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Is there life after Buckley's Formocresol? Part I – A narrative review of alternative interventions and materials

V. SRINIVASAN[1], C. L. PATCHETT[1] & P. J. WATERHOUSE[2]

[1]*Department of Child Dental Health, Newcastle Dental Hospital and* [2]*School of Dental Sciences, University of Newcastle upon Tyne, Newcastle upon Tyne, UK*

Summary. *Objectives.* (1) To present a narrative review of the currently available alternative interventions and materials to formocresol pulpotomy for the management of extensive caries in the primary molar, and (2) to produce a clinical protocol for pulp therapy techniques in the extensively carious primary molar.

Introduction. The International Agency for Research on Cancer has recently classified formaldehyde as carcinogenic to human beings. Since Buckley's Formocresol contains 19% formaldehyde in its full strength and, therefore, 1% in a 20% dilution, a safer alternative should be identified.

Methods. A narrative review of the published literature for primary molar pulp therapy techniques was undertaken following an extensive and appropriate literature search. A specialist group of paediatric dentists was formed to arrive at a consensus and establish an evidence-based protocol for the management of extensively carious primary molar teeth. Part I of this paper explores the currently available alternative interventions and materials to formocresol in the form of a narrative review. The second part of the paper will present the formation of a specialist group to arrive at a consensus and establish an evidence-based protocol for the management of the extensively carious primary molar.

Conclusions. After consideration of a review of extensively searched literature, a protocol and key points document have been developed to assist clinicians in their treatment planning. Further long-term studies with the highest level of evidence (i.e. randomized controlled trials) are required to enable us to identify acceptable alternatives which can replace formocresol.

Introduction

The disquiet among the dental profession over the use of formocresol in the management of primary teeth has led in the past to the evaluation of possible alternatives to the medication. Following the criticism from the Cochrane Review of Pulp Therapy [1] regarding the paucity of appropriately designed, statistically assessed investigations, and the lack of long-term outcomes, many studies have been reported, and several others have begun to contribute to the literature.

Furthermore, the International Agency for Research on Cancer (IARC) classified formaldehyde as carcinogenic to humans in June 2004 [2], leaving the profession to look for other viable alternatives to formocresol. An expert working group of the IARC evaluated the available evidence on the carcinogenicity of formaldehyde, an ingredient in Buckley's Formocresol solution, which is used as a pulpotomy medicament in the management of extensive caries in the primary molar. Based on the information made available, the expert working group has determined that there is now sufficient evidence that formaldehyde causes nasopharyngeal cancer in humans, a rare cancer in developed countries, limited evidence for cancer of the nasal cavity and paranasal sinuses, and 'strong but not sufficient evidence' for leukaemia.

Correspondence: C. L. Patchett, Department of Child Dental Health, Newcastle Dental Hospital, Richardson Road, Newcastle upon Tyne NE2 4AZ, UK. E-mail: c.l.patchett@ncl.ac.uk

Materials and methods

The different techniques employed to manage the cariously exposed vital primary tooth with reversibly inflamed coronal pulp and healthy radicular pulp tissue will be reviewed in this section. The procedure used must result in clinical and radiographic success, and any techniques or agents used should be biocompatible with the pulp and surrounding tissues.

This is a traditional narrative review that aims to consider and discuss alternative interventions to

formocresol as a pulpotomy medicament in primary teeth. It differs from a systematic review in involving general discussion of the subject and has no stated hypothesis [3]. An extensive search of the reported literature from January 1966 to September 2004 was produced using the Medline, Embase and PubMed databases. The search strategy employed key words, which were each of the alternatives to formocresol considered in this paper in combination with each other and with formocresol. Although the Cochrane Review of Pulp Therapy covered similar ground [1], the authors hope to review the literature that has been made available since the review, and also to highlight information that could have been lost because of the rigour of the Cochrane Review.

