

Review Article**Pulpotomy Medicaments: An Outlook**

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**ABSTRACT:** Pulpotomy therapy is the treatment of choice for cariously exposed vital primary molars. Pulpotomy therapy for the primary dentition has developed along three lines: devitalization, preservation, and regeneration. Controversies surrounding formocresol which enjoys good clinical success as a pulpotomy medicament has triggered the search for better alternatives. Of the three categories, regeneration is expected to develop the most rapidly in the coming years. Advances in the field of bone morphogenetic protein have opened new vistas in pulp therapy. The objective of this narrative review is to provide an overview of the materials that have been studied as alternatives to formocresol to aid clinicians in making an informed choice of medicament for pulpotomy.

**Keywords:** Bone morphogenetic proteins; Pulpotomy; Devitalization; Preservation; Regeneration.

**INTRODUCTION**

If caries removal process leads to pulp exposure, a pulpotomy is undertaken since direct pulp capping in cariously exposed primary teeth has been shown to have poor success.<sup>1</sup> A pulpotomy is performed in a primary tooth with extensive caries without evidence of radicular pathology when caries removal results in a carious or mechanical pulp exposure.<sup>1</sup> In particular, the vital pulpotomy procedure has been a topic of debate for decades. While pulpotomy therapy evolved slowly over the first 40 years, the pace of change since the 1960s has continued to accelerate. A simple chronological detailing of the advances in pulpotomy therapy without an attempt to categorize the underlying mechanism of action, does not permit the clinician to adequately weigh the pros and cons of current and future treatment options. The primary objective of pulp therapy is to maintain the integrity and health of the teeth and their supporting tissues. It is a treatment objective to maintain the vitality of the pulp of a tooth affected by caries, traumatic injury, or other causes. Especially in young permanent teeth with immature roots, the pulp is integral to continue apexogenesis. Long term retention of a permanent tooth requires a root with a favorable crown/ root ratio and dentinal walls that are thick enough to withstand normal function. Therefore, pulp preservation is the primary goal for treatment of the young permanent dentition. A tooth without a vital pulp, however, can remain clinically functional.<sup>2</sup>

The indications, objectives, and type of pulpal therapy depend on whether the pulp is vital or nonvital, based on the clinical diagnosis of normal pulp (symptom free and normally responsive to vitality testing), reversible pulpitis (pulp is capable of healing), symptomatic or asymptomatic irreversible pulpitis (vital inflamed pulp is incapable of healing), or necrotic pulp. The clinical diagnosis is derived from:

1. A comprehensive medical history.
2. A review of past and present dental history and treatment, including current symptoms and chief complaint.
3. A subjective evaluation of the area associated with the current symptoms/chief complaint by questioning the child and parent on the location, intensity, duration, stimulus, relief, and spontaneity.
4. A objective extraoral examination as well as examination of the intraoral soft and hard tissues.
5. If obtainable, radiograph(s) to diagnose pulpitis or necrosis showing the involved tooth, furcation, periapical area, and the surrounding bone.
6. Clinical tests such as palpation, percussion, and mobility.<sup>3</sup>

A pulpotomy is performed in a primary tooth with extensive caries but without evidence of radicular pathology when caries removal results in a carious or mechanical pulp exposure. The coronal pulp is amputated, and the remaining vital radicular pulp tissue surface is treated with a long-

term clinically-successful medicament such as Buckley's Solution of formocresol or ferric sulfate. Several studies have utilized sodium hypochlorite with comparable results to formocresol and ferric sulfate. Don M. Ranly classified pulpotomy based on treatment objectives into devitalization, (Mummification, Cauterization), preservation (minimal devitalization, noninductive) and regeneration (inductive, reparative). Non chemical methods of pulpotomy include use of electro surgery and lasers.<sup>4</sup>

**Devitalization Pulpotomy:** The first approach to pulpotomy treatment of primary teeth was devitalization. The multiple-visit formocresol technique, as introduced by Sweet's was designed to mummify the tissue completely. When completely fixed, the radicular pulp was theoretically sterilized and devitalized, thereby obviating infection and internal resorption. Apparently this protocol was highly successful.<sup>5</sup>

Pulpotomy using formocresol was introduced by Buckley in 1904. Since then various modifications have been tried and advocated regarding the techniques of FC pulpotomy and the concentrations.<sup>6</sup> Buckley's formula of formocresol includes formaldehyde 19%, Cresol 35%, glycerine 15%, and water with an approximate pH of 5.1. Currently 1:5 dilution of Buckley's formocresol is commonly used. A diluent consisting of 3 parts of glycerine (90 ml) added to one part distilled water (30 ml) is prepared. Later 4 parts of diluent (120 ml) is mixed with one part of Buckley's FC (30 ml).<sup>7</sup> Commercially available products vary in concentrations of their ingredients, for example Sultan formocresol available in India consists of 48.5% formaldehyde, 48.5% cresol and 3% glycerine.

