Clinical and Radiographic Evaluation of Pulpotomies In Primary Molars With Formocresol, Glutaraldehyde and Ferric Sulphate

Raghavendra Havale[1], Rajesh T Anegundi[2], KR Indushekar[3], P Sudha[4]

[1]MDS, BDS. Reader, Department of Paediatric and Preventive Dentistry, AME's Dental College, Hospital, and Research Centre, Raichur, Karnataka, India. [2]MDS, BDS. Professor and Head, Department of Paediatric and Preventive Dentistry, SDM College of Dental Sciences and Hospital, Dharwad, Karnataka, India. [3]MDS, BDS. Principal and Head, Department of Paediatric and Preventive Dentistry, Sudha Rustagi College of Dental Sciences and Research, Haryana, India. [4]MDS, BDS. Professor and Head, Department of Paediatric and Preventive Dentistry, College of Dental Surgery, Mangalore, Karnataka, India.

Abstract

Aims: This *in vivo* study aimed to assess and compare the relative clinical and radiographic success of formocresol, glutaraldehyde and ferric sulphate as medicaments following pulpotomies in primary molars at three-monthly intervals over one year.

Methods: The study was carried out on 90 primary molars in 54 children aged from 3 to 9 years. Selected teeth were equally distributed and randomly assigned to formocresol, glutaraldehyde and ferric sulphate pulpotomy medicament groups (30 in each group). The teeth were then evaluated clinically and radiographically at three-monthly intervals over one year. The resulting data were tabulated and statistically analysed using the chi-square test.

Results: After one year, the clinical success rate was 100% with glutaraldehyde, 96.7% with ferric sulphate, and 86.7% with formocresol. The radiological success rate gradually decreased over the year in all pulpotomy medicament groups. Radiological success rates in formocresol, glutaraldehyde, and ferric sulphate groups were 56.7%, 83.3%, and 63.3%, respectively.

Conclusion: Two per cent glutaraldehyde may be recommended as a more effective alternative to formocresol and ferric sulphate as a pulpotomy medicament.

Key Words: Pulpotomy, Formocresol, Glutaraldehyde, Ferric Sulphate

Introduction

No area of treatment in paediatric dentistry has been more controversial than pulp therapy [1] The diagnosis and subsequent management of pulp pathology in carious primary teeth remain challenging [2]. Pulpotomy is currently the accepted standard of care for carious exposures of asymptomatic vital primary teeth [3]. The procedure involves coronal pulp amputation and the remaining vital radicular tissue surface is treated with long-term clinically evaluated medicaments to preserve the vitality and function of radicular pulp [4].

The original aim of pulpotomy for primary teeth was devitalisation. In 1904, Buckley introduced formocresol to treat non-vital permanent teeth [1]. In 1930, Sweet intoduced the formocresol pulpotomy technique. Formocresol has subsequently become a popular pulpotomy medicament for primary teeth. Initially, the technique involved five visits. By 1960, a single visit procedure was advocated [5]. There are concerns over the use of formocresol regarding cytotoxicity, allergencity, mutagenicity, carcinogenicity, and teratogenic effects on animals [6], chromosomal damage to the dental pulp cells in tissue culture [7], chromosomal breaks and aberrations in peripheral lymphocytes [8] and mutagenesis of stem cells [9,10]. In the presence of formaldehyde, an increased risk of myeloid leukaemia has been found [11]. These problems have caused concern among dental professionals over the use of formocresol. In June 2006, the International Agency for Research on Cancer published a report [12,13]. In June 2011, the United States Department of Health and Human Health Services issued a report [14] that classified formaldehyde as a carcinogen for humans.

Corresponding author: Raghavendra Havale, Department of Paediatric and Preventive Dentistry, AME's Dental College, Hospital, and Research Centre, Raichur, Karnataka, India; e-mail: raghavendrahavale@yahoo.co.in

Sufficient evidence on formaldehyde carcinogenicity and the mechanism of carcinogenicity has been established from studies in humans [11]. The dental profession has therefore looked for alternative pulpotomy medicaments that are both clinically and biologically more acceptable [15].