The various procedures and medicaments reported in the literature have been previously classified by Ranly according to the treatment objectives [4]. The interventions reported in current literature can also be classified applying the same criteria as follows: devitalization (formocresol, glutaraldehyde, electrocoagulation), preservation (ferric sulphate, calcium hydroxide, mineral trioxide aggregate, lasers) and remineralization (indirect pulp therapy, bone morphogenic proteins, collagen) of the dental pulp in the primary molar with extensive caries. The action of certain medicaments is however arguable, for example glutaraldehyde (devitalisation or preservation) or calcium hydroxide (preservation or remineralisation). In addition to the above interventions, this review also includes pulpectomy (root canal therapy), which is indicated in teeth with irreversible radicular pulp inflammation or necrosis.

Literature review

Devitalization

Glutaraldehyde. Glutaraldehyde was proposed as a new pulp tissue fixative by's-Gravenmade in 1975 [5] and has been reported to be a better tissue fixative than formocresol [6]. This dialdehyde has a limited shelf life and a cross-linking ability superior to that of formocresol, eliciting a different pulpal response to the latter. Although this tissue effect is indicative of advantages as a pulpotomy agent, such benefits have yet to be adequately substantiated. Its systemic distribution from pulpotomy sites [7,8], cytotoxicity [9] and mutagenicity [10,11] have been reported to be similar to formocresol.

Clinical studies have evaluated the use of 2% buffered glutaraldehyde applied for 5 min over the pulp tissue of primary teeth to achieve the fixative effect. A 98% success rate was reported in a prospective study after a follow-up for 19–42 months [12] with equal effectiveness for 1–3-min applications. Fuks *et al.* [13] reported a success rate of 94·3% over 6 months that decreased to 82% after 25 months, which is significantly lower than that reported for formocresol. Shumayrikh and Adenubi [14] reported the overall success rate for glutaraldehyde as 92·9% for an Intermediate Restorative Material dressing (IRM, Dentsply, Weybridge, UK) and 73·6% for a calcium hydroxide dressing after 12 months.

With similar toxic effects to formocresol, and no strong evidence of improved success rates, glutaraldehyde has not been accepted as an appropriate alternative to formocresol.

Electrosurgery. Electrosurgery is a nonpharmacological, haemostatic technique used for the amputation of the inflamed coronal pulp prior to placing a lining material [15]. In 1982, Anderman [16] described the electrosurgical pulpotomy in primary teeth as a time-efficient method that is relatively free from postoperative complications. In electrosurgery, different currents producing different amounts of heat may be used to produce a surgical incision, coagulation or electrofulguration (destruction of tissue by electric sparks). The procedure carbonizes and denatures the pulp tissue, producing a layer of coagulative necrosis, which acts as a barrier between the lining base material placed and the healthy radicular tissue beneath.

Electrocoagulation has been evaluated and compared to formocresol on caries-free primary and permanent teeth in primates [17–19]. These animal studies are of limited benefit since primary molars requiring pulpotomy are cariously exposed in the clinical situation. It has also been suggested that contaminated pulp tissue might not promote adequate current penetration [18].

Conflicting reports have resulted from human clinical trials. From the study by Sheller and Morton [20], it was concluded that the success depended on the pre-existing pulpal status. However, Mack and Dean [21] reported a high clinical and radiographic success rate in a study where teeth were reviewed from one to 70 months following electrocoagulation pulpotomy. The electrosurgical process cannot eliminate

inflammation of the radicular pulp. Therefore, the success of the electrosurgical pulpotomy depends on the initial pulp status.

Preservation

Ferric sulphate. Ferric sulphate (15·5%) has been investigated widely and reported in animal and human studies as a haemostatic agent in pulpotomy procedures. On contact with blood, a ferric ion-protein complex is formed, and the membrane of this complex seals the cut vessels mechanically, producing haemostasis, and the agglutinated protein complex forms plugs which occlude the capillary orifices, preventing blood clot formation [22,23].