As such, the only rationale for using formocresol is empirical and it succeeds more often than it fails. Reducing the concentration of formocresol used in pulpotomies, spurred by a series of toxicity and systemic distribution studies, has served only to move us further from the original objective, *s.* While reducing formocresol is laudable, using a diluted form merely

extends the empiricism. Despite half a century of research, we are still unable to explain why two toxic agents such as formaldehyde and cresol can be used beneficially.<sup>8</sup>

IARC (June 2004) classified formocresol as carcinogen that has potency to cause leukemia and nasopharyngeal carcinoma. However, Ranly calculated the formocresol concentration following pulpotomy and reported that 3000 pulpotomies will have to be performed in same individual to reach toxic levels.<sup>9</sup> In two stage devitalizing pulpotomy entire coronal and radicular pulp tissue is fixed. It is used when shorter appointments are required and for better patient management.

Miyamoto advocated two visit pulpotomy for effective management of uncooperative children.<sup>10</sup> During the first visit the material containing formalin or paraformaldehyde is placed in contact with the pulp, left for 5-7 days and pulpotomy is completed under local anesthesia in the second visit. Materials used are Gysi Triopaste (Tricresol 10 ml, cresol 20 ml, glycerine 4ml, paraformaldehyde 20 ml, zinc oxide eugenol 60 g), Easlick's Paraformaldehyde paste (paraformaldehyde 1 g, Procaine base 0.03 g, Powdered asbestos 0.05 g, Petroleum jelly 125 g, Carimine to color) and Paraform devitalizing paste (Paraformaldehyde 1g, Lignocaine 0.06g, Propylene glycol 0.5g, Carbowax 1.3g, Carmine to color).

Another form of nonchemical devitalization emerged during the last decade: electrosurgical pulpotomy.<sup>11</sup> While mummification eliminates pulp infection and vitality with chemical crosslinking and denaturation, electrocautery carbonizes and heat denatures pulp and bacterial contamination. Electrosurgery does little to improve on the formocresol pulpotomy save avoiding chemicals. Experimentally, electrosurgery has been shown to incite pathologic root resorption and periapical/furcal pathology and a spectrum of pulpal effects including acute and chronic inflammation, edema, fibrosis, and diffuse necrosis.<sup>11</sup> It may prove to be more diagnosis and technique sensitive, and it may not be suitable if apical root resorption

has occurred 2° Remarkably, Mack and Dean reported a very high success rate with the technique. It is difficult to explain why burned tissue is tolerated by the residual vital pulp. Nonetheless, despite the bleak histologic picture and perpetuated empiricism, electrosurgery will undoubtedly gain in popularity. In the future, laser energy might be able to overcome the histologic deficits of electrosurgery. Ideally, laser irradiation would create a superficial zone of coagulation necrosis that remained compatible with the underlying tissue and that isolated the pulp from the vagaries of the subbase. Thus far, only exploratory research has been done with lasers in pulp therapy.<sup>12</sup>

**Preservative Pulpotomy:** Materials used in preservative pulpotomy technique produce minimal insult to orifice tissue, thereby maintaining vitality and normal histological appearance of radicular pulp. The materials included in this category are ZOE, glutaraldehyde, ferric sulfate.<sup>13</sup>

Zinc oxide-eugenol (ZOE) was the first agent to be used for preservation. Because this cement was such a workhorse in early dentistry, it is little wonder that it was adapted to pulpotomies. But because it was so popular, we will probably never know who initiated the practice. While earlier studies revealed some negative aspects of ZOE pulpotomies, it was the comprehensive histologic analysis by Magnusson that best demonstrated the resultant inflammation and internal resorption. We now know that eugenol possesses destructive properties, and cannot be placed directly on pulp.<sup>14</sup> Although an obtundent, ZOE does not apparently suppress metabolism adequately or self-limit its irritative properties.

Zinc Oxide Eugenol (ZOE) was the first agent to be used for preservation. Earlier studies have shown that teeth treated with a pulpotomy using ZOE base demonstrated internal resorption and inflammation at the pulpotomy amputation site.<sup>15</sup> ZOE acted as obtundent but apparently failed to suppress the metabolism adequately.

It has been assumed that internal resorption is associated with eugenol. When ZOE is used as a sub-base following pulpotomy,

eugenol directly contacts with the vital tissue and causes moderate to severe inflammatory response. Products such as IRM and ZOE B&T are reinforced ZOE materials with improved mechanical properties.<sup>16</sup> Reinforced ZOE contains polymethyl methacrylate, zinc oxide, acetic acid, and eugenol. Fuks et al. found that 73% of pulpotomized primary teeth of baboons treated with IRM presented with mild or no inflammation.<sup>17</sup>

Glutaraldehyde for pulp fixation was proposed by s-Gravenmade in 1975. This dialdehyde has a limited shelf life and a cross-linking ability superior to that of formocresol. In recent years, glutaraldehyde has been proposed as an alternative to formocresol based on its superior fixative properties, self-limiting penetration, low antigenicity, low toxicity and elimination of cresol. Garcia-godoy reported that despite of high success rates the drawbacks in using glutaraldehyde includes the cost and inadequate fixation that leaves a deficient barrier susceptible for sub base irritation resulting in internal resorption.<sup>18</sup> In recent years, glutaraldehyde has been proposed as an alternative to formocresol based on: its superior fixative properties, self-limiting penetration, 3° low antigenicity, low toxicity, and the elimination of cresol. The histologic picture of a glutaraldehyde-treated pulp shows a zone of superficial fixation with very little underlying inflammation.<sup>19</sup>

A non-aldehyde chemical, ferric sulfate, has received some attention recently as a pulpotomy agent. This hemostatic compound was proposed on the theory that it might prevent problems encountered with clot formation and thereby minimize the chances for inflammation and internal resorption. It has not been explained how clotting itself could curtail these activities. Possibly the metal-protein clots at the surface of the pulp stumps, acts as a barrier to the irritative components of the subbase. If true, the ferric sulfate may function solely in a passive manner. An earlier 12-month clinical evaluation of ferric sulfate pulpotomies showed an excellent success rate, but the results reported from a more recent study were considerably less

favorable. That heavy metal coagulation with ferric sulfate is somehow able to subdue the pulp when the high pH-coagulation of calcium hydroxide cannot, remains to be verified.<sup>20</sup>

**Preservative Pulpotomy:** It is also called as inductive pulpotomy or reparative pulpotomy. This mechanism encourages the radicular pulp to heal and form a dentin bridge/hard tissue barrier. Ranly, stated that "Ideal pulpotomy treatment should leave the radicular pulp vital and healthy. Also completely enclose within an odontoblast lined dentin chamber." Additionally, the odontoclasts of an uninflamed pulp could enter into the exfoliative process at the appropriate time and sustain it in a physiologic manner. Unlike the other two categories i.e devitalization and preservation, the rationale for developing regeneration is based on sound biologic principle.<sup>21</sup> Materials used in regenerative pulpotomy are Calcium hydroxide, mineral trioxide aggregate, bone morphogenic protein (BMP 2, 3, 4, 5, 6, 7 and OP-2), Collagen.

Unlike the other two categories for pulp treatment, the rationale for the developing field of regeneration is actually based on sound, biologic principles. In 1972, Vostatek published an article in which he called his era of pulpotomy treatment the "Biological Era." In truth, we are only now entering it.<sup>22</sup>

Calcium hydroxide was the first agent used in pulpotomies that demonstrated any capacity to induce regeneration of dentin. The rationale that prompted its use by Zander was fundamentally erroneous, he attributed the action of calcium hydroxide to a modification of the solubility product of Calcium, phosphate and a precipitation of salt into an organic matrix. The main drawback of this alternative intervention is internal resorption. 70% success rate was reported by Subramaniam P with the use of thick paste of Ca(OH) and water. Schroder et al. and Doyle et al. reported dentine bridge formation and complete healing of the pulp stumps but some cases showed treatment failure in form of internal resorption. Magnusson obtained less

impressive results with use of calcium hydroxide for pulpotomy.<sup>23</sup>

Bone Morphogenic Proteins (BMP) is thought to induce reparative dentin with recombinant dentinogenic proteins similar to the native proteins of the body. This exciting era was based on two classic observations made many years ago. Huggins reported urinary tract epithelia implanted into the abdominal wall of dogs evoked bone formation. Urist observed that demineralized bone matrix, stimulated new bone formation when implanted in ectopic sites such as muscle. However due to its existence in such minute quantities and high affinity for the bone matrix, progress has been slow. Only very recently, with techniques of molecular biology significant progress has been made. Although tightly associated with collagen of matrix, BMPs are classified as non-collagenous proteins. Rutherford studied pulp response in monkey teeth and stated recombinant human BMP-2 and BMP-4 induce differentiation of adult pulp cells into odontoblasts. Silva et al. reported that rhBMP7 did not show favorable results and there was failure to form dentin bridge. Loren K et al. elicited the role RhBMP-2 in pulpal healing of experimental subjects. Currently animal studies using recombinant human BMP's are being tested, however no suitable product for human use is available yet.<sup>24</sup>

Mineral Trioxide Aggregate (MTA) has shown good success rates as pulpotomy agent. MTA was introduced by Torabinejad. Studies on MTA reveal that it not only exhibits good sealing ability, excellent long term prognosis and good biocompatibility but favors tissue regeneration as well. MTA has a pH of 10.2 immediately after mixing and increases to 12.5 after 3 hours of setting. MTA in contact with pulp tissue encourages dentin bridge formation. Dominguez et al. following histological evaluation reported that MTA caused minimal pulpal inflammation. However drawback of most studies were short follow up period and dropouts in follow up.<sup>25</sup>

Fortunately, the era of chemicals like calcium hydroxide may be coming to an end. Recent advances in the field of bone and

dentin formation have opened exciting new vistas for pulp therapy, and we are fast approaching a rational period in the treatment of pulp tissue. We now have the prospect of being able to induce reparative dentin with recombinant dentinogenic proteins similar to the native proteins of the body. This exciting new era is founded on two classic observations made many years ago, Huggins noted that urinary tract epithelia implanted into the abdominal wall of dogs evoked bone formation. Some years later, Agamy observed that demineralized bone matrix stimulated new bone formation when implanted in ectopic sites such as muscle<sup>26</sup> Yaman, concluded that bone matrix contains a factor capable of auto-induction, and he named this factor bone morphogenetic protein (BMP). Since that time, countless labs have attempted to purify the factor, or factors, but because it exists in such minute quantities and has such a high affinity for the bone matrix, progress has been slow. Only very recently, with techniques of molecular biology, has significant progress been made. We now know that there is a family of proteins that has bone inductive properties, and BMP is a generic term for this family.<sup>27</sup>

**Recent Advancements:** Sodium hypochlorite (NaOCl) has been successfully used for decades in endodontic therapy as an irrigant. Cox et al reported that hemostasis is best achieved with NaOCl. Chompu-Inwai et al. reported similar success rate of NaOCl/RMGIC when compared to FC/ ZOE in their 3 month evaluation . Vargas et al. showed promising results from a pilot study using 5% NaOCl as a primary molar pulpotomy agent . Various studies have shown a good success rate with NaOCl as pulpotomy agent ranging from 82 to 100% . Histologically Roza et al. noted mild inflammation and also dentin bridge formation after 2 months following NaOCl pulpotomy.<sup>28</sup>

Calciumphosphate cement falls in the class of hydraulic cements, which self-harden to hydroxyapatite (HA), the bone mineral. Several formulations of CPC have been successfully designed for various orthopedic and dental applications. CPCs possess the combination of biocompatibility, osteo-

conductivity and mouldability. Moreover, they are non-toxic and non-immunogenic and do not have any mutagenic or carcinogenic potential. Animal studies reported the capacity of calcium phosphate to form dentin without areas of necrosis.<sup>29</sup>

Propolis is a wax cum resin substance that is produced by bees. It is shown to have antibacterial, antiviral, antifungal, immunostimulation hypotensive and cytostatic activity mainly due to the presence of flavonoids (2-phenyl- 1,4-benzopyrone), aromatic acids, and esters. As an anti-inflammatory agent, it inhibits prostaglandin synthesis. Carmen et al. compared the effectiveness of 10% propolis tincture and formocresol pulpotomy in primary molars and showed that 10% propolis tincture was as effective as FC. Lima et al. following histological analysis concluded that the inflammatory response was less severe, the area of pulp necrosis was smaller, and more frequent formation of a mineralized tissue barrier was evident. Ozorio et al. in their histologic study noted the complete calcific bridge formation in propolis group.<sup>30</sup>

Pulpotec is a newly available radiopaque, non resorbable paste that is used for pulpotomy treatment. It is available as powder liquid system (Produits Dentaires SA, Vevey, Switzerland). Powder consists of polyoxymethylene, iodoform and liquid consists of dexamethasone acetate, formaldehyde, phenol, guaiacol. Its mode of action is by cicatrization of the pulpal stump at the chamber-canal interface, while maintaining the structure of underlying pulp. Previous histological studies reported no signs of inflammation, but there was a discontinuity in the odontoblastic layer lining along the dentin walls. However more clinical trials to evaluate clinical and radiographic success are needed.<sup>31</sup>

Nano Hydroxy Apatite has been introduced for augmentation procedures in osseous defects and is attracting increasing interest in medicine and dentistry. NHA is biocompatible and non-irritating to pulp tissue. Shayegan et al. following histological evaluation reported that there was a significant difference between NHA and FC in terms of pulp response. The results of the

study show that NHA appears to be more biocompatible and provokes only mild inflammatory reaction in pulp tissue in both pulpotomy and direct pulp capping treatments.<sup>32</sup>

Bioactive glass has been studied more than 30 years as a bone substitute. It reacts with aqueous solution and form a carbonate apatite layer. Originally BAGs were considered as osteo-conductive. Recent evidence suggests that they are osteo-inductive. BAGs are biocompatible, antibacterial and stimulate osteoblasts. Some authors state odontoblast stimulation and subsequent reparative dentin formation; however studies are ongoing to prove exact mechanism of bridge formation. Animal study by Salako et al., reported that BAG showed localized areas of inflammation in the pulp especially in the mid root portion and four week old samples showed comparative better results where the inflammation was resolved and odontoblastic layer was evident.

Lyophilized freeze dried platelet acts as signaling proteins that get involved in regulation of cell proliferation, migration and extracellular matrix production. It contains transforming growth factor, platelet derived growth factor, bone morphogenic proteins and insulin growth factor. These regulate key cellular processes like differentiation, mitogenesis and chemotaxis. Kalaskar and Damle compared the efficacy of lyophilized freeze dried platelet derived preparation with calcium hydroxide as pulpotomy agents in primary molars and reported that the success rate of lyophilized freeze-dried platelet derived preparation was better than calcium hydroxide.<sup>33</sup>

Ankaferd Blood Stopper (ABS) is a herbal extract obtained from five different plants: *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum*, and *Urtica dioica*. Each of these plants has some effect on the endothelium, blood cells, angiogenesis, cellular proliferation, vascular dynamics and also as cell mediators. ABS-induced protein network formation with blood cells particularly erythrocytes covers the primary and secondary haemostatic system without disturbing individual

coagulation factors. Studies on pulpotomy with ABS have shown success rate ranging from 89% to 100%. However, long term studies are required in this regard.<sup>34</sup>

Bovine preparations would not be suitable for human teeth. Fortunately, molecular biology techniques can circumvent the necessity of isolating BMP fractions from human bone. Both recombinant human BMP-2 and OP-1 have been purified and characterized, and both demonstrated cartilage and bone inductive potential in ectopic sites of rats. And furthermore, hOP-1 has been shown to elicit reparative dentin in exposed pulps of monkey teeth. We are now entering an era when commercially available recombinant human BMPs will be available for experimentation and clinical trials. A combination of BMPs may be necessary to ensure maximal and predictable reparative dentinogenesis, but these are details to be determined in logical steps. Covey describes the scenario where groups of people can become so involved in hacking through the underbrush that they overlook which jungle they are in. This describes much of the activity associated with pulpotomy research through the years.<sup>35</sup> But technology has now enabled us to climb a tree and look around. I think that we are in the right jungle at last. Success of pulpotomy depends on various vital factors like case selection, clinical diagnosis, intraoperative diagnosis and most importantly the material used for the pulpotomy procedure. The so called "Ideal Pulpotomy material" is not yet been identified. Formocresol Pulpotomy enjoys very good clinical and radiographic success rates, and is still a popular pulpotomy material despite the concerns raised due to its toxicity, mutagenicity and carcinogenicity. Clinical studies report good success rates of Ferric sulfate 15.5% and MTA as alternatives to FC. One of the major limitations of using MTA is its high cost and its use in pediatric dentistry practice can become almost prohibitive in some circumstances. Hence, FS can still be considered a valid and inexpensive solution for pulpotomies in primary teeth.<sup>36</sup>

**CONCLUSION:** The cost of MTA may prohibit its use in pediatric dentistry and

therefore newer medicaments which are as effective as MTA but are economic in use are being introduced. These newer medicaments are both preservative and regenerative. A newer medicament which is ABS (herbal), an turkish material can be future of pulpotomy.

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**How to cite this article:** Katiyar A, Gupta K, Solanki S, Gupta S, Pandey M, Srivastava S, Pulpotomy Medicaments: An Outlook. *Rama Univ J Dent Sci* 2016 Dec;3(4):19-26.

**Sources of support:** Nil

**Conflict of Interest:** None declared