CONTEMPORARY PULPOTOMY AGENTS IN PEDIATRIC DENTISTRY: A REVIEW

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Abstract

Pulpotomy therapy is a widely used therapy used in various clinical settings. It is used for treating the cariously exposed vital primary tooth. Formocresol is the most widely used pulpotomy agent inspite of being a subject of many controversies. This has led to the development of various alternatives to formocresol. The objective of this narrative review is to put forward overview of the materials used as alternative to formocresol thus, providing the clinicians with better alternatives to select from the following materials for use.

Keywords

Dental pulp, pulpotomy, medicaments.

Introduction

Preservation of deciduous teeth is very important until the required age as it maintains the arch length for the permanent teeth to erupt.^[1] Caries, injuries causing trauma to teeth and various treatment procedures makes the vital pulp tissue vulnerable to exposure which can severely reduce the function and lifespan of the deciduous teeth. Pulpotomy is a dental clinical procedure performed on a vital deciduous tooth with an inflamed

and widespread carious lesion having infected coronal pulp but a healthy and normal radicular pulp. Pulpotomy is also done in vital carious deciduous tooth with mechanical exposure. Pulpotomy of the deciduous teeth is not only the most frequent endodontic treatment performed on children but also the most controversial ^[1]. Pulpotomy is recommended in those individuals who complain of spontaneous pain only, showing clinical evidence of wide area of caries and radiographic evidence of coronal pulp infection without any radicular and periapical infection. The procedure of pulpotomy involves the elimination of the infected and inflamed coronal pulp and preservation of the healthy radicular pulp using various pulpotomy agents. Formocresol is the most commonly used pulpotomy agent clinically. Concerns about formocresol have shown it to be cytotoxic, mutagenic and carcinogenic in animal experiments by Lewis in 1981^[2]. In view of these controversies surrounding FC, various alternatives have been studied ^[3]. The objective of this review is to throw some light on these alternatives.

History

The Europeans were the first to introduce pulpotomy procedures. Table 1.lists the history and chronology of various pulpotomy agents ^[3].

Table1. History and chronology of various pulpotomy agents

1885	Leptowski: Formalin was introduced as a fixative and mummifying agent.
1886	The exposed vital pulp was covered using gold foil
1889	Gysi: Paraformaldehyde was introduced as a Pulpotomy agent by Gysi
1904	Buckley: Initiated the use of formocresol as Pulpotomy medicament
1930	Hermann: Found calcium hydroxide as calxyl(pulp capping agent), was also used for pulpotomy
1975	S'Gravenmade: was the first to found the use of gluteraldehyde as Pulpotomy medicament and also stated that glutaraldehyde has a potential to replace formocresol

1980	Nevins AJ: described the use of collagen-calcium phosphate gel in pulpotomy procedure
1981	Bimstein E: used enriched collagen solution as Pulpotomy medicament.
1983	Ruemping et al.: showed the use of electrosurgery in Pulpotomy procedure
1985	Shoji:showed application of carbon dioxide laser in pulpotomy
1991	Nakashima: application of bone morphogenic protein in Pulpotomy procedure
1993	Torabinejad: Initiated the use of MTA for the repair of perforation. MTA was used for various vital pulp therapy procedures including pulpotomy

Classification:

Don M Ranley in 1994 classified pulpotomy according to the treatment objectives:

1. Devitalisation (mummification, cauterization) ^[2]
2. Preservation (minimal devitalisation, non conductive)^[2]
3. Regeneration (inductive, reparative) ^[2]

Devitalisation pulpotomy

This is the first method of pulpotomy done with the intention of “mummifying” the radicular pulp tissue by chemically treating the pulp using pulpotomy agents like: Formocresol, GysiTrio paste, Easlick’s formaldehyde, paraform devitalizing paste.

FORMOCRESOL was introduced by Buckley in 1904. At present, 1:5 dilution or 1/5th concentration of buckley’s formula is used in clinical practice. Buckley’s formula includes: 19% formaldehyde, 3% cresol, 15% glycerine, and 31% water.

MECHANISM OF ACTION: Formocresol shows good efficacy as a bacteriocidal agent. The tissue autolysis is prevented due to bonding of formocresol to the bacterial proteins ^[2]. The microorganisms and the residual vital tissue gets converted by formocresol ^[4].

Three zones were seen histologically seen after a 7 to 14 days application which was demonstrated by MASSLER and MANSUKHANI in 1959. These zones are as follows:

1. A wide eosinophilic area of fixation directly beneath the medicament where it is placed ^[2, 4]
2. An atrophied wide pale- staining zone which shows poor cellular clarity ^[2].
3. A broad zone of persistent inflammation extending apically into the normal pulp tissue ^[2].