The first animal study with ferric sulphate was carried out in monkey teeth by Landau and Johnsen in 1988 [24] to investigate usage prior to the placement of calcium hydroxide over amputated pulps. It was intended to produce haemorrhage control in order to improve the efficacy of calcium hydroxide since its failure was attributed to the persistence of an extrapulpal blood clot [25]. Subsequent animal studies were carried out in baboons [26] and rats [27]. Fuks and her co-workers compared the pulpal responses of ferric sulphate and formocresol in baboon teeth [26]. Outcomes for both medicaments were equal after 6 weeks, with 60% of teeth in each group presenting with mild inflammation. Working in rat teeth, Cotes and co-workers [27] confirmed similar inflammation in response to ferric sulphate and formocresol. Although there was more reparative dentine and fibrosis with ferric sulphate, these findings occurred in less than 40% of teeth treated.

Fei *et al*. reported the combined clinical and radiographic success at the end of a one-year prospective human trial [28] as 96% for ferric sulphate and 78% for formocresol. Ibricevic and Al-Jame reported results first at the end of 20 months [29] and later at 48 months [30] for teeth treated with ferric sulphate and formocresol. Although the overall success rates were similar to those from Fuks and her co-workers [31], the radiographic success rates for ferric sulphate fell from 97·2% after 20 months to 92% after 48 months follow-up. Despite this, success rates were higher than those reported in the two retrospective studies by Burnett and Walker [32], and Smith *et al*. [33].

The ferric sulphate used in all the above studies was 15·5%, except in the study by Casas *et al*. [34], where a 16% ferric sulphate equivalent in an aqueous vehicle was evaluated in comparison to pulpectomy (root canal therapy) in primary molars. Although this group reported statistically significant success rates in favour of root canal therapy in their sample at the end of 2 years (teeth recommended for extraction: 39% for ferric sulphate and 9% for root canal treatment), the same sample size was insufficient to show significant results at the end of 3 years.

Based on the available evidence so far, ferric sulphate and formocresol produce equivalent outcomes. An evidence-based assessment of clinical trials of ferric sulphate and formocresol with meta-analysis [35] concluded that, in human carious primary molars with reversible coronal pulpitis, pulpotomies performed with either formocresol or ferric sulphate are likely to have similar clinical/radiographic success. This finding agreed with the Cochrane Review [1] of the pulp treatment for extensive decay in primary teeth.

Calcium hydroxide. Calcium hydroxide has been proposed as an alternative to formocresol for pulpotomies in primary teeth [36]. The main drawback of this alternative intervention is internal resorption, which was thought to be stimulated by calcium hydroxide. Since the observed resorption has been ascribed to a blood clot intervening between the material itself and the pulp tissue, various unsuccessful attempts have been made to prevent the formation of the extrapulpal blood clot. These have included minimizing the trauma to major pulp vessels and the resultant clots by performing a partial pulpotomy [25,37], the use of a haemostatic agent prior to the placement of calcium hydroxide [24,38] and pulp amputation by electrocoagulation [39].

Various animal studies have been carried out to evaluate the pulpal response to calcium hydroxide, but since several animal models have been utilized, comparison is difficult. The consensus of opinion from these studies appears to be that complete and incomplete dentine bridges are formed in amputated pulps beneath calcium hydroxide, which are similar in morphology to osteodentine. A fibrous layer and vital pulp tissue are found beyond the calcific bridge [40–42]. Calcium hydroxide, therefore, can promote either preservation and/or remineralisation, hence an overlap between the two intervention categories.

Published data regarding the degree of clinical success of calcium hydroxide vital pulpotomy technique are varied. A success rate of 70% was obtained using a thick paste of calcium hydroxide

and water, as reported by Teuscher and Zander [43]. Via [44], Schröder [25], Schröder *et al*. [37] and Doyle *et al*. [36] concluded that the calcium hydroxide treatment was associated with dentine bridge formation and complete healing of the stump of the amputated primary dental pulp; however, when the treatment failed internal resorption was the cause. There was no such dentine bridge or healing process seen with formocresol in these studies.