Glutaraldehyde has been suggested as an alternative to formocresol as a pulpotomy medicament [16-18]. It is a colourless solution that has a mild odour and a boiling point of 183°C to 187°C, is soluble in water and produces a mild acidity on contamination [19]. Glutaraldehyde is a chemically bifunctional reagent, which forms strong intra- and intermolecular protein bonds, leading to superior fixation by cross linkage [5]. Penetration into surrounding periapical tissue is limited primarily by protein cross-linkage formation. Thus, systemic distribution of glutaraldehyde is limited [20-22]. Glutaraldehyde is less necrotic, dystrophic, cytotoxic and antigenic, is a better bacteriocide, and fixes the tissue instantly [5]. Unlike formaldehyde, glutaraldehyde exhibits very low tissue binding and is readily metabolised [21]. Unfortunately, a buffered solution of glutaraldehyde is unstable due to short shelf life and it has to be freshly prepared [23].

Monsel's solution [24], which is a 20% ferric sub-sulphate, is widely used as a strong styptic agent in skin and mucosal biopsies. It causes reactive and degenerative changes when used as a styptic agent. However, another form of this chemical, ferric sulphate [25], produces local and reversible inflammatory response to oral soft tissues, but no toxic or harmful effects have been published in dental or medical literature [24,26,27]. In contact with the blood, ferric ions form a ferric complex and the membrane of this complex seals the cut blood vessels mechanically and provides haemostasis and an agglutinated protein complex, which produces a blood clot that occludes the capillary orifices [25,28]. This non-aldehyde chemical (ferric sulphate) has therefore been proposed as a pulpotomy agent as its mechanism of controlling haemorrhage might minimise the chances of inflammation and internal resorption and it is believed to be associated with physiologic clot formation [29]. Fie *et al.* (1991) demonstrated good clinical results using ferric sulphate in human primary teeth [25]. Since then, it has been used as an alternative pulpal medicament.

Aims

Against this background, this *in vivo* study aimed to assess and compare the relative clinical and radiographic success of formocresol, glutaraldehyde and ferric sulphate as medicaments in primary molars at three-monthly intervals over one year.

Methods

The 90 carious primary molars that formed the sample for this study were in the mouths of 54 children aged between three and nine years who visited the Department of Paediatric Dentistry, Sri Dharmasthala Manjunatheshwar (SDM) College of Dental Sciences and Hospital, Sattur, Dharwad, India (study duration between January 2005 and April 2007). The Ethics Committee of the SDM College of Dental Sciences approved the study.

The inclusion criteria, based on clinical and radiographical screening, were:

1. Healthy and cooperative children with one or more primary molar with a carious lesion involving vital pulp.
2. Primary molars with vital carious exposures that bled upon pulp extirpation on entering the pulp chamber.
3. No evident clinical symptoms of pulpal necrosis such as pain on percussion, continuous pain, history of swelling, and sinus tract.
4. No radiographic evidence of internal and external resorption, pulp stone, and interradicular or periapical pathology.
5. The structure of the tooth would be restorable with a stainless steel crown.

The complete treatment procedure, its possible discomfort, risks and benefits were explained to the parents/guardians of the patients. Informed consent prior to participation in the study was obtained. The selected primary molars were randomly assigned and divided into three test groups according to the pulpotomy medicament used. The pulpotomy technique, including local anaesthesia, placement of rubber dam and treatment procedure, was explained to the child. Children's confidence was gained before starting the procedure. The conventional and standard pulpotomy technique was performed [30]. The amputated pulp stumps were treated with one of the following medicaments.

Group FC: A sterile foam pellet no. 4 (Pele Tim; Voco, Cuxhaven, Germany), first saturated with formocresol (formalin 20% w/v, cresol 32.0% w/v, glycerine base 0.5; forsol 20 ml; Vishal Dentocare, Ahmedabad, Gujarat, India), later compressed twice between gauze to remove excess solution (dampened), was placed for five minutes on ampu-

tated pulp stumps. Following the brownish to black discoloration of fixed radicular pulpal tissue on the orifice, a thick mix of zinc oxide eugenol (DPI, Mumbai, India) was placed.

