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Original Article

Clinical evaluation of 3 Mix and Other Mix in non-instrumental endodontic treatment of necrosed primary teeth

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ABSTRACT

Problem considered: The objective was to evaluate and compare the clinical and radiographic efficacy of two different combinations of antibacterial drugs when used in non-instrumental endodontic treatment of necrosed primary teeth.

Materials and method: Forty teeth were randomly divided into two groups, viz. groups A and B having 20 teeth each. In Group A, 3 Mix (ciprofloxacin, metronidazole, and minocycline) and in Group B, Other Mix (ciprofloxacin, ornidazole, and minocycline) mixed with propylene glycol were used. Medication cavities of Group-A and B were filled with 3 Mix and Other Mix respectively followed by restoration of teeth. Clinical evaluation was done at 3 months whereas, clinical and radiographic evaluation was done at 6 and 12 months, respectively.

Results: Both the groups showed 100% clinical success whereas, radiographic success rate was 81% with 3 Mix and 92% with Other Mix but, was not statistically significant.

Conclusions: Both the antibacterial pastes can be used effectively in non instrumental endodontic treatment of necrosed primary teeth and require more clinical trials to prove its efficacy.

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1. Introduction

Periapical pathosis is one of the main causes for bacterial infection of the periradicular tissues. In order to improve the prognosis, the bacteria remaining in the root dentine or in the periradicular tissues should be eliminated without damaging the tissues.¹ Bacteria in superficial layers of infected root canal walls can be easily removed by conventional root canal treatment, while bacteria in the deep layers of root canal dentine may leak out to periapical regions and cause complications. In order to sterilize infected root dentine, especially the deep layers, antibacterial medicaments are useful.²

Cariology Research Unit of Niigata University School of Dentistry has developed the concept of Lesion sterilization and tissue repair (LSTR) therapy that employs a mixture of antibacterial drugs for disinfection.³ The infection of the root canal system is considered to be a polymicrobial infection, consisting of both aerobic and anaerobic bacteria. It is unlikely that any single antibiotic could result in an effective sterilization of the canal due to the complexity of the root canal infection. Since the overwhelming majority of bacteria in the root canal wall consist of obligate anaerobes, metronidazole should be selected as first choice among the antibacterial drugs as it has a wide spectrum of bactericidal action against oral obligate anaerobes. However, metronidazole even at higher concentrations fails to eradicate all the bacteria from carious lesions and some bacteria remain resistant to metronidazole, indicating the necessity of some additional drugs like ciprofloxacin and minocycline to sterilize these lesions.¹ Ornidazole has been reported to have a longer duration of action, with better efficacy and slower metabolism compared with metronidazole.⁴ The application of antibacterial drugs may represent a way to eradicate bacteria during root canal treatment. Hence this study was conducted to evaluate two combinations of drugs each comprising of three antibiotics in non instrumental endodontic treatment (NIET) of necrosed primary teeth.

2. Methods

Forty necrosed primary molars either due to caries or trauma, indicated for pulpectomy showing one or more signs and symptoms such as pain, tender to percussion, mobility (grade I, II), presence of abscess or sinus tract and radiolucency in furcation area, were selected from 38 healthy children with age group of 4–10 years. Teeth excluded from the study were showing radiographic evidence of excessive internal or external root resorption, perforated pulpal floor, excessive bone loss in furcation area involving underlying tooth germ and non restorable teeth. The children were randomly divided into two groups, Group A and Group B having 20 teeth each. In Group A, medication cavities were filled with 3 Mix (ciprofloxacin, metronidazole and minocycline), whereas in Group B, Other Mix (ciprofloxacin, ornidazole and minocycline) was used.

Antibacterial drugs such as ciprofloxacin, metronidazole, minocycline, and ornidazole in pure salt form (KAN HEALTH CARE PVT. LTD. NEW DELHI, INDIA) were used. These drugs were kept separately in tightly capped porcelain containers to

prevent exposure to light and moisture. A small amount of silica gel in a bag was placed inside the container to maintain low humidity and stored in refrigerator. The drugs were used within a month of preparation and the antibacterial paste was prepared just before use.

2.1. Group A

The drugs (ciprofloxacin, metronidazole and minocycline) were mixed in the ratio of 1:3:3 (by weight, measured by mono pendulum micro weighing machine) with 1 part of propylene glycol on glass slab with glass spatula to form a paste.

2.2. Group B

The drugs (ciprofloxacin, ornidazole and minocycline) were mixed in the ratio of 1:3:3 (by weight, measured by mono pendulum micro weighing machine) with 1 part of propylene glycol on glass slab with glass spatula to form a paste.

The clinical procedure was performed under rubber dam isolation. As the teeth in the study were non-vital therefore did not require local anesthesia to be administered prior to procedure. In each tooth the cavity was prepared depending upon the extent of the lesion and caries was removed, making sure that no overhanging tooth structure left in order to provide good access to coronal pulp. Access opening was done with No. 014 round carbide bur under slow speed and roof of the pulp chamber removed followed by extirpation of necrotic coronal pulp, under copious irrigation with normal saline (0.9% w/v) and drying with cotton pellets to ensure visualization of the canal orifices.