Magnusson [45] obtained less impressive results, with 12% clinical and 33% radiographic success from 120 pulpotomies in primary mandibular molars. Waterhouse *et al*. [46] reported a statistically insignificant difference in treatment outcomes between formocresol and calcium hydroxide pulpotomy. This group of workers implemented strict tooth selection criteria in their study, i.e. an absence of clinical signs and symptoms of coronal and radicular pulp necrosis, including a lack of spontaneous pain, in addition to an absence of radiographic signs of pulp necrosis. Working only within this remit of tooth selection criteria, they concluded that calcium hydroxide in its pure powder form was a clinically acceptable alternative to formocresol but recommended further research.

Mineral trioxide aggregate. Mineral trioxide aggregate (MTA) was first described in the dental literature in 1993 [47] for repair of lateral root perforations. Since then, the material has been evaluated in animal models for several applications in dentistry including root end fillings [48,49], direct pulp caps [50–52], perforation repair in furcations [53,54] and apexification [55,56]. These histological animal studies report optimum biocompatibility with the periapical tissues [48,49] and the pulp [50–52] in addition to the material's sealing ability [49].

Mineral trioxide aggregate (ProRoot, Dentsply Tulsa Dental, Tulsa, OK, USA) is available as ProRoot Grey or ProRoot White [57]. White ProRoot has been introduced as an aesthetic improvement over the original material, for placement in anterior teeth. The major components of White MTA are tricalcium silicate, dicalcium silicate, tricalcium aluminate, calcium sulphate dehydrate and bismuth oxide (Dentsply Tulsa Dental). However, the manufacturer does not disclose the ingredients responsible for masking the greyness of the original ProRoot.

Torabinejad *et al*. [58] have described some of the physical and chemical properties of MTA. It is biocompatible, and provides a better seal than zinc oxide-eugenol and amalgam. It is available in powder form, which sets in the presence of moisture, with a setting time of 4 h. Koh *et al*. [59] demonstrated that MTA has the ability to stimulate cytokine release from bone cells, indicating that it actively promotes hard tissue formation. Torabinejad and Chivian [60] proposed MTA as a potential medicament for pulpotomy procedures as well as capping of pulps with reversible pulpitis in addition to many other applications in dentistry.

Mineral trioxide aggregate was first tested on traumatically exposed pulps in monkey teeth as a pulp capping material and was found to produce favourable results [61]. No pulpal inflammation was observed after 5 months in comparison to calcium hydroxide, which elicited pulpal inflammation in all samples.

Eidelman and co-workers [62] reported a study in which MTA was compared to formocresol. Follow-up evaluation was reported for a period ranging from 6 to 30 months and revealed only one failure in a molar treated with formocresol and no failures in teeth treated with MTA. Although pulp canal obliteration was observed in two out of 15 teeth treated with formocresol (13%) and seven out of 17 teeth treated with MTA (41%), it was not regarded as an unfavourable outcome. Although the sample sizes were small, MTA was proposed as a suitable alternative to formocresol in primary teeth.

More recently, Agamy *et al*. [63] reported a prospective clinical trial comparing White MTA, Grey MTA and formocresol. Grey MTA appeared to be superior to both White MTA and formocresol as a pulp dressing for pulpotomized primary teeth. This study found a high percentage of pulp canal obliteration (58% with the Grey MTA and 5% with White MTA), but no obliteration in the group treated with formocresol. There was a significant difference in the clinical and radiological outcomes between the White MTA and Grey MTA groups, with the latter performing better. However, comparable outcomes were achieved with the White MTA and formocresol at the end of 12 months. Histologically, both types of MTA successfully induced a thick dentine bridge at the amputation sites, while formocresol induced thin, poorly calcified dentine.