Group GA: A sterile foam pellet no. 4 (Pele Tim; Voco, Cuxhaven, Germany), first saturated with freshly prepared 2% glutaraldehyde solution (2% glutaraldehyde in one litre with a solution activator of 6.5 g Bioclenz-G; PSK Pharma, Karnataka, India) prepared according to the manufacturer's instructions and later compressed twice between gauze to remove excess solution (dampened), was placed for five minutes on amputated pulp stumps. Following the brownish to black discoloration of fixed radicular pulp tissue on the orifice, a thick mix of zinc oxide eugenol (DPI, Mumbai, India) was placed.

Group FS: A sterile foam pellet no. 4 (Pele Tim; Voco, Cuxhaven, Germany), first saturated with 15.5% ferric sulphate (Astringedent 60 ml; Ultradent Products, South Jordan, UT, USA) and later compressed twice between gauze to remove excess solution (dampened), was placed for 15 seconds—as quoted by original study of Fie *et al.* (1991) [25], FS is an astringent; its mechanism of action to produce a blood clot is 15 seconds—on amputated pulp stumps. After the brownish to black discoloration of fixed radicular pulp tissue, the ferric sulphate was flushed from the pulp chamber with a copious amount of water and then a thick mix of zinc oxide eugenol (DPI, Mumbai, India) was placed.

All teeth in the three groups were restored with a stainless steel crown (3M) cemented with glass-ionomer cement (GC Fuji I, GC America, Alsip, IL, USA). The children were recalled for clinical and radiographical evaluation at three-monthly intervals for a period of one year. The first author (RH) performed all the treatment and second and third authors (RTA and KRI) evaluated all the post-operative follow-ups. The post-operative clinical success was evaluated for pain (P), tenderness. (T), swelling (Sw), fistula formation (Fi), and pathologic mobility (PM). Post-operative radiographic success was evaluated by looking for a lack of widening of the periodontal ligament space (WPLS), internal root resorption (IR), external root resorption (ER), pathological interradicular radiolucency (PIR) and calcification of canal (CC). If the tooth exhibited any one of these features, the pulpotomy was considered to be a failure (F); otherwise, it was regarded as a success (S). In this study, all children attended for a follow-up evaluation.

The results were analysed using descriptive statistics and making comparisons between treatment groups with respect to demographics and clinical and radiographic parameters. Proportions were compared using chi-square test. Statistical significance was set at a *P*-value of =0.05.

Results

Fifty-four children (27 female, 27 male) were included in the study, from which 90 primary molars (15 upper and 75 lower) were selected.

Clinical evaluation

At the end of the 12-month follow-up period, clinical failures were found in the FC and FS groups. However, the GA group was free from clinical failures. The FS group had one tooth (3.3%) and the FC group had seven teeth (23.3%) with clinical failures. In the FC group, clinical failure rates were: 1/30 (3.3%) at three months, 2/29 (6.9%) at six months, 1/27 (3.1%) at nine months, and 3/2 (11.5%) at twelve months. In the FS group, only one tooth 1/30 (3.3%) showed clinical failure at nine months. The clinical failure rate of three groups at three, six and nine months was not statistically significant. At 12 months, it was statistically significant ($P<0.05$) (*Table 1*).

Radiographical evaluation

Radiological failures were seen in all three groups. The GA group had lowest number of failures followed by the FS group and the FC group. After 12 months, the GA group had 5/30 (16.7%) "radiographic" failures, the FS group 11/30 (36.7%) and the FC group 13/30 (43.3%). In the FC group the radiographic failures were 6/30 (20%) teeth at three months, 6/24 (25%) teeth at six months, and 1/18 (5.6%) tooth at nine months. In total, 13 FC group teeth had failed by the end of one year. In the FS group, radiographic failures were 5/30 (16.7%) at three months, 2/25 (8%) at six months and 2/23 (4.5%) at twelve months. Thus nine teeth in the FS group had exhibited radiographic failures at the end of one year. In the GA group, radiographic failures were 3/30 (10%) teeth at three months, and 2/27 (7.4%) teeth at six months, a total of five teeth failures at the end of one year. The radiographic failure rate of three groups at the third, ninth and twelfth months was not statistically significant ($P>0.05$); however, it was statistically significant at the end of sixth months ($P<0.05$). The radiographic failures