Complete loss of vitality was seen in the root canal's apical one third region ^[4].When the formocresol in low concentration comes

in contact with the polymorphonuclear cells, it causes stimulation of the PMN cells thus resulting in chronic inflammatory change ^[5].In 1930 Sweet formulated the multivisit FC pulpotomy technique in human pulp with the intention of the tissue being mummified completely ^[6].Theoretically, it showed the entirely fixed radicular pulp to be sterilised and devitalised thereby precluding infection and internal resorption ^[6]. Doyle et al. in1962 introduced the 2 visit FC pulpotomy technique where FC was applied in the first visit.A base of zinc-oxide eugenol cement mixed with paraformaldehyde and restoration was placed in the second visit ^[7]. Spedding et al. in 1965 and Redig in1966 started using 5 min. FC pulpotomy^[6].Instead of absolute mummification ,this procedure left the pulp partially devitalized. In other words, the pulp remained partially dead and partially vital and persistently inflamed ^[6].Venham in 1967 proposed 15 seconds procedure^[2].Gracia Godoi in 1991 recommended the 1 min. single visit pulpotomy^[3]. A study conducted by Prof. Amitabha Chakraborty in 2018 using the 1 min. single visit technique showed 89.4% clinical and radiographic success ^[7].

Electrosurgery:- This is a non-pharmacological hemostatic single sitting devitalisation pulpotomy procedure. It was introduced by Anderman in 1982.Mark was the first US dentist to routinely perform electrosurgical pulpotomies in 1993 and had a success rate of 99% for primary molars^[2].When the electric arc is placed 1 to 2mm above the pulp stump, it in turn denatures and carbonizes the pulp which leads to coagulation necrosis^[4]. In 2006, clinical trial was performed which evaluated the clinical and radiographic success of ES showing 100% clinical and 84% radiographical success ^[8].

Laser:- The use of laser was first initiated in the early 1960s. Besides being a haemostatic, it also has cell stimulating and antimicrobial properties. Saltzman et al., in 2005 in a study used diode laser and achieved hemostasis, but reported less radiographic success compared to formocresol pulpotomy^[4]

The two stage devitalisation pulpotomy technique uses materials such as Easlick’s paraformaldehyde paste (composition:- Paraformaldehyde 1g , procaine base 0.03g , powdered asbestos 0.5g , petroleum jelly 125g , and carmine to color) , Gysi Triopaste(composition:- Tricresol 10ml , cresol 20ml , glycerine 4 ml, paraformaldehyde 20g , zinc oxide eugenol 60g) , Paraform

devitalizing paste (composition:- paraformaldehyde 1g, lignocaine 0.06g, propylene glycol 0.5g, carbowax 1.3g, carmine to color).

Studies have shown formocresol therapy to have a clinical success rate between 70% and 90%^[4]. Still, concerns exist in the view of the safety with respect to mutagenicity, carcinogenicity, immune sensitization potential and also regarding the effectiveness seen of formocresol use. In June 2004 International Agency for Research and Cancer classified Formaldehyde as carcinogenic to humans. It has a potential to cause leukemia and nasopharyngeal carcinoma^[9]. WHO classified formaldehyde as a known human carcinogen^[9]. Ranley DM in 1994 calculated that over 3000 pulpotomy has to be carried out in a same individual for the formocresol to achieve noxious level. Milnes in 2006 in his publication of an expansive and comprehensive review of the more recent research on the pharmacokinetics, metabolism and carcinogenic effect of formaldehyde deduced formaldehyde as a non-potent human carcinogen when used under conditions of low exposure^[2]. Formaldehyde has been shown to be distributed upto 10% of the same in dogs following formocresol pulpotomy^[10]. An association between Dentigerous cyst and FC Pulpotomy was seen^[11]. No association was demonstrated between FC pulpotomy and cancer^[12].

PRESERVATIVE PULPOTOMY: - Preservative pulpotomy involves maintaining of the maximum vital tissue, without reparative dentine being induced, thus maintaining the vitality and normal histological property of the root pulp.

1. ZINC OXIDE EUGENOL:- The first medicament to be used in preservation was zinc oxide eugenol. Earlier many studies revealed some negative aspects of ZOE pulpomoties but it was the comprehensive histologic analysis by Magnusson which best demonstrated the resultant internal resorption and inflammation^[6].

