Formocresol and Alternative Pulpotomy Medicaments used in Primary Teeth: A Review

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Abstract

Background: Pulpotomy is a common procedure to treat asymptomatic reversible pulpitis in primary molars. Several pulpotomies medicaments have been used to devitalize remaining pulp or maintain pulp vitality and promote healing.

Objectives: To review different material used so far for pulpotomy that has appeared in previously published papers.

Search Methods: An electronic search was undertaken on Cochrane Database, PubMed, Science Direct, and Google Scholar for articles on medicament agent used in pulpotomy in children. All electronic searches were last updated in May 2021. Search terms used were pulpotomy, formocresol, electrosurgery, mineral trioxide aggregate, zinc oxide-eugenol, calcium hydroxide, laser, glutaraldehyde, ferric sulfate, sodium hypochlorite, Portland cement and Biodentine.

Results: All significant pulpotomy agents were being found from 57 published papers. All these medicaments had been compared with the standard pulpotomy agents and their success rates has been demonstrated.

Conclusion: The use of formocresol or formaldehyde-based medicaments should be replaced with more biocompatible medicaments possessing antimicrobial and pulpal regenerative properties. There is a continual search on finding an ideal material with good success rate.

Keywords: Formocresol; Medicaments; Primary Teeth; Pulp; Pulpotomy

Abbreviations

FC: Formocresol; FS: Ferric Sulfate; ES: Electrosurgery; GA: Glutaraldehyde; Ca (OH)2: Calcium Hydroxide; MTA: Mineral Trioxide Aggregate; NaOCl: Sodium Hypochlorite

Introduction

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 (FC). The coronal pulp chamber is then filled with a suitable base and the tooth is restored with a restoration that seals the tooth from microleakage. Numerous agents have
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been utilized as pulpotomy agents such as electrosurgery (ES), laser, glutaraldehyde (GA), calcium hydroxide (Ca(OH)₂), ferric sulfate (FS), mineral trioxide aggregate (MTA), and sodium hypochlorite (NaOCl) [1].

The materials to be used for pulpotomies should be bactericidal, harmless to the pulpal tissue and surrounding structures, promote healing of the radicular pulp or keep the tissue without inflammation, and should not interfere with the physiological process of root resorption [2]. The aim of this review was to review different material used so far for pulpotomy that has appeared in previously published papers.

**Review Search methodology**

Electronic databases, “Cochrane Database”, “PubMed”, “Science Direct”, and “Google Scholar”, were searched to identify relevant studies published in English until 2021. Abstracts and full texts were explored to identify studies that described the pulpotomy and compare formocresol with other medicament agents were included in the review. Appropriate MeSH headings and key words related to different aspects of pulpotomy in primary dentition were used in the search.

**Formocresol**

Formocresol (FC) was introduced approximately a century ago into endodontic therapy as a formulation of equal parts of formalin and tricresol [3]. In 1930 Sweet advocated the use of FC for pulpotomy of primary teeth, and it is still considered the most universally taught and preferred pulp treatment for primary teeth in both predoctoral pediatric dentistry programs and pediatric dentistry specialists in USA and Canada [1,4]. It is frequently used due to its ease of use, antibacterial effect and fixative properties [5]. FC is derived from two active components, formaldehyde and cresol, both having completely different properties. Formaldehyde is a well-known fixative that reacts with the proteins of the pulp and bacteria. It presumably denatures the toxins and the autolytic enzymes with converts an acute inflammation into a chronic state [6]. On the other side is cresol, which is a caustic, phenol-like drug that dissolves cell membranes and homogenizes the pulp [7].

Multiple clinical studies have shown that a 20% FC dilution produces results that are equal to, or better than, those of full-strength FC [8,9].

During recent times, concern has arisen overusing FC as a pulpotomy medicament and no longer used in some countries, mainly as a result of its toxicity, post-operative systemic transport of FC, effects on the enamel structure of their permanent successors, radiographic changes in treated teeth, the possibility of reversible fixation leading to auto antibody formation, and potential carcinogenicity [10,11]. Other possible problems with FC include liver toxicity and genotoxicity [12]. Formaldehyde testing reveals DNA breakage and crosslinking activity. Dosage is also a problem, with packages listing only estimated percentages and coming in varying sizes across the world. The relationship between milligrams per liter and parts per million has been wrongly interpreted by many clinicians. As a result, the actual dose is often unknown [12].