Table 1. *Clinical failures*

Pulpotomy groups	Follow-up								Grand total	
	3 months		6 months		9 months		12 months			
	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)
FC	30	1 (3.3%)	29	2 (6.9%)	27	1 (3.1%)	26	3 (11.5%)	30	7 (23.3%)
GA	30	0 (0%)	30	0 (0%)	30	0 (0%)	30	0 (0%)	30	0 (0%)
FS	30	0 (0%)	30	0 (0%)	30	1 (3.3%)	29	0 (0%)	30	1 (3.3%)
χ^2 value	2.02		4.233		1.086		7.057		11.799	
P-value	0.3637‡		0.1204‡		0.5809‡		0.029*		0.0027*	

Statistically significant at $P<0.05$. *Significant; ‡Not significant

Table 2. *Radiological failures*

Pulpotomy groups	Follow-up								Grand total	
	3 months		6 months		9 months		12 months			
	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)	Total teeth N	Failures N (%)
FC	30	6 (20%)	24	6 (25%)	18	1 (5.6%)	17	0 (0%)	30	13 (43.3%)
GA	30	3 (10%)	27	2 (7.4%)	25	0 (0%)	25	0 (0%)	30	5 (16.7%)
FS	30	5 (16.7%)	25	2 (8.0%)	23	2 (8.7%)	21	2 (4.5%)	30	11 (36.7%)
χ^2 value	1.184		4.309		2.15		4.13		5.291	
P-value	0.5531‡		0.1159*		0.342‡		0.1267‡		0.070‡	

Statistically significant at $P<0.05$. *Significant, ‡Not significant

Table 3. *Success and failure of clinical features at the end of one year (N=30)*

Pulpotomy groups	Clinical features						
	P	T	Sw		Fi	PM	
	S	S	S	F	S	S	F
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
FC	30 (100%)	30 (100%)	26 (86.7%)	4 (13.3%)	30 (100%)	26 (86.7%)	4 (13.3%)
GA	30 (100%)	30 (100%)	30 (100%)	0	30 (100%)	30 (100%)	0
FS	30 (100%)	30 (100%)	29 (96.7%)	1 (3.3%)	30 (100%)	30 (100%)	0

S = success, F = failure, N (%) = number of teeth and percentage, P = pain symptoms, T = tenderness, Sw = swelling, Fi = fistulation, PM = pathologic mobility, FC = formocresol, GA = glutaraldehyde, FS = ferric sulphate

were significantly higher than clinical failures ($P>0.05$) (*Table 2*).

Clinical and radiographic features of failure at the end of one year

At the end of one year, clinical failure symptoms of post-operative swelling were reported with 4/30 (13.3%) in the FC group, 1/30 (3.3%) in the FS group, and swelling-free in the GA group. Pathologic mobility was reported only in the FC group (4/30; 13.3%) of teeth. Pain, tenderness and fistulation were not reported in the entire follow up period (*Table 3*).

In radiographic evaluation, the most common finding over time in all groups was internal resorption. It was 5/30 (16.6%) in the FC group, 6/30 (20%) in the FS group, and 5/30 (16.6%) in the GA group. External resorption was only seen in the FC group (5/30; 20%). Pathological interradicular radiolucency was seen in the FC group (7/30; 23%) and the FS group (2/30; 6.7%), but not in the GA group. Calcification of canals was not seen in the FC or GA groups but was seen in the FS group (4/30; 13%). Widening of periodontal ligament was not seen with any of the groups at recall (*Table 4*).

Table 4. *Success and failure of radiographical features at the end of one year (N=30)*

Pulpotomy groups	Radiographical features								
	WPLS	PIR		IR		ER		CC	
	S	S	F	S	F	S	F	S	F
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
FC	30 (100%)	23 (76.6%)	7 (23.3%)	25 (83.3%)	5 (16.66%)	24 (80%)	6 (20%)	30 (100%)	Nil
GA	30 (100%)	30 (100%)	0	25 (83.3%)	5 (16.66%)	30 (100%)	0	30 (100%)	Nil
FS	30 (100%)	28 (93.33%)	2 (6.66%)	24 (80.0%)	6 (20%)	30 (100%)	0	26 (86.66%)	4 (13.33%)

S = success, F = failure, N (%) = number of teeth and percentage, WPLS = widening of periodontal ligament, PIR = pathological interradicular radiolucency, IR = internal resorption, ER = external resorption, CC = calcification of canals, FC = formocresol, GA = glutaraldehyde, FS = ferric sulphate