ZOE used as a sub base after pulpotomy, eugenol contacts the vital tissues and causes modest to critical inflammatory response. Reinforced ZOE contains polymethyl methacrylate, zinc oxide, acetic acid, and eugenol^[3]. In a clinical study done in 2013, 94% clinical success was seen in ZOE pulpotomy when compared with FC pulpotomy^[4].

2. GLUTARALDEHYDE:- S. Gravenmade in 1975 proposed glutaraldehyde (GA) as pulpotomy medicament^[3]. Glutaraldehyde was suggested instead of FC because of its ability to cause superior surface fixation, self-limiting penetration, and causes less necrosis of the pulp substance and removal of cresol^[3]. Mutagenicity and antigenicity is also less compared to FC. Glutaraldehyde also has the property of low tissue binding, is readily metabolized, and eliminated in urine. The main disadvantage of glutaraldehyde is that, it needs to be immediately prepared before use due to its short life span of 14 days^[4]. Glutaraldehyde produces speedy fixation of the surface underlying pulpal tissue^[2]. Hill described the minimum antimicrobial concentration of glutaraldehyde as 3.125%^[4]. Ranly, Gracia Godoy in 1987 observed that increased concentration and prolonged time enhances the fixative property and recommended the use of 4% glutaraldehyde for 4 minutes or 8% glutaraldehyde for 2 minutes^[4]. In a recent study by Havale et al., the relative clinical and radiographic success of FC, GA, and Ferric Sulphate (FS) pulpomoties were compared at 3-month intervals over one year. The clinical success rates of FC, FS, and GA were 86.7, 96.7, and 100% respectively. The radiographic success rates in FC, GA, and FS were 56.7, 83.3, and 63.3%, respectively^[12]. Fuks et al. in 1990 carried out a pulpotomy study with 2% glutaraldehyde showed an average of 83% success rates. Tsai et al. in 1993 carried out a pulpotomy study with 5% and 2% unbuffered and buffered glutaraldehyde showed an overall of 79% success rate^[13]. The following table (TABLE 2.) shows the clinical and radiographical success rates of glutaraldehyde shown in various studies^[6].

Table 2. Clinical studies related to glutaraldehyde

Investigators	Clinical success rate (%)	Radiographic success rates (%)	Duration (months)
1. Gracia Godoy	100	98	42
2. Alcam	96	92	12
3. Guiliana	96	96	12
4. Prakash et al.	100	100	6
5. Fuks et al.	96	82	25

FERRIC SULPHATE:- Ferric sulphate ($\text{Fe}_2(\text{SO}_4)_3$) is a chemical compound utilized as an agent of Pulpotomy procedure in the form of 15.5% solution^[2]. Ferric sulphate's mechanism of action is still under debate, but the reaction of blood with the ferric and sulphate ions results in agglutination of blood proteins. The capillary orifices are sealed with the help of these agglutinated proteins, hence, preventing clot formation^[4]. Most common pathology that has been observed is calcific metamorphosis and internal resorption^[4]. A higher percentage of internal resorption is the major failure of FS pulpotomies reported by Papagiannoulis^[12]. Landau and Johnson were the first to study the pulpal response from ferric sulphate in monkey teeth^[14]. The two human clinical studies using ferric sulphate has been done by following two investigators. Fei et al. in 1991 used 15.5% FS+ZOE on 29 human molars and 1:5 dilution 5 min FC+ZOE on 27 human molars. After an observation period 3 to 12 months, a clinical success of 100% in FS and 96% in FC was found. A radiographical success of 97% in FS and 78% in FC was observed. Calcific metamorphosis of 48% in FS and 44% in FC was also observed^[14]. Fuks et al. in 1997 also performed a similar study using similar concentrations of FC and FS for a period of 6 to 34 months. A radiographical success of 93% in FS and 84% in FC was observed. An internal root resorption of 7% and calcific metamorphosis of 18% was seen in FS. Similarly, internal root resorption of 5% and calcific metamorphosis of 11% has been seen in FC^[14]. Therefore, ferric sulphate maybe suggested as a suitable substitute for formocresol^[12].

Regenerative Pulpotomy: Regenerative pulpotomy is the procedure that stimulates the radicular pulp to cure and results in the formation of a dentin bridge barrier^[3]. Calcium hydroxide, mineral trioxide aggregate, bone morphogenic protein are used in regenerative procedures^[3].