In a case-control study in which FC pulpotomies were performed in 20 children by using Buckley’s original formula, blood samples were taken before (control) and after treatment to observe the mutagenic potential of FC on lymphocytes cultures [10]. No statistically significant differences could be observed in the cultured lymphocytes. FC was mutagenic for one patient which leading the authors to raise doubts about the desirability of using this technique in children [10].

In summary, FC has been used as the medicament of pulpotomy in primary teeth since decades. Because of the biological concerns, several materials have been introduced to be an alternative to FC. Because of the long history of clinical and biological studies done on FC, FC is still the most universally taught medicament in the treatment of pulpotomy in primary teeth.
Zinc oxide-eugenol

Zinc oxide-eugenol (ZOE) was the first agent used for the preservation of pulp tissue in early dentistry [13]. Eugenol is an essential oil, which has a pleasant smell, germicidal activity and some degree of local anesthetic effect. When mixed with zinc oxide, the setting of ZOE cements is the result of formation of zinc eugenol ate crystals [14].

Previous investigation reported that ZOE used as a pulpotomy agent on permanent teeth results in internal resorption [15]. Similar study also revealed some negative aspects of ZOE pulpotomies; it was the comprehensive histologic analysis by Magnusson that best demonstrated the resultant inflammation and internal resorption [16]. Based on the studies, it has been concluded that eugenol possesses destructive properties, and cannot be placed directly on pulp [17].

In summary, ZOE was not found to be a suitable medicament in the pulpotomy of primary teeth since the direct placement of the ZOE material with the pulp tissue resulted in chronic inflammation and necrosis [15-18].

Calcium hydroxide

Calcium hydroxide Ca(OH)\(_2\) is a material that has been used for a variety of purposes since its introduction into dentistry by Hermann in 1920. Ca(OH)\(_2\) was considered most favored as a pulpotomy agent in the 1940s and mid-1950s and was named “vital” pulpotomy because it was thought to be more biologically acceptable owing to the fact that it promoted reparative dentin bridge formation and pulp vitality was maintained [19]. Ca(OH)\(_2\) is the material used routinely for pulpotomy of permanent teeth, therefore might be considered to be the material of choice for primary teeth, because it promotes healing and stimulates secondary dentine formation [20]. Published data regarding the degree of clinical success of Ca(OH)\(_2\) as a primary tooth pulpotomy medicament reported varying success rates from 33% to 87% [9,18,21]. A summary of clinical studies which investigated Ca(OH)\(_2\) as a pulpotomy medicament and compared it with FC is shown in table 1.

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Number</th>
<th>Time periods: Months</th>
<th>Percent Success</th>
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<tbody>
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<td></td>
<td></td>
<td>Clinical</td>
</tr>
<tr>
<td>Waterhouse., et al</td>
<td>2000</td>
<td>84</td>
<td>To exfoliation</td>
<td>FC: 84</td>
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<td></td>
<td></td>
<td>Ca(OH)(_2): 77</td>
</tr>
<tr>
<td>Huth., et al</td>
<td>2005</td>
<td>200</td>
<td>24</td>
<td>FC: 96</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ca(OH)(_2): 87</td>
</tr>
<tr>
<td>Yildiz and Tosun</td>
<td>2014</td>
<td>147</td>
<td>Up to 30</td>
<td>FC:100</td>
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<td></td>
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<td>Ca(OH)(_2): 85</td>
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</tbody>
</table>

**Table 1: Clinical studies using Ca(OH)\(_2\)**

In all investigations, failure was the result of chronic pulpal inflammation and internal resorption because Ca(OH)\(_2\) has no healing effect on chronically inflamed pulp tissue[9,20,22]. Internal resorption may result from overstimulation of the primary pulp by the highly alkaline Ca(OH)\(_2\). This alkaline- could cause metaplasia within the pulp tissue, leading to the formation of odontoclasts. In addition, undetected microleakage could allow large numbers of bacteria to overcome the pulp and cancel out the beneficial effects of Ca(OH)\(_2\) [22].

In summary, the Ca(OH)\(_2\) pulpotomy technique cannot be generally recommended for primary teeth owing to its low success rate.