Discussion

Dental caries is one of the most common pathologies to affect paediatric dental health. When comparing the structure of primary teeth to permanent teeth, enamel and dentine are thinner, enamel is more porous, dental tubules are wider, and the pulp chamber is higher and larger [30]. Added to this, there is frequently inadequate maintenance of oral hygiene and consumption of sugars, leading to more rapid spread of caries and early involvement of pulp in primary teeth than in permanent teeth. When pulpal inflammation is confined to coronal pulp, the treatment that has attained wide acceptance clinically and radiologically is pulpotomy.

Thus, the present study was designed to assess and compare the relative success of formocresol (FC), glutaraldehyde (GA) and ferric sulphate (FS) as pulpotomy medicaments in primary molars. The study demonstrated the relative success of gluteraldehyde, both clinically and radiographically, as a pulpotomy medicament in primary teeth, followed by ferric sulphate and formocresol. It was interesting to note that at the end of one year the clinical success rate was 100% in the GA group (comparable to Kopel *et al.* (1980) [16], who reported 100% success), 96.7% in the FS group—comparable to Fuks and Holan (1997) [31] and Erdem *et al.* (2011) [2], who reported 92.7% and 100% success, respectively—and 86.7% in the FC group—comparable Huth *et al.* (2005) [32] and Ruby *et al.* (2012) [3], who reported 96% and 100% success, respectively. In the present study, clinical failure symptoms were post-operative swelling and pathologic mobility, which were reported in the FC and FS groups. These symptoms were also noted in previous studies [33-35]. They may be attributed to chronic inflammation of pulp and periapical tissue leading to oedema, which progresses into pathologic mobility.

Surprisingly, the radiographic success rate was drastically reduced in comparison with the clinical successes rate in all three groups. This result is in accordance with other studies. After 12 months the radiographic success rate was 83.3% in the GA group—comparable to Shumayrikh and Adenubi (1999) who reported 75.8% radiologic success [36]). In the FS group, it was 63.3%—comparable to Fuks and Holan (1997) [31] and Odabaş *et al.* (2012) [37], who reported 74.5% and 78.2 % radiological success, respectively. In the FC group, it was 56.7%, compared with Thaliyath and Joseph (1996) [18] and Ansari and Ranjpour (2010) [38] who reported 67.75% and 85% radiological success, respectively.

Failure of pulpotomy is normally detected radiographically, as the tooth may be asymptomatic clinically. The first sign of failure may be internal resorption of the root adjacent to the pulpal medicament. This may be accompanied by external root resorption, especially as the failure progresses. In primary molars, pathological interradicular radiolucency develops in the bifurcation or trifurcation area; in anterior teeth radiolucency may develop at the apex or laterals to the root. With more destruction, the tooth becomes mobile or a fistula may develop [39].

In the present study, the glutaraldehyde group was free from pathological interradicular radiolucency (PIR) after 12 months. However, seven teeth (23.3%) in the formocresol group and two teeth (6.7%) in the ferric sulphate group showed PIR. This cause of failure has also been reported in various previous studies [18,31-33,36,38,40,41]. The PIR failures in the formocresol group may have been due to the smaller molecular size of formocresol, which may cause seepage into the apical region through the pulpal canal(s) or into the furcation area via accessory canals or the pulpal floor, as it is

thin, porous and permeable in nature, in deciduous molars [30,42]. PIR was not seen in the glutaraldehyde group, possibly because of the larger molecular size of the medicament, which may not able to seep into the furcation area [43,44].

In the present study, internal resorption was noted in all the three pulpotomy medicament groups. This pulpal response has also been noticed in previous studies [18,31-33,36,38,40,41,45-47]. Internal resorption may be due to a chronically inflamed pulp, to variation in the pulpotomy techniques used, or to lack of predentine [48]. In the current study, the formocresol was in contact with vital pulp tissue for five minutes. This period may be too short to produce complete mummification. This in turn may lead to half-dead, half-vital, and/or chronically inflamed pulp tissue. The resulting pulp can be susceptible to abscess formation and internal resorption [49]. In the case of glutaraldehyde, the penetration is limited due to the rapid bonding to proteins and may cause inadequate fixation. This leaves a deficient barrier to sub-base irritation, resulting in internal resorption [17]. Ferric sulphate is not a fixative agent; this may be the reason for internal resorption. The zinc oxide eugenol base is in direct contact with the pulpal surface and may play an important role in diffusing the eugenol to vital pulp and irritating the pulpal tissue [40,50]. It has been suggested that the eugenol initially produces a vascular change that leads to an inflammation and formation of granulation tissue. It may be accompanied by metaplasia of normal connective tissue and macrophages to form osteoclast-like giant multinuclear odotoclasts, which may cause internal resorption [51].

