Is there sufficient evidence to support the long-term efficacy of mineral trioxide aggregate (MTA) for endodontic therapy in primary teeth?

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Abstract

Several papers have been published to illustrate the effectiveness of mineral trioxide aggregate (