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REVIEW ARTICLE

AN UPDATE ON PRIMARY TEETH PULPOTOMY MEDICAMENTS

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ABSTRACT

This article reviews the pulpotomy medicaments which were studied in the dental literature and discusses their advantages and disadvantages. Many of the newly suggested medicaments have shown promising results in vitro and in vivo in the short run; however, the evidence is still insufficient to identify one superior pulpotomy medicament. There is clearly a need for long-term studies with the highest level of evidence (randomised controlled trials) to identify the best medicament for pulpotomy of primary teeth .It is important to identify a novel, effective and preferably natural pulpotomy medicament to increase the therapeutic arsenal and successfully perform pulpotomy procedures.

INTRODUCTION

Vital pulpotomy procedure in primary teeth has been a topic of great interest in pediatric dentistry and it has generated many opinions and controversial concepts. Vital pulpotomy includes applying a medicament over the residual radicular pulp tissue to promote healing and to allow normal tooth physiology to continue. (Bahrololoomi *et al*., 2008) Many factors must be considered in choosing the appropriate medicament such as clinical efficacy, cost, and sensitivity of placement technique (Block, 2009). The purpose of this article is to review the information available regarding various medicaments used in pulpotomy of primary teeth. Pulpotomy in this article will be discussed only as a procedure for the primary dentition, not in terms of young permanent teeth. For the reader's convenience, the medicaments will be categorized based upon their historical introduction in the dental literature.

Formocresol

Buckley's formocresol has been widely used as a pulpotomy medicament due to its bacteriostatic and fixative properties. (Waterhouse *et al*., 2000) Formocresol is available as full strength Buckley's formocresol (19% formaldehyde, 35% tricresol, 15% glycerol, and 31% water). (Block, 2009) Single five minutes treatment with dilutions of the full strength of 1:5 became and has remained the gold standard against which all new modalities are compared (Peng *et al*., 2006).

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(Peng *et al*., 2006) Formocresol pulpotomies have a reported success rate which might reach 100%. (Waterhouse, 2000; Fallahinejad Ghajari *et al*., 2008). Recently, concern was raised over formocresol as a pulpotomy medicament due to the "aldehyde" constituent in its composition. Several investigations have led to the conclusion that formaldehyde is potentially carcinogenic, mutagenic and immune sensitive. (Casas *et al*., 2005). However, the definitive evidence to prove that formocresol used in one or more pulpotomies would pose a risk to the child is still lacking because of the brief duration of exposure (5minutes) and the low concentration dose (1/5 dilution). Therefore, up till now, and until a biologic and reparative alternative is identified that is clearly and reproducibly superior to formocresol, formocresol is still an essential, safe and efficacious pulpotomy medicament.

Calcium Hydroxide

Calcium hydroxide has been called into question as a pulpotomy medicament due to the occurrence of internal root resorption following pulpotomy. In such cases, treatment is considered to be a failure, as internal root resorption is viewed as an indication of chronic inflammation of the residual pulp. (Sönmez and Durutürk, 2008). A summary of clinical studies which investigated calcium hydroxide as a pulpotomy medicament and compared it with formocresol is shown in Table 1. However, it should be emphasized that calcium hydroxide gave inferior outcomes than formocresol in all of the studies.

Table 1. Clinical studies using calcium hydroxide

Name	Year	N	Time period: months	Percent success	
				Clinical	Radiographic
Waterhouse *et al*	2000	FC: 44 CH: 35	To exfoliation	FC: 84% CH: 77%	FC: 84% CH: 77%
Huth *et al*	2005	FC: 48 CH: 38	24	FC: 96% CH: 87%	FC: 90% CH: 66%
Markovic *et al*	2005	FC: 33 CH: 34	18	FC: 91% CH: 82%	FC: 85% CH: 76%
Moretti *et al*	2008	FC: 15 CH: 15	Up to 24	FC: 100% CH: 36%	FC: 100% CH: 36%
Yildiz and Tosun	2014	FC: 35 CH:35	Up to 30	FC: 100% CH: 85%	FC: 95.2% CH: 85%

