



Review Article

Clinical Uses of Metronidazole in Paediatric Dentistry

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ABSTRACT

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Metronidazole has been widely used in clinical dentistry, is specifically anti-anaerobic in nature and known for its effective antibacterial activity against anaerobic cocci as well as Gram-negative and Gram-positive bacilli. It has been used both systemically and topically in the treatment of periodontal disease. Application of its uses in paediatric dentistry is limited. The importance of metronidazole in paediatric dentistry has not been clearly demonstrated. Hence, the purpose of this short communication was to review uses of metronidazole in children with dental problems.

KEY WORDS: metronidazole, antimicrobial, paediatric dentistry, children

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1. INTRODUCTION

Antibacterial activity against clinically important anaerobes has been found with nitroimidazole derivatives. Metronidazole, 1-(2-hydroxyethyl)-2-methyl-5-nitroimidazole, which is a nitroheterocyclic compound, is specifically anti-anaerobic in nature and has a broad spectrum of activity against protozoa and anaerobic bacteria.¹ Metronidazole was introduced as an anti-trichomonal agent via classical pharmaco-chemical steps, but has progressed as a useful

drug in a variety of disparate fields. It was first used in clinical trial in 1958, after its synthesis from a crude extract of streptomycete.² Durel and co-workers³ further reported its use in the treatment of infections caused by *Trichomonas vaginalis*. Subsequently, it was used in the infections caused by *Entamoeba histolytic* and *Giardia lamblia*. Inference of metronidazole on oral diseases was initially done by Shinn⁴ as he observed successful resolution of acute ulcerative gingivitis in patients receiving concurrent metronidazole for trichomoniasis.² Nonetheless, metronidazole had been progressed from near ideal anti-trichomonal agent to far more useful drug in a variety of heterogeneous fields. The advantages of metronidazole have been shown in Table 1.

Metronidazole is available as oral, intravenous, vaginal, and topical formulations. It is well absorbed after oral administration, and reaches peak plasma concentrations within 1–2 hours after consumption. The drug itself is a major component in plasma with the limited amount of active metabolites.⁶ Main therapeutic advantage of metronidazole is removal of pathogenic anaerobes, without disturbing protective aerobic flora. The drug does not develop resistance among anaerobes as suggested by the consensus of clinical and experimental evidence, which is due to decreased uptake of drug, reduced drug efficiency or prevention of entry of the drug or efflux.^{2,6} There is no problem of re-administration of metronidazole. Hence, its use in dentistry does not exclude its immediate reuse systemically, which has made the drug as 'priority drug'.²

2. APPLICATION IN PAEDIATRIC DENTISTRY

2.1 AS ORAL MEDICAMENT:

Metronidazole is the most commonly prescribed antibiotic for pulpal infections in both primary and permanent teeth after amoxicillin. Two main reasons for its use in Paediatric dentistry are control of oral infection and prevention of subacute bacterial endocarditis. It is primarily prescribed as an adjunct to the treatment in abscess condition where periapical tissue becomes involved. Main purpose of its prescription in this condition is to limit swelling, as well as metastasis of infection to vital organs.⁷ Tanwir and co-workers⁸ conducted a cross sectional study to evaluate the pattern of antibiotic and painkiller prescription as per diagnosis by dentists and concluded that amoxicillin and metronidazole were the most commonly prescribed antibiotics for dental problems such as caries/pulpitis. This drug has been prescribed under the trade name of Flagyl at a dosage of 200 mg (BID).

2.2 ENDODONTIC REGENERATIVE PROCEDURE:

Regenerative procedure is an alternate clinical approach for apexification and involves the use of triple antibiotic paste (metronidazole, ciprofloxacin, and minocycline) as a dressing to sterilise the root canal before the induction of bleeding to create a matrix for the in growth of new vital tissue in the pulp canal space.⁹

Advantages of using triple antibiotic paste prior to endodontic regenerative procedure may conserve any viable tissue and allows the root thickness and length, resembling normal maturation of the root.¹⁰ Bose and co-workers¹¹ compared triple antibiotic paste, calcium hydroxide and formocresol as intra-canal medicament in non-vital young permanent teeth, and reported highest percentage of increase in dentin wall thickness in triple antibiotic paste group. The paste mainly contains bactericidal (metronidazole, ciprofloxacin) and a bacteriostatic (minocycline) agent that aid in successful revascularisation and also helps to promote functional development of pulp dentin complex.¹²

2.3 INTRACANAL MEDICAMENT:

Metronidazole can be used as an effective intra-canal medicament. Siqueira and de Uzeda¹³ evaluated the antibacterial activity of 0.12% chlorhexidine gel, 10% metronidazole gel, calcium hydroxide plus distilled water, calcium hydroxide plus camphorated paramonochlorophenol (CPMC) and calcium hydroxide plus glycerine using an agar diffusion test. Authors found that, metronidazole caused inhibition of growth of all obligate anaerobes tested and showed better effectiveness than calcium hydroxide/ CMPC paste against two of the strains, whereas, calcium hydroxide/ CMPC paste and chlorhexidine were effective against all bacterial strains tested.