After this, canal orifices were enlarged to receive medication termed as “medication cavity” which was 1 mm in diameter and 2 mm deep. This was accomplished using a round bur, following which cavities were cleaned and irrigated with normal saline and dried using cotton pellets. Then, the medication cavities of Group-A and Group-B were filled with 3 Mix and Other Mix respectively and teeth restored with glass ionomer cement (Type-IX) followed by S.S Crown. The whole procedure was completed in one visit and an immediate post operative IOPA radiograph was recorded.

In each patient clinical evaluation was done at 3 months whereas, clinical and radiographic evaluation was done at 6 months and 12 months respectively (Figs. 1 and 2). The treated cases were considered clinically successful if there was absence of spontaneous pain, tenderness to percussion, mobility, abscess and sinus tract. Radiographically, success in the cases was considered when radiolucency decreased or remained same. Increase in radiolucency at subsequent visit was considered a radiographic failure.

3. Results

Discrete (categorical) data were summarized as number (no.) and percentage (%). Categorical groups were compared by Fisher's exact test or chi-square (χ^2) test wherever applicable. A two-sided ($\alpha = 2$) p value less than 0.05 ($p < 0.05$) was considered statistically significant. The observations were based on clinical and radiographic evaluation.

Fig. 1 – Radiological evaluation of 3 Mix.

In Group A out of 20 teeth, all teeth (100%) exhibited pain and tenderness on percussion, 14 teeth (70%) had sinus tract, 11 teeth (55%) showed mobility, 15 teeth (75%) had abscess and 16 teeth (80%) showed inter-radicular radiolucency. Whereas in Group B out of 20 teeth, all teeth (100%) exhibited pain and tenderness on percussion, 16 teeth (80%) had sinus tract, 12 teeth (60%) showed mobility, 18 teeth (90%) had abscess and 12 teeth (60%) showed inter-radicular radiolucency ([Table 1](#)).

Three-months post-operatively there was complete resolution of clinical signs and symptoms, such as pain, tenderness on percussion, sinus tract, mobility, and abscess in both the groups. At 6 and 12 months both the groups showed 100% clinical success, therefore any statistical test is not applicable (NA) ([Table 2](#), [Fig 3](#)).

After 6 months, the bone regeneration and no bone changes were found in 15% and 65% in Group A while 20% and

Fig. 2 – Radiological evaluation of Other Mix.

Table 1 – Presence of clinical signs and symptoms in two groups at different time periods.

Periods	Pain (n = 40)		Tenderness on percussion (n = 40)		Sinus tract (n = 40)		Mobility (n = 40)		Abscess (n = 40)	
	Group A (n = 20)	Group B (n = 20)	Group A (n = 20)	Group B (n = 20)	Group A (n = 20)	Group B (n = 20)	Group A (n = 20)	Group B (n = 20)	Group A (n = 20)	Group B (n = 20)
Pre-op	20 (100%)	20 (100%)	20 (100%)	20 (100%)	14 (70%)	16 (80%)	11 (55%)	12 (60%)	15 (75%)	18 (90%)
After 3 months	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
After 6 months	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
After 12 months	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

40% in Group B respectively; however, increase in bone loss was absent (0%) in both the groups, thus Fisher's exact test revealed statistically similar observations in both the groups ($p = 0.418$) though the bone regeneration was 5% higher in Group B as compared to Group A.

At 12 months, the bone regeneration was found in 30%, no bone changes in 35% cases and increase in bone loss in 15% in Group A whereas it were 35%, 20% and 5% in Group B respectively. Comparing the radiological changes (regeneration of bone/no bone changes/increase in bone loss) of two groups, χ^2 test revealed statistically similar observations in both the groups ($\chi^2 = 1.35$, $p = 0.509$), though the increase in bone loss was 10% lower in Group B as compared to Group A.

Moreover, radiological success rate was statistically similar in both the groups ($p = 0.613$), though it was 11% higher in group B as compared to Group A (Table 3, Fig 4).

4. Discussion

Pulp therapy in primary teeth is difficult for reasons like difficulty of behavior management, differences in morphology of primary teeth, complexity of root canals, desired timely resorption of primary teeth, and difficulties with root canal filling materials.⁵ The goal of successful pulpectomy is to eliminate all bacteria in root canal systems. According to Grossman (1972) the application of antibacterial drugs to endodontic lesions is one of the clinical procedures that may be used to sterilize lesions.

Systemic and topical use of antibiotics has been utilized in both medicine and dentistry for years. Chronic alveolar infections are associated with pulpless teeth and since no blood supply reaches the pulp space, the systemic administration of an antibiotic allows only a negligible concentration to reach the root canal, which is unlikely to be beneficial. Local

antibiotics offer an advantage as systemic consequences and complications are prevented and substantially higher concentrations can be utilized.⁶

Cariology Research Unit of Niigata University School of Dentistry developed the concept of lesion sterilization and tissue repair (LSTR) therapy that employs a mixture of antibacterial drugs for disinfection.³ LSTR or Non Instrumental Endodontic Treatment (NIET) are new biologic approaches in the treatment of carious lesions with or without pulpal and periapical involvement using a mixture of antibacterial drugs. LSTR has no mechanical instrumentation. This prevents too much enlargement of root canals, unnecessary irritation of periapical tissues, reduces chair time and requires only one treatment visit.