The lack of internal resorption in the above studies in the teeth treated with MTA contrasts with the studies which have reported internal resorption in response to zinc oxide eugenol [64], ferric sulphate [31,33] and calcium hydroxide [36,38]. The lack of

internal resorption in addition to the biocompatibility, sealing ability and promotion of hard tissue formation seem to favour further research involving long-term follow-up on the use of MTA for pulp therapy in primary molars.

Presently, a drawback to the clinical use of MTA is its cost relative to other agents and perceived problems with its storage. A carton of ProRoot MTA contains, five, one-gram sachets of the material costing approximately £121·45 (€178·00, US$232·52). The composition of MTA is similar to that of the cement used in the building industry to make concrete. Such a material should be kept dry during storage since moist air leads to the phenomenon of air-setting [65], which reduces the strength of the mix. Once such a material is opened from the air-seal packaging, it should be sealed in an air-tight and water-proof container. Significant strength losses begin to occur after 4–6 weeks. The same could be applied to MTA when used in dentistry. The manufacturer recommends the marketed one-gram sachet for single use, which would result in considerable wastage of the material. Once the sachet is opened and the required amount used, the remaining material may be stored for up to 4 weeks in a water- and airtight container such as an Eppendorf tube (Eppendorf UK Ltd, Cambridge, UK; J. M. Whitworth, personal communication. 2004).

Lasers. Since the development of the ruby laser in 1960, different forms of lasers have been evaluated in animal studies for their applications in dentistry. However, their use in pulpotomies was first published in 1985, when Shoji *et al*. [66] evaluated the carbon dioxide laser in canine models.

Subsequent studies showed conflicting results with respect to pulpal healing following laser pulpotomy [67–69]. While Shoji *et al*. [66] reported no detectable change in the radicular portion of the pulps, Wilder-Smith and Dang *et al*. [68] found that secondary dentine was formed and a regular odontoblast layer was present. A carbon dioxide laser was compared to the neodymium: yttrium aluminium garnet (Nd:YAG) laser by Jukic *et al*. [70], who reported that laser irradiation caused carbonisation, necrosis, inflammatory infiltration, oedema and haemorrhage in the pulpal tissues. Further animal studies have been published evaluating other types of lasers, i.e. ND:YAG lasers [71,72], the gallium arsenide laser [73], the argon laser [74] and the erbium: yttrium aluminium garnet laser [75]. The results from the different animal studies disagreed with respect to the histological evidence of repair with a newly formed dentinal bridge.

The only randomised controlled human clinical trial using a laser pulpotomy technique involved caries-free primary cuspids, which were scheduled for serial extraction [76]. These teeth were subjected to either formocresol or carbon dioxide laser pulpotomy. The teeth were evaluated clinically and radiographically at 28 and 90 days, and histologically after extraction. Carbon dioxide laser treatment compared favourably to formocresol for pulpotomy in caries free primary teeth.

Although animal studies have been carried out, further human clinical trials are recommended, which will take the use of laser for pulpotomy in primary molars to the next stage of research.

Ledermix. Ledermix (Lederle Pharmaceuticals, Wolfrathausen, Germany) contains the steroid triamcinolone acetonide as its primary active component as well as the broad-spectrum antibiotic calcium demethylchlortetracycline. The product is available as a single tube cream and two-component tube cement.

In the canine model, Ledermix has been evaluated for its effect on the pulp tissue exposed as a result of trauma [77] in comparison to formocresol, which is a fixative, and tetrandrine, which is a bibenzylisoquinoline alkaloid with broad-spectrum anti-inflammatory properties, with saline as a control. Histological evaluation after 3 days for acute inflammation (neutrophil infiltration) and 6 weeks for chronic inflammation (lymphocytic infiltration) revealed a statistically significant ($P > 0{\cdot}01$) difference between the medicaments. Both acute and chronic inflammatory responses were achieved in the following ascending order: Tetrandine, Ledermix, Buckley's Formocresol and saline.