FC, formocresol; CH, calcium hydroxide

Table 2. Clinical studies using ferric sulphate

Name	Year	N	Time period: months	Percent success	
				Clinical	Radiographic
Fei *et al*	1991	FS: 29 FC: 27	Up to 12	FS: 100% FC:96%	FS:81% FC:96%
Fuks *et al*	1997	FS: 55 FC: 37	Up to 34	FS:93% FC: 84%	FS: 93% FC:80%
Ibricevic and Al-Jame	2000	FS: 35 FC: 35	20	FS: 100% FC: 100%	FS: 97.2% FC: 97.2%
Ibricevic and Al-Jame	2003	FS: 84 FC: 80	42-48	FS:96% FC:97%	FS:92% FC:94%
Markovic *et al*	2005	FS: 37 FC: 34	18	FS:89% FC: 91%	FS:81% FC:85%
Huth *et al*	2005	FS: 50 FC: 50	24	FS: 100% FC:96%	FS:86% FC:90%
Havale *et al*	2013	FS: 30 FC: 30	12	FS: 96.7% FC: 86.7%	FS: 63.3% FC: 56.7%

FC, formocresol; FS, ferric sulphate

Glutaraldehyde

Many studies have suggested that glutaraldehyde should replace formocresol as the medicament of choice for pulpotomy procedures in primary teeth based on its superior fixative properties, self-limiting penetration, low antigenicity, low toxicity, and the elimination of cresol (Ranly, 1994). However, it was found that glutaraldehyde results in high failure rate in long-term follow-up (3 years) which indicates that clinicians should be cautious before extensively using glutaraldehyde as a pulpotomy medicament (Tsai *et al*., 1993).

Ferric Sulphate

Ferric sulphateis a non-aldehyde hemostatic chemical which was introduced as a 15.5% acidic solution (Prabhu and Munshi, 1997). When it is applied for 15 seconds, ferric sulphate produces the same effect as formocresol without any toxic effect and it is easy to manipulate. (Ibricevic and Al-Jame, 2000) The exact mechanism of action of ferric sulphate is still debatable, but it was assumed that the reaction of blood with ferric sulphate ions causes agglutination of blood proteins forming a metal protein complex, this metal protein complex is capable of occluding the capillaries and causing hemostasis. (Smith *et al*., 2000) Therefore, the problems of excessive bleeding will be minimized, and consequently the chances of having inflammation and internal resorption will be less. (Ranly, 1994) The most important advantages of ferric sulphate over formocresol are the minimized working/ manipulation time. (Ibricevic and Al-Jame, 2000).

In addition, ferric sulphateis less pungent making it easier to be used with children, and it is readily available. Ferric sulphate has also bactericidal properties. (Prabhu and Munshi, 1997). A summary of clinical studies which investigated ferric sulphate and compared it with formocresol is shown in table 2. Ferric sulphate was better than formocresol in some studies and similar to formocresol in others.

Mineral Trioxide Aggregate (MTA)

MTA has several properties which meet the requirements of an ideal pulpotomy medicament. It is a mixture of portland cement, bismuth oxide, and gypsum. MTA's powder is commonly mixed with sterile water in a 3:1 powder/liquid ratio. (Roberts *et al*., 2008) Hydration of the powder results in a colloidal gel which solidifies into a hard structure in less than three hours. (Salako *et al*., 2003; Witherspoon *et al*., 2006) Several in vitro and in vivo studies have shown that MTA prevents micro leakage, is biocompatible, has excellent sealing ability and antimicrobial properties, (Torabinejad and Chivian, 1999; Peng *et al*., 2006) is able to form dentine bridge, and promotes regeneration of the original tissues when it is placed in contact with the dental pulp or periradicular tissues. (Eidelman *et al*., 2001) Nevertheless, the working properties of MTA are less than ideal; MTA has poor handling characteristics and delayed setting time which depends on the material's contact with water. (Salako *et al*., 2003; Witherspoon *et al*., 2006) Therefore, a moistened cotton pellet and an interim restoration should be left in the treated tooth until the final restoration can be commenced. (Karimjee *et al*.,

2006; Jafarnia *et al*., 2009) In addition, MTA is costly, which may prohibit its global use as a pulpotomy medicament (Block, 2009). A summary of clinical studies which investigated MTA as a pulpotomy medicament and compared it with formocresol is shown in Table 3. Almost all the studies comparing MTA with formocresol showed that MTA presented better results even though in some of them there was no statistical difference as a result of the small number of teeth tested.