Due to the complexity of the root canal infection, possibility of any single antibiotic to be effective in sterilization of the canal is rare. A combination is needed to combat the diverse flora, and decrease the likelihood of development of resistant bacterial strains.⁷ Such a promising combination may consist of ciprofloxacin, metronidazole and minocycline. Sato² investigated this drug combination *in vitro* and found sterilization of carious lesions, necrotic pulps, and infected root dentin of deciduous teeth when this combination was used. Hoshino¹ tested the antibacterial efficacy of these drugs alone and in combination against the bacteria of infected dentin, infected pulps, and periapical lesions *in vitro*. None of the drugs resulted in complete elimination of bacteria when used alone, but when used in combination, they were able to consistently sterilize all samples.¹

In this study both the combinations gave the 100% clinical success but there was difference in radiographic success rate,

Table 2 – Overall clinical evaluation in two groups at different time periods.

Periods	Group A (n = 100) ^b	Group B (n = 100) ^b	p value
Pre-op.	80 (80%)	86 (86%)	0.259
After 3 months	0 (0%)	0 (0%)	NA ^a
After 6 months	0 (0%)	0 (0%)	NA ^a
After 12 months	0 (0%)	0 (0%)	NA ^a
Success rate	100%	100%	NA ^a

^a NA: not applicable.

^b n = sum of clinical signs and symptoms.

Fig. 3 – Overall clinical evaluation in both groups at different time periods.

Table 3 – Radiological evaluation in both groups at different time periods.

Periods	Bone changes	Group A (n = 20) ^a	Group B (n = 20) ^a	p value
Pre-op.	Radiolucency in furcation area	16 (80%)	12 (60%)	0.301
After 6 months	Regeneration of bone	3 (15%)	4 (20%)	0.418
	No bone changes	13 (65%)	8 (40%)	
	Increase in bone loss	0 (0%)	0 (0%)	
After 12 months	Regeneration of bone	6 (30%)	7 (35%)	0.509
	No bone changes	7 (35%)	4 (20%)	
	Increase in bone loss	3 (15%)	1 (5%)	
Success rate		81%	92%	0.613

^a n = sum of teeth. **Fig. 4 – Radiological evaluation in both groups in different time periods.**

which was 81% with 3 Mix and 92% with Other Mix, indicating that Other Mix was the best. Fidalgo⁸ in an “in vitro” study concluded that 3 Mix has a potent bacterial growth inhibitor, whereas Takushige⁹ also observed good clinical outcome of 95% with 3 Mix. Good clinical and radiographic outcome¹⁰ when 3 Mix was used in endodontic retreatment of previously obturated teeth using non instrumental endodontic treatment. Results of the present study were similar to another study¹¹ who reported 100% clinical and 76% radiographic success with 3 Mix. But there was dissimilarity in the results of another study¹² with an observation of 75% of clinical success and poor radiographic success of 36.7% with 3 Mix. The poor success rate could be attributed to the fact that radiolucent areas were often seen in the areas of erupting succedaneous teeth at the time of root resorption and it was difficult to differentiate the cause of the radiolucency.

A clinical study¹³ evaluated the antimicrobial effect of ornidazole on 20 primary molars with infected pulp and concluded the 94.53% reduction in bacterial count. Pinky¹⁴ when compared the clinical and radiographic evaluation of

two different combinations i.e. 3 Mix (ciprofloxacin, metronidazole and minocycline) and Other Mix (ciprofloxacin, ornidazole and minocycline) in non-instrumental endodontic treatment of necrosed primary teeth reported a higher success rate of Other mix then 3 Mix, but there was no statistically significant difference. Similar results were observed in the present study which revealed that there was no statistically significant difference between 3Mix and Other Mix, although there was a difference in radiographic success rate.

Good clinical success in the study for two combinations could be attributed to the fact that in primary teeth, the presence of accessory canals, porosity and permeability in the pulpal floor region indicate a probable connection between pulpal and periodontal tissues. Combination of antibacterial drugs can easily dissipate through these regions and induce a sterile zone, which is expected to promote tissue repair.¹² The penetration ability of these drugs was improved by mixing these drugs with propylene glycol.¹⁵ Good radiographic success rate with Other Mix could be due to presence of ornidazole which has a longer duration of action ($t^{1/2}$ –12–14 h),

slower metabolism and better efficacy than metronidazole. Hence both the combinations were equally efficacious clinically.

5. Conclusion

Use of 3 Mix or Other Mix could be a good alternative to conventional pulpectomy and root filling. More clinical trials should be performed on primary teeth using 3 Mix/Other Mix as there are less number of studies.

Conflicts of interest

All authors have none to declare.

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