Kargul and co-workers⁵ conducted a clinical trial, where metronidazole has been used as intra-canal medicament combined with pulpectomy in infected primary molars. When freshly mixed metronidazole cream was applied as intra-canal medicament for one week, it has shown success rate of 85% after 24 months, which proves metronidazole's effectiveness against endodontic bacteria which are mainly obligate anaerobes. Hoshino and co-workers⁹ evaluated the antibacterial efficacy of mixture (Metronidazole, Ciprofloxacin and Minocycline, with and without Rifampicin) on the bacteria from infected dentin of root canal walls, and authors reported that this drug combination is sufficiently potent in eradicating bacteria from infected dentin of root canals. Although, metronidazole can be used as intra-canal medicament causing inhibition of growth of all obligate anaerobes and more effective than other intra-canal medicaments in eliminating obligate anaerobes with in root canal.

2.4 OBTURATING MATERIAL:

Metronidazole has been used as an obturating material along with two other antibiotic drugs in lesion sterilization and tissue repair (LSTR) therapy or non-instrumentation endodontic treatment (NIET). This is a new biologic approach in the treatment of carious lesions with or without pulpal and periapical involvement. When the conventional endodontic therapy is not possible or if the teeth show presence of external or internal resorption, this technique is used as adjuvant. This concept employs a mixture of three antibiotic drugs viz. ciprofloxacin, metronidazole and minocycline in a ratio of 1:3:3, which can sterilize carious

lesions, necrotic pulps, and infected root dentine of primary teeth. LSTR technique prevents unnecessary irritation of the periapical tissues, as there will be no mechanical instrumentation of the root canals. Metronidazole cannot eradicate all bacteria from the carious lesions even in maximum concentration. Hence, there is necessity of additional drugs to make the lesion sterile.¹⁴ The triple antibiotic (3 Mix) powder is mixed along with macrogel and propylene glycol, acts as a vehicle and enhance the penetration ability of the drug into infected root canal dentin.¹⁵ Triple antibiotic paste is biocompatible with tetracycline inhibiting collagenases and matrix metalloproteinases, whereas metronidazole and ciprofloxacin in triple antibiotic paste generate fibroblasts.¹⁰ Kayalvizhi and co-workers¹⁶ conducted a literature review on LSTR therapy in primary teeth and concluded, successful resolution with 3 Mix paste in LSTR therapy. The antibiotic drugs used in LSTR offer a few disadvantages when used alone, as ciprofloxacin has reduced activity against anaerobes, while metronidazole was ineffective against facultative bacteria and minocycline may cause tooth discoloration

Table 1: Advantages of Metronidazole.

Advantages of Metronidazole

Ready availability
Rapid bactericidal action
Good tissue penetration
Cost effectiveness
Acceptable pharmacokinetics and pharmacodynamics
Undiminished antimicrobial activity
Inability of susceptible organisms to develop resistance

2.5 OTHER APPLICATIONS:

Metronidazole has also been used along with dental materials to provide antibacterial properties which can prevent the harmful effects caused by bacteria. Antibacterial glass ionomer cement (GIC) when used as a liner had delivered preservation of dental tissue and reduced risk of pulp exposure, need of repairing the remaining dentin is consistent with in the limits of minimal invasive dentistry.¹⁷ Ferreira and co-workers,¹⁸ had evaluated the performance of GIC added with antibiotics (1% metronidazole, ciprofloxacin and cefaclor) for sealing infected dentin in atraumatic restorations of primary molars. They found showed higher success rate for glass ionomer with antibiotics rather than conventional, which shows its reasonable use as a liner when used in primary molars.

3. CONCLUSION

Thus metronidazole has several uses in paediatric dentistry for decades, such as an obturating material, an intra-canal medicament, oral administration during pulp therapy as well as in triple antibiotic paste for endodontic regenerative procedure and many other varied uses. Further studies were recommended on metronidazole and its uses in paediatric dentistry.

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