The effects of calcium hydroxide have been compared to a combination of calcium hydroxide and Ledermix [78] on cariously exposed canine pulps. Both these interventions showed no difference in inflammation after 7 and 30 days, with no inflammation after 90 days. Other workers [79] have also reported similar findings in monkey teeth.

The histological effects of Ledermix cream and cement on the unexposed and traumatically exposed pulp in permanent teeth have been reported [80]. The histological changes observed beneath cavities without pulp exposure were localised to the

odontoblast-predentine area, and the reactions to the cement were less conspicuous than those to the cream. When placed directly on traumatically exposed pulps, preparations rarely produced any histological changes in the soft tissue. However, moderate to severe inflammation has been reported as a possible response to Ledermix when it is placed as a wound dressing following pulpotomy in cariously exposed vital primary teeth [81].

The anti-inflammatory effect of corticosteroids used locally in the pulp capping of permanent teeth was widely reported in 1960. Hansen and co-workers [81] reported the only available clinical study of Ledermix as a dressing to cover the pulpal wound following pulpotomy of cariously exposed primary teeth. This study compared the effect of Ledermix and zinc oxide eugenol as wound dressings following vital pulpotomy in primary molars over an observation period from one to 42 months. Seventy-nine per cent of the teeth treated with Ledermix and 57% of the teeth treated with zinc oxide eugenol were reported to be clinically and radiographically successful. Teeth exhibiting internal and external resorption were deemed to be treatment failures, extracted and subsequently evaluated histopathologically. Less significant inflammation was observed beneath the pulp wounds dressed by Ledermix in comparison to the zinc oxide eugenol group. No difference was observed in the inflammation present in the apical part of the roots of the teeth studied.

From the literature, there appears to be minimal data to support the use of Ledermix as a wound dressing following pulpotomy in the primary teeth.

Remineralisation

Indirect pulp therapy. Indirect pulp therapy (IPT) involves the removal of caries, leaving a thin layer of stained dentine at the deepest sites of a cavity where complete caries removal would result in pulp exposure [82,83]. Removal of caries from the lateral wall ensures complete sealing of the tooth and restorative material interface, thereby isolating the bacteria from their nutrient source, resulting in a reduction in their number or death [84–87].

The indication of IPT is limited to teeth which have no signs of irreversible pulp pathology based on a clinical and radiographic examination and direct evaluation of the cavity preparation [88–90]. In addition to careful case selection, knowledge of tooth anatomy, clinical experience and a good understanding of the process of caries progression are required [91]. The use of an antibacterial agent such as calcium hydroxide and restoration of the cavity with adequate marginal seal will eliminate any bacteria, which remain.

Studies in permanent teeth [92–95] have reported that the remaining deep dentine in teeth treated by IPT is mostly remineralized and hardened. These studies suggest that optimal coronal seal prevents caries progression beneath the restorations. Therefore, in view of the thinner dentine in primary teeth compared with permanent teeth, reopening a restoration for removal of the suspected residual caries is more likely to cause pulpal exposure, and hence, is inappropriate.

A prospective study by Falster *et al*. [91] in primary molar teeth, where two groups of teeth were restored with a composite resin, reported that a total etch technique without the placement of a calcium hydroxide lining may produce a similar effect upon residual bacteria to that of calcium hydroxide. All restorations were placed using the optimal isolation of dental dam. Success rates at 2 years were 96% for the total etch technique and 83% for the calcium hydroxide lining technique. The high success rate was attributed to the correct diagnosis, case selection and appropriate restorative technique rather than the placement of a calcium hydroxide lining *per se*.

Two retrospective human clinical studies using IPT in primary teeth, reported success rates exceeding 90% over a mean follow-up time of 4·2 years [90,96] and a range of 2 weeks to 73 months [97]. The first group of workers reported a comparative 82% success rate for formocresol pulpotomy in comparison to IPT. Indirect pulp therapy is a promising technique that warrants further prospective clinical evaluation.