The present study showed no external root resorption with the glutaraldehyde and ferric sulphate groups during entire period of follow-up. Only the formocresol group showed external resorption, in a total of six teeth. This failure was demonstrated in previous studies [33,35,38]. It is well documented that the mechanism of external root resorption with the use of formocresol is not clearly understood. One explanation [52] is the cell-mediated reaction to normal tissue by formocresol irritation. Thus, irritation potentiates external root resorption. The higher molecular weight of (two active aldehyde molecules) glutaraldehyde limits its tissue penetration and hence it may reduce the extension of inflammatory response [43-45].. Therefore, in the majority of glutaraldehyde cases external resorption was limited.

In the present study, calcification of canals was not seen in the glutaraldehyde and formocresol groups. However, in the ferric sulphate group four teeth manifested calcification of the canals, a side effect previously noticed in various other studies [2,3,25,31,33,34,38,40,41]. Canal calcification can be described as a reaction of dentine, which represents an effort by pulp tissue to repair, after experiencing an injury [53]. The other reason could be because eugenol seepage was faster than the glutaraldehyde into pulpal canals and it led to irritation and exaggerated the odontoblastic activity leading to canal calcification [50,54].

Failures in pulpotomised teeth—such as pathological radiolucency, interradicular radiolucency, external resorption, calcification of canals, swelling, pain, tenderness, abscesses and cysts—emphasise the importance of periodic follow-up [39].

The diagnosis of failure is mainly based upon clinical judgement; it includes pre- and intra-operative assessment of pulp status. The texture and colour of the pulp tissue as well as cessation of bleeding after coronal amputation have been used in paediatric dentistry as indicators of the status of the radicular pulp. Because more precise diagnostic tools are not available in the clinical situation, some pulpotomies performed on teeth would be histologically contra-indicated [55]. This may be the reason attributed for the pulpotomy failure.

Previous studies have shown a gradual decrease in success rate with time [33,40,41,56], as was noticed in the current study. This could be attributed to physiological resorption, accelerated root resorption, and the approach of the time for exfoliation of primary molars.

Generally it is believed that free eugenol, as found in freshly prepared zinc oxide eugenol mix, could cause significant irritation to vital pulp tissue [57], leading to a reduction in success rates. To overcome this, polycorboxylate cement can be used as sub-base, due to its larger molecular size and less irritation to vital pulp.

Comparison with previous studies may sometimes be difficult due to varied selection criteria regarding cases, clinical, radiographical, methodology, materials, concentration of medicaments, timing of application and the duration of evaluation, which may affect the final outcome.

Conclusions

The following conclusions were drawn from the present study:

1. No significant difference was shown between formocresol, glutaraldehyde, and ferric sulphate as medicaments for use following pulpotomy. However, the result achieved following the application of 2% glutaraldehyde was promising when compared to ferric sulphate and formocresol. The limitation of glutaraldehyde is that it has to be freshly prepared.
2. Internal resorption was a common radiographic finding in all pulpotomy medicament groups.
3. At recall, pulpotomised teeth should be assessed radiographically to monitor any pathological changes.
4. In the present study, the clinical success rate was higher than the radiological success. From this observation, it can be assumed that from the point of view of a clinician as well a parent, clinical success may count more than radiologic changes.

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Contributions of each author

- RH performed all the pulpotomies in this study and wrote the full manuscript.
- RTA and KRI performed the blind valuation of post-operative clinical and radiographical aspects of pulpotomies and checked the draft and gave necessary guidance for this study.
- PS helped in writing the paper and designed the study.

Statement of conflict of interest

As far as the authors are aware, there is no conflict of interest.

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