Electrosurgery

Electrosurgery (ES) is a nonpharmacological hemostatic method often utilized in dentistry and has been suggested to give favorable results in pulpotomy procedures [23]. ES used different currents to produce different amount of heat which is used to produce a surgi-
cal incision, coagulation for the coronal pulp tissue prior to placing a lining material [24]. The rationale for ES pulpotomy is that after the removal of infected coronal pulp tissue, a layer of coagulation necrosis caused by ES application provides a barrier between healthy radicular tissue and the base material placed in the pulp chamber [25].

ES has been compared to FC as a pulpotomy medicament in a number of previous clinical studies [26,27]. Dean et al. (2002) did study compared ES pulpotomies vs. FC pulpotomies in human vital primary molar teeth. Fifty children were randomly divided into two groups, 25 receiving an ES pulpotomy and 25 receiving FC pulpotomy. After at least 5 months postoperative observation time, the clinical and radiographic success rates for the ES group, 96% and 84%, respectively; and for the FC group, 100% and 92%, respectively. This study failed to demonstrate a difference in the success rate between the ES and FC pulpotomy techniques [26].

In summary, ES has been suggested to give favorable results in pulpotomy procedures with a primary advantage that it can be performed quickly, that there is no pharmacotherapeutic agent used which may produce undesirable local or systemic effects and one of the techniques recommended by AAPD [1,27].

Laser

Laser is an acronym for light amplification by the stimulated emission of radiation. It is a device that transforms light of various frequencies into a chromatic radiation in the visible, infrared, and ultraviolet regions with all the waves in phase capable of mobilizing immense heat and, power when focused at close range [28]. The first challenge for the use of laser in dentistry dates back to the late 1960s, but it was not until the early 80s that laser saw its first use in clinical practice for soft and hard dental tissues treatment [29]. It has been shown that the laser application has advantages and disadvantages which are the same as for electrosurgery [30]. Subsequent studies showed conflicting results with respect to pulpal healing following laser pulpotomy [31,32].

In summary, it could be concluded that laser has been used to achieve hemostasis and achieve pulpotomy in primary teeth with variable success rate [28,33]. However, more controlled clinical and histological investigations are needed to address the variables of power settings, application times, continuous versus pulsed modes of application, and degree of heat dissipation in the radicular pulp and surrounding hard tissues.

Glutaraldehyde

Glutaraldehyde (GA) was proposed as early as 1972 as alternative to FC in the management of carious exposed pulp in primary molars [34]. It has been suggested by many authors that GA probably could substitute for FC because it is more active chemically, rapidly forms cross linkages, more limited penetration, less dystrophic pulp calcification, no evidence of ingrowth of granulation tissue into root apex, less apical damage and less necrosis [35]. The clinical success rates of GA as a pulpotomy agent have been established in several studies and has ranged from 94% - 100% [36,37]. Several studies have assessed the systemic distribution, cytotoxicity and mutagenicity of GA as pulpotomy agent [38,39]. To assess the toxicity of GA, Seow and Thong (1986) evaluated the effect of pulpotomy medicaments commonly used in pediatric dentistry on Polymorphonuclear (PMN) adherence. The results showed that GA did not produce PMN lysis at high concentration; also, not cause activation of PMN adherence at low concentration [39].

In summary, GA has shown comparable success to FC. In spite of that, GA has not been accepted as an appropriate alternative to FC because it has similar toxic effects to FC, availability, required fresh preparation, and no strong evidence of improved success rates [11].

Ferric sulfate

Ferric sulfate (FS) is a strong hemostatic agent which was first used in a military hospital as Basic Ferric Sulfate Solution or Monsel’s solution (20% FS) in Bordeaux, France in 1857 [40]. FS, a nonaldehyde chemical, has been proposed as a pulpotomy agent by Landau and
Johnsen in 1988 [41]. It acts as a hemostatic agent but its exact mechanism of action is not completely understood. It is thought that iron and sulfate ions chemically react with blood proteins, causing them to agglutinate and form plugs over the capillary orifices, without the presence of a blood clot thereby minimizing the chances for inflammation and internal resorption [42]. Thus, in the treatment of vital pulpotomies, the known action of FS is merely hemostatic rather than bactericidal or fixative [40].

Promising results of FS pulpotomy have been reported in many animal and human studies [18,43-45]. A summary of clinical studies which investigated FS as a pulpotomy medicament and compared it with FC is shown in table 2.

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Number</th>
<th>Time periods: Months</th>
<th>Percent Success</th>
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</thead>
<tbody>
<tr>
<td>Fuks., et al.</td>
<td>1997</td>
<td>96</td>
<td>Up to 34</td>
<td>FC: 84</td>
<td>FS: 93</td>
<td>FC: 80</td>
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<td></td>
<td></td>
<td>FS: 93</td>
</tr>
<tr>
<td>Ibricevie and AlJame</td>
<td>2000</td>
<td>70</td>
<td>20</td>
<td>FC: 100</td>
<td>FS: 100</td>
<td>FC: 97.2</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>FS: 97.2</td>
</tr>
<tr>
<td>Huth., et al.</td>
<td>2005</td>
<td>200</td>
<td>24</td>
<td>FC: 96</td>
<td>FS: 100</td>
<td>FC: 90</td>
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<td></td>
<td></td>
<td></td>
<td>FS: 86</td>
</tr>
<tr>
<td>Ozmen and Bayrak</td>
<td>2017</td>
<td>45</td>
<td>24</td>
<td>FC: 87</td>
<td>FS: 100</td>
<td>FC: 80</td>
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<td></td>
<td>FS: 87</td>
</tr>
</tbody>
</table>

**Table 2: Clinical studies using FS.**

In summary, based on the available evidence so far, FS and FC produce equivalent outcomes. However, histological studies have shown that FS produce severe inflammatory response also had a high incidence of premature loss due to internal resorption, external resorption or abscess formation [42,44,45].

**Mineral trioxide aggregate**

Mineral trioxide aggregate (MTA) was proposed as new biocompatible a pulp capping material and approved in 1998 by the U.S. Food and Drug Administration (FDA). The MTA material appears to be an improvement over other materials for some endodontic procedures that involve root repair and bone healing [46]. Koh., et al. (1995) demonstrated that MTA has the ability to stimulate cytokine release from bone cells, indicating that it actively promotes hard tissue formation [47]. Furthermore, multiple studies investigated on the performance of MTA as a pulpotomy dressing agent for primary molars and reported over 90% clinical and radiographic success rate [21,48-50]. A summary of clinical studies which investigated MTA as a pulpotomy medicament and compared it with FC is shown in table 3.

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Number</th>
<th>Time periods: Months</th>
<th>Percent Success</th>
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<th></th>
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</thead>
<tbody>
<tr>
<td>Holan., et al.</td>
<td>2005</td>
<td>62</td>
<td>Up to 74</td>
<td>FC: 83</td>
<td>MTA: 97</td>
<td>FC: 83</td>
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<td></td>
<td></td>
<td></td>
<td>MTA: 97</td>
</tr>
<tr>
<td>Yildiz and Tosun</td>
<td>2014</td>
<td>147</td>
<td>Up to 30</td>
<td>FC: 100</td>
<td>MTA: 96.4</td>
<td>FC: 95.2</td>
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<td></td>
<td></td>
<td>MTA: 96.4</td>
</tr>
<tr>
<td>Olatosi., et al.</td>
<td>2015</td>
<td>25</td>
<td>12</td>
<td>FC: 81</td>
<td>MTA: 100</td>
<td>FC: 81</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>MTA: 96</td>
</tr>
<tr>
<td>Lin et al</td>
<td>2019</td>
<td>90</td>
<td>12</td>
<td>FC: 93.3</td>
<td>MTA: 100</td>
<td>FC: 90</td>
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<td></td>
<td>MTA: 100</td>
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</tbody>
</table>

**Table 3: Clinical studies using MTA.**

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In summary, the lack of internal resorption in primary teeth treated with MTA, in addition to the biocompatibility, sealing ability and promotion of hard tissue formation seem to favor the use of MTA for pulp therapy in primary molars [21,48-50]. However, the common drawbacks to the clinical use of MTA in pulpotomy of primary teeth are cost, not easily available and storage problems [11].

**Sodium hypochlorite**

Sodium hypochlorite (NaOCl) is the most favored endodontic irrigant in modern practice because of its tissue dissolution capacity, antimicrobial effect, lubricant properties and acceptable biologic compatibility in less concentrated solutions [51]. The antimicrobial effectiveness of NaOCl, based in its high pH (pH > 11) which is similar to the mechanism of action of Ca(OH)$_2$ [51].

However, only few clinical trials evaluated the efficacy of NaOCl as a medicament in pulpotomy of primary teeth. Accorinte., et al. (2005) evaluated FS, NaOCl, Ca(OH)$_2$ and saline as hemostatic agents in the response of human pulps premolars capped restored with adhesive and composite resin. They result showed that no subjects receiving NaOCl have reported any pain or sensitivity [52].

Preliminary reports showed NaOCl could be a promising alternative to pulpotomy medicament of primary teeth [53-56]. A summary of clinical studies which investigated NaOCl as a pulpotomy medicament and compared it with FC is shown in table 4.

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Number</th>
<th>Time periods: Months</th>
<th>Percent Success</th>
<th>Clinical</th>
<th>Radiographic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruby., et al.</td>
<td>2013</td>
<td>47</td>
<td>12</td>
<td>FC: 100</td>
<td>NaOCl: 100</td>
<td>FC: 90</td>
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<td></td>
<td></td>
<td></td>
<td>NaOCl: 80</td>
<td></td>
<td></td>
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<tr>
<td>Almutairi and Bawazir</td>
<td>2013</td>
<td>84</td>
<td>12</td>
<td>FC: 92.1</td>
<td>NaOCl: 94.6</td>
<td>FC: 86.8</td>
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<td></td>
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<td></td>
<td>NaOCl: 96</td>
<td></td>
<td>NaOCl: 86.5</td>
</tr>
<tr>
<td>Shabzendedar., et al.</td>
<td>2013</td>
<td>100</td>
<td>12</td>
<td>FC: 100</td>
<td>NaOCl: 100</td>
<td>FC: 93</td>
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<td></td>
<td>NaOCl: 85</td>
<td></td>
<td>NaOCl: 92</td>
</tr>
<tr>
<td>Chauhan., et al.</td>
<td>2017</td>
<td>40</td>
<td>6</td>
<td>FC: 100</td>
<td>NaOCl: 100</td>
<td>FC: 90</td>
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<td>NaOCl: 85</td>
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</table>

**Table 4: Clinical Studies using NaOCl.**

**Alternative medicaments**

A variety of materials have been discovered to make vital pulp therapy a realistic therapeutic option; however, each of the materials described above has its own set of limitations. There is a need to adopt better materials in order to broaden the reach and improve treatment outcomes. Alternative medications have been studied as possible primary molar pulpotomy medications in a few studies. Materials like Biodentine and Theracal have been put to use for pulpotomy and direct pulp caps in recent times [57,58].

In 2018, Taha et colleagues conducted a prospective trial on pulpotomy with biodentine on carious exposed young permanent teeth with irreversible pulpitis. An overall success rate of 95% was observed with a recall time of 6 months and 1 year [57]. M Cannon., et al. conducted a research in four primates in which they compared the effectiveness of Theracal LC to pure Portland cement, resin-based calcium hydroxide, and glass ionomer cement as pulp capping agents. Theracal LC and Portland cement generated a considerable hard tissue barrier and mild pulpal inflammation which was acceptable to be used as a pulp capping agent after 28 days, according to the findings [58].

When it comes to materials like calcium phosphate, Jose., et al. (2013) compared histologically the efficacy of calcium phosphate cement as a pulpotomy medicament with that of FC, they found that calcium phosphate cement formed better dentine bridge, therefore it was suggested that calcium phosphate cement is more compatible to pulp tissues than FC and it shows good healing potential [59].

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Another biocompatible material with a neutral pH of 7.0 is hydroxyapatite. Of all the synthetic calcium phosphate ceramics, it is the most thermodynamically stable. It may also be utilized to support newly generated mineralized tissue as a scaffold [60]. Many other materials, such as growth factors (recombinant insulin-like growth factor - I), simvastatin, stem cells, and propolis (Russian penicillin), are indicated as part of vital pulp treatment. However, further study is needed before they may be used in clinical practice [60].

Conclusion

In conclusion, more biocompatible medicaments with antibacterial and pulpal regenerating properties should be used instead of FC or formaldehyde-based medicaments. There is yet to be identified an ideal pulpotomy agent. Many pulpotomy medications have been researched and used, each with its own set of advantages and disadvantages. The success of a pulpotomy is largely dependent on case selection and clinical diagnosis. Clinicians must choose cases carefully, utilize medications based on clinical judgment, and experiment with new medications to achieve the highest results.

Acknowledgments

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Conflicts of Interest

The author declares no conflict of interest.

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