It is important to appreciate the difference between IPT and atraumatic restorative treatment (ART). The latter involves excavating cavitated dentine caries with hand instruments only and restoring the cavity with a chemically adhesive restorative material, and sealing any associated fissures and pits. The technique was initially recommended in countries where highly trained dentists and the electricity needed for clinic equipment are not readily available [98]. Although IPT and ART share the similar concept of sealing the cavity from the oral environment, leading to a reduction in the number of microorganisms, ART can be practised in cavitated teeth, especially those with single surface

decay only. Furthermore, glass ionomer cement, the material of choice in ART, has inadequate physical and mechanical properties which influence the long-term survival of the restorations.

Bone morphogenic proteins. Bone morphogenic protein (BMP) is a generic term for a family of proteins which have bone-inductive properties. It was observed as early as 1965 that demineralized bone matrix was capable of stimulating bone formation when implanted in ectopic sites [99]. It was concluded that factors capable of autoinduction were present in the bone matrix and the term BMPs was proposed. Bone morphogenic proteins are osteogenic proteins which form part of the tumour growth factor (TGF-β). They are implicated in cell differentiation, tissue morphogenesis, regeneration and repair. Bone-morphogenic-protein-like activity has been identified in dentine matrix, and BMP genes are expressed during tooth development and dentinogenesis [100].

Promising results have been published in this area of research based on animal models in permanent teeth with non-inflamed pulps. It has been proposed that BMP stimulates the induction and differentiation of mesenchymal cells with varying degrees of dentine bridge formation [100–102] in swine, monkey and canine teeth. Although these studies have suggested that reparative dentine can be induced on contact with BMP, dentine bridge formation itself is not a sign of pulpal healing, and healing pulps are evident in teeth where dentinal bridge formation does not occur [103].

Collagen. Collagen products have been evaluated in animal studies as pulp medicaments. Cross-linked collagen gel [104] and enriched collagen solution [105,106] have been reported as pulpotomy medicaments in animals. Varying histological responses have been demonstrated, including complete regeneration of pulpal tissue and dentine bridge formation. These were experiments carried out on non-inflamed pulps, and not a true reflection of the response of a pulp exposed by caries. However, presently, no clinical studies have been reported on the use of collagen as a medicament to be used as an alternative to formocresol.

Pulpotomy medicaments: conclusions

From the published data available, the authors conclude that ferric sulphate, MTA and IPT appear to be promising alternatives to the single-visit formocresol pulpotomy for cariously exposed vital primary molar teeth. Ferric sulphate use is arguably technique-sensitive and MTA has cost implications. The use of lasers and electrosurgery is not routine in all dental settings and may not be readily available. In view of the promising results obtained so far, its relatively user-friendly technique for the operator and the patient in comparison to ferric sulphate and its expense in comparison to MTA, IPT emerges as one of the potential alternatives. This is especially so in asymptomatic primary molars with no radiographic signs of pathology. However, further research is required to increase our knowledge of the clinical efficacy, histological effects and systemic impact of all the possible alternatives reviewed here, in addition to providing a sufficient evidence base for developing policy documents and guidelines. Therefore, long-term studies with the highest level of evidence (randomised controlled trials) are required to enable us to identify acceptable alternatives which can replace formocresol.

Pulp removal

The final section of this review will consider the available literature on pulpectomy (root canal therapy) since it could be considered as an option in primary molars with varying degrees of coronal and radicular inflammation in addition to those with necrotic pulp which are, therefore, nonvital.

Pulpectomy

Previously, teeth with irreversible radicular inflammation or necrotic pulp tissue could be treated with formocresol in a non-vital pulpotomy technique. The authors accept that this is perhaps no longer an option, and hence, we must seek alternative non-vital techniques.