Table 3. Clinical studies using MTA

Name	Year	N	Time period: months	Percent success	
				Clinical	Radiographic
Agamy *et al*	2004	MTA: 19 FC: 20	12	MTA: 100% FC: 90%	MTA: 100% FC: 90%
Farsi *et al*	2005	MTA: 38 FC:36	24	MTA: 100% FC: 97%	MTA: 100% FC: 86%
Holan *et al*	2005	MTA: 33 FC: 29	≤ 74	MTA: 97% FC: 83%	MTA: 97% FC: 83%
Naik and hegde	2005	MTA: 24 FC: 23	6	MTA: 100% FC: 100%	MTA: 100% FC: 100%
Noorollahian	2008	MTA: 18 FC: 18	Up to 24	MTA: 100% FC: 100%	MTA: 94.4% FC: 100%
Moretti *et al*.	2008	MTA: 15 FC: 15	Up to 24	MTA: 100% FC: 100%	MTA: 100% FC: 100%
Godhi *et al*.	2011	MTA: 25 FC: 25	Up to 12	MTA: 100% FC: 100%	MTA: 96% FC: 88%
Mettlach *et al*	2013	MTA:119 FC:133	42	MTA: 98% FC: 95%	MTA: 90% FC: 47%
Yildiz and Tosun	2014	MTA:41 FC: 35	Up to 30	MTA: 96.4% FC: 100%	MTA: 96.4% FC: 95.2%

FC, formocresol; MTA, mineral trioxide aggregate

Table 4. Clinical studies using sodium hypochlorite

Name	Year	N	Time period: months	Percent success	
				Clinical	Radiographic
Vargas *et al*.	2006	5% SH: 14 FS: 12	Up to 12	5%SH: 100% FS: 85%	5%SH: 79% FS: 62%
Ruby *et al*.	2012	3% SH:34 FC: 31	Up to 12	3%SH: 100% FC: 100%	3%SH: 80% FC: 90%
Shabzendedar *et al*	2013	3% SH: 50 FC:50	Up to 12	3%SH: 100% FC: 100%	3%SH: 92% FC:93%
Al-Mutairi and Bawazir	2013	82 overall	Up to 12	5%SH: 94.6% FC: 92.1%	5%SH: 86.5% FC: 86.8%

FS, ferric sulphate; SH, sodium hypochlorite; FC, formocresol

Bioactive glass

Bioactive glass consists of biocompatible and antibacterial materials; therefore, it might be considered as an ideal pulpotomy medicament. Salako *et al.* (2000) evaluated histologically the efficacy of bioactive glass as a pulpotomy medicament with MTA, formocresol, and ferric suphate in rat molar teeth. However, their results weren't very promising; they found that bioactive glass was inferior to MTA since it induced an inflammatory response after 2 weeks which was severe enough to cause periapical abscess in one of the tested teeth and root resorption in another tooth. After 4 weeks, most of bioactive glass sample teeth showed regular pulpal histology; however, there were specimens which showed complete necrosis. Clinical studies on bioactive glass are also required since up to date no clinical studies are present to assess its efficacy as a pulpotomy medicament.

Sodium hypochlorite

Few clinical studies investigated sodium hypochlorite as a pulpotomy medicament and compared it with either formocresol or ferric sulphate (Table 4). Two concentrations were tested; five percent and three percent sodium hypochlorite. All studies reported that sodium hypochlorite had comparable clinical and radiographic success rates to formocresol. In one study, sodium hypochlorite showed better clinical and radiographic success rates than ferric sulphate. (Vargas *et al*., 2006) Nevertheless, further clinical studies with long-term follow-up are required before recommending sodium hypochlorite as a pulpotomy medicament since the follow up interval in all of the studies didn't exceed 12 months.