CALCIUM HYDROXIDE:- Calcium hydroxide was introduced to dentistry in 1838 by Nygren. In 1930, Hermann showed that calcium hydroxide stimulated the formation of new dentin when placed in contact with human pulp tissue^[12]. Schroder et al. in 1978 conducted pulpotomy studies with calcium hydroxide base showed 59% success. Heilig et al. in 1984 conducted a pulpotomy study with calcium hydroxide base which showed 88% success. Gruythuysen and Weerheijm in 1997 conducted pulpotomy study with calcium hydroxide base, showed 80% success^[13]. The major disadvantage of this alternate intervention is internal resorption^[3].

MINERAL TRIOXIDE AGGREGATE (MTA):- Lee et al. introduced MTA and patented in 1995 by Torabinejad and White^[12]. It is a ash colored powder primarily made of fine hydrophilic particles of tricalcium aluminate, tricalcium silicate, silicate oxide, tricalcium oxide, and bismuth oxide is added for radiopacity. It is available commercially as ProRoot MTA (Dentsply Tulsa Dental, Tulsa, Okla)^[2]. Freshly mixed MTA has a pH of 10.2 which rises to 12.5 after 3 hours of setting^[3].

The major benefits of MTA are biocompatibility, being bacterial and induction of cementogenesis. MTA is used for various clinical treatments like DPC, apexification and apexogenesis in immature

teeth. A study done by E. Stringhini Junior et al. assessed the scientific evidence of pulpotomy in deciduous teeth MTA, calcium hydroxide, ferric sulphate, and electrosurgery with FC. The rate of success of MTA (94.6%) was higher than that of FC (87.4%). MTA was clinically and radiographically superior to FC^[15].

BONE MORPHOGENIC PROTEIN (BMP):- BMP are members of highly conserved family of signaling molecules that have been used repeatedly during evolution to mediate tissue interactions during embryonic development^[6]. Reparative dentin can be induced using BMP with the help of recombinant proteins^[3]. Urist (1965) reported of a factor with the ability of self-induction present in the bone matrix and named it as bone morphogenetic protein^[3]. A study was done by Rutherford on the pulpal response in the teeth of monkey which stated that recombinant human BMP-2 and BMP-4 can result in differentiation of mature pulp cells into odontoblasts^[3].

Newer Materials:

a. Lyophilized freeze dried platelet regulates the multiplication of cells, migration and extracellular matrix production by acting as signalling protein^[3]. An in vivo study conducted by N Venugopal Reddy to compare and evaluate the clinical, radiographical and histological success of FC, Propolis (PS), and Platelet derived growth factor (PDGF) as pulpotomy agents. The study showed clinical and radiographical success for PDGF group as 96.3% and 88.89% respectively, followed by PS group (96.3%, 88.4%) and FC group (76%, 72%). Histological examination showed deep and uninterrupted formation of dentin bridge with minimum inflammation in both PS and PDGF^[16].

b. Enamel Matrix Derivative (EMD) is formed from embryonic enamel as amelogenin^[3]. The capability of EMD to facilitate the regenerative process is conclusively proved. EMD, obtained of stimulating periodontal ligament cell proliferation faster than gingival fibroblasts and bone cells^[1]. At present, emdogain gel (Sturmann, Switzerland) has been effectively used for pulpotomy procedures^[3]. A report given by Jumana and Ahmed showed a success rate of 93% using emdogain gel for Pulpotomy^[3].

c. Biodentine is a calcium silicate based material composed of tricalcium silicate having dentin replacement property. It has the potential to induce apposition of reactionary dentin by stimulating odontoblasts and reparative dentin by induction of cell differentiation^[17]. It has a pH of 12, giving it a bacteriostatic property. Biodentine is mechanically more strong, less soluble and produces tight seals. This certified it for avoiding three main drawbacks of calcium hydroxide, i.e., material resorption, mechanical instability and the resultant failure of preventing microleakages^[17].

d. Propolis is a beehive product which is resinous and has an antioxidant, antibacterial and anti-inflammatory action. Park YK, in 2002 in his study reported that collagen synthesis and wound healing can be achieved by propolis^[4]. Lima et al. after histological

analysis, deduced that the inflammatory response was less severe, smaller area of pulp necrosis, and evidence of more periodic formation of a mineralised tissue barrier^[3].

Conclusion:

The pulpotomy procedure is widely practiced in clinical settings as it helps in the preservation of natural teeth. Pulpotomy depends on a number of factors such as case selection, the material used, clinical diagnosis. The pulpotomy using formocresol is in use even today as a pulpotomy medicament despite the worries raised due to its mutagenicity, toxicity, and cariogenicity. Clinical reports have exhibited better rates of success with Ferric sulphate and MTA.

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