The aim of pulpectomy is to attempt to retain a tooth that would otherwise be extracted, and in doing so, prevent space loss and disturbance to the permanent dentition [107]. Pulpectomy is indicated where the radicular pulp is non-vital or irreversibly inflamed [108]. It is not suitable when there is evidence of extensive internal or external root resorption, or if more than one-third of the root length has been lost [83]. Single-visit pulpectomy is also an acceptable alternative to formocresol pulpotomy [34].

A number of root-filling materials have been suggested. An ideal material for root canal therapy of the primary molar should resorb at a similar rate to the primary root, be rapidly eliminated if accidentally extruded through the apex, harmless to the periapical tissues and the succedaneous tooth germ, easy to manipulate in order to fill the root canals, easily removable, radiopaque, and not result in discolouration of the tooth [109]. The most commonly used medicaments for primary molar root canal therapy are zinc oxide eugenol (ZnOE) paste, iodoform paste and calcium hydroxide.

Pure ZnOE paste has been shown to produce high clinical success rates, which are comparable to those of calcium hydroxide [110]. Casas *et al*. found that survival rates for primary molars treated with ZnOE pulpectomy were significantly greater than those treated with ferric sulphate pulpotomies at 3 years of age [34]. Until recently, ZnOE has been the material of choice, but concerns have been expressed regarding the difference between its rate of resorption, and that of the tooth and its slow absorption when pushed into the apical tissues [107]. It is not known whether this has a significant clinical effect. Some studies have identified patients in whom use of ZnOE in the primary tooth has resulted in deflection of the permanent successor [111], and Coll and Sandrian suggested that this may occur in as many as 20% of cases [112].

Several authors have reported the use of KRI paste (Pharmachemie, Haarlem, the Netherlands), which is a mixture of iodoform, camphor, parachlorophenol and menthol [113,114]. This medicament resorbs rapidly and does not appear to have an adverse effect on the permanent successor. Its success rates have been reported as being between 84% and 100% [113,114]. Studies have found unfavourable responses of periapical tissues to KRI paste and increased cytotoxicity when compared with ZnOE [115,116]. Maisto's paste has also been described [115]. It is essentially KRI paste with the addition of zinc oxide, thymol and lanolin.

Calcium hydroxide has favourable antibacterial effects, is easily resorbed and causes no foreign body reaction. Mani *et al*. [110] showed high clinical success rates over a 6-month period, and although a depletion of material from the root canals was noted, this did not appear to be clinically significant. Recent research [111] has investigated the use of a premixed calcium hydroxide and iodoform paste (Vitapex, Neo Dental Chemical Products Co., Tokyo, Japan). This study demonstrated a combined clinical and radiographic success rate of 100% for Vitapex in comparison to 78·5% for ZnOE. These high clinical success rates, as well as a lack of toxic effects and deleterious effects on the succedaneous tooth, combined with its radiopacity and resorbability, have led authors to herald this as a nearly ideal primary tooth filling material [117,118].

What this paper adds

- This paper highlights the evidence since the Cochrane review of pulp therapy in 2001 and evidence that could have been lost in the rigour of such a review.
- A narrative review of the currently available alternative interventions and materials to formocresol pulpotomy is presented following an appropriate literature search.

Why this paper is important for paediatric dentists

- The IARC (International Agency for Research on Cancer) in June 2004 has classified formaldehyde as carcinogenic to humans leaving the dental profession to look for other viable alternatives to formocresol.
- From the published data available it is concluded that ferric sulphate, MTA (Mineral Trioxide Aggregate) and IPT (Indirect Pulp Therapy) appear as promising alternatives to the single visit formocresol pulpotomy.

Conclusion

This review of the currently available literature highlights the advantages and disadvantages of the alternative interventions and materials for the management of the extensively carious primary molar in comparison to formocresol. The process of the literature review promoted debate, which facilitated the development of a local clinical protocol.

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