Alternative medicaments

Alternative medicaments have been assessed in few studies as possible primary molar pulpotomy medicaments. These are principally bioactive glass, (Salako *et al*., 2000) alendronate, (Cengiz *et al*., 2005) enamel matrix derivative, (Sabbarini *et al*., 2008) portland cement, (Conti *et al*., 2009) calcium phosphate cement, (Jose *et al*., 2013) and propolis. (Lima *et al*., 2012; Ozório *et al*., 2013; Al-Haj Ali, 2015)

Alendronate

Alendronate sodium is a biphosphonate known to favor hard tissue turnover. In one study, Cengiz *et al*. (2005) compared the histological response of alendronate, calcium hydroxide and formocresol in pulpotomized rat molar teeth; they found

that alendronate was capable of maintaining pulpal vitality and potentially stimulating odontoblastic activity while promoting hard tissue formation in a similar manner to calcium hydroxide. However, further research in the form of randomized controlled clinical trials is needed to confirm this finding and to evaluate the ideal concentration for stimulation of odontoblasts before alendronate can be used as an alternative vital pulpotomy material.

Enamel matrix derivative

Enamel matrix derivative is a purified enamel matrix protein product which was tested for induction of reparative dentine formation. (Weishaupt *et al*., 2008) In one study, Sabbarini *et al*. (2008) compared the clinical and radiographic success rates of enamel matrix derivative with formocresol pulpotomy; they found comparable clinical success rates after a follow up period of 6 months. On the other hand, enamel matrix derivative demonstrated superior radiographic success rate (60%) than formocresol (13%). However, enamel matrix derivative has gel consistency which makes its application rather difficult. In addition, it is impossible to condense any material over it. These issues may raise concern over the practicability of using enamel matrix derivative as a pulpotomy medicament. Moreover, further clinical studies are required with long term follow up to confirm enamel matrix derivative's efficacy as a pulpotomy medicament.

Portland cement

Portland cement was evaluated as a pulpotomy medicament in few studies with promising results. (Shayegan *et al*., 2008; Conti *et al*., 2009; Sakai *et al*., 2009; Oliveira *et al*., 2013) In one study, portland cement successfully maintained pulpotomised teeth symptom free, it preserved pulpal vitality with successful dentine bridge formation after 12 months follow up (Conti *et al*., 2009). When portland cement was compared with MTA, they both gave 100% clinical and radiographic success rates after follow up intervals which reached 24 months. (Sakai *et al*., 2009; Oliveira *et al*., 2013) In addition, both MTA and portland cement demonstrated favorable pulpal response and hard tissue formation in pulpotomized primary pig teeth compared to ferric sulphate and formocresol which irritated the pulp tissue and provoked more inflammatory response. (Shayegan *et al*., 2008) However, further randomized clinical trials with human teeth are required in order to determine the suitability of portland cement before unlimited clinical use can be recommended.

Calcium phosphatecement

In one study, Jose *et al*. (2013) compared histologically the efficacy of calcium phosphate cementas a pulpotomy medicament with that of formocresol, they found that calcium phosphate cementformed better dentine bridge, therefore it was suggested that calcium phosphate cement is more compatible to pulp tissues than formocresol and it shows good healing potential.

Propolis

Propolis is a strongly adhesive resinous hive substance produced by honeybees from collected plant products. (Gulinelli *et al*., 2008) Few in vitro studies evaluated the efficacy of propolis as a pulpotomy medicament in primary teeth. (Lima *et al*., 2011; Ozório *et al*., 2012; Esmeraldo *et al*., 2013). Al-Haj Ali (2015) has recently found that propolis had similar biocompatibility to MTA on human fibroblasts and that both propolis and MTA were more biocompatible than formocresol and ferric sulphate. In addition, Al-afandy (2014) found that propolis was successful as a pulp capping agent on primary molars after a follow up period of up to 12 months with a success rate approaching 87%. Propolis is a natural, valid and inexpensive material when compared to MTA, therefore, further clinical studies with long term follow up are needed to evaluate and compare the efficacy of propolisas a pulpotomy medicament with other primary teeth pulpotomy medicaments.

Conclusion

The dental literature is replete with articles about primary teeth pulpotomy medicaments; however, it seems that up till now there is no evidence to identify one superior pulpotomy medicament clearly. Two medicaments may be preferable: MTA or ferric sulphate. The cost of MTA may prohibit its use in pediatric dentistry and therefore ferric sulphate could be a suitable alternative. Unlike other suggested pulpotomy medicaments, propolis is a natural, valid and inexpensive alternative for pulpotomy in primary teeth. However, further clinical studies with long term follow up are needed to confirm its efficiency as a pulpotomy medicament.

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