over floor of the pulp chamber. They found higher clinical and radiographic success rate (100%) in the group where both coronal and radicular pulp was removed than the group where only coronal pulp was removed.(9)

Reynolds K et. al. (2009) suggested a novel approach to seal dentinal tubules of the pulp chamber to avoid crown discoloration . The inner surface of the coronal access was etched, rinsed, bonding agent applied and cured.(10)

Mohammadi, Z. Abbott, P.V. (2009) reported that antibiotics are mainly prescribed primarily to control active microbial infections, not for preventing the possibility of infections, unless the patient is medically compromised. In endodontics, systemic antibiotics are prescribed to suppress the infection in the pulp space and / or periapical area. For systemic antibiotic to kill bacteria, it has to be carried by the blood circulation in the pulp space to come in direct contact with the bacteria. Hence in an infected or necrotic pulp due to lack of blood supply, topical antibiotics may be effective in a highly constrained and restricted pulp space.(11)

Nakornchai, S. et al.(2010) reported clinical studies in infected primary teeth suggesting 3Mix to be an effective root canal treatment material. Both 3Mix and vitapex had been suggested to be effective root canal treatment material for primary teeth as there was no statistical significance in radiographic success. Both groups showed 100% and 96% clinical success at 6 and 12 months, respectively.(12)

Kim et al. (2010) identified that, though the triple antibiotic paste eradicates bacteria in the root canal, it had a disadvantage of causing aesthetic problem leading to tooth discoloration. He identified the discoloration was caused by minocycline in an in vitro study.(13)

Trope et al. (2010) suggested that Arestin can be used as substitute for minocycline to markedly reduce discoloration.(14)

Thomson, A. and kahler, B. (2010) substituted amoxicillin for minocycline in his case report to avoid discoloration.(15)

Madhubala MM et. al.(2011) compared the antimicrobial activity of calcium hydroxide, tri-antibiotic mixture, and an ethanol extract of propolis as intra-canal medicaments on *Enterococcus faecalis*-infected root canals. The percentage reduction in colony forming unit was reported to be highest for propolis showing 100% reduction on day 2 followed by tri-antibiotic mixture showing 82.5%, 92.2%, and 98.4% of reduction on days 1, 2, and 3, respectively. Calcium hydroxide showed a gradual increase in antibacterial activity with a maximum of 59.4% on day 7.(16)

Pinky, C et al.(2011) replaced metronidazole with Ornidazole as it had longer duration of action, better efficacy and slower metabolism when compared with metronidazole. The study concluded that there was no statistical difference between metronidazole and ornidazole groups. Group containing ornidazole was reported to exhibit better results during the evaluation period of 3, 6 and 12 months in infected primary teeth.(17)

Trairatvorakul C et al.(2012) suggested that non instrumentation endodontic treatment using 3Mix –MP cannot replace conventional root canal filling material as a long term therapy in primary teeth. In their clinical study non-instrumentation endodontic treatment using 3Mix-MP in primary mandibular molars showed good clinical success but had a low success rate based on radiographic evaluation at 2- year follow-up.(18)

Lenherr et al. (2012) investigated the discolouration potential of various endodontic materials in bovine tooth model. The most severe discolouration was reported to be detected after 12 months in triple antibiotic paste group followed by ledermix paste indicating the effect of tetracycline group.(19)

Miller EK et al.(2012) performed internal bleaching to remove the cervical discolouration from the triple antibiotic paste six months later.(20)

Lenherr, P. Weiger, R. et al. (2012) had suggested an alternative to substitute minocycline by cefaclor. This modification of the current clinical protocol (Sato et al. 1996, Banchs & Trope 2004) has been promulgated to avoid crown discolouration. This innovative method covers the dentinal tubules of the root dentin, thus preventing any interaction between tri -antibiotic paste and root dentin walls.(19)

Jaya AR et.al.(2012) evaluated and compared the clinical and radiographic effectiveness of Ciprofloxacin, Minocycline, Metronidazole combination with Ciprofloxacin, Minocycline and Tinidazole combination when used for Lesion Sterilization and Tissue Repair in primary teeth .After a 24 month follow up, they found no statistical difference between the groups and concluded that primary teeth with the peri-radicular lesions, can be conserved by using combination of Ciprofloxacin, Minocycline and Tinidazole antibacterial drugs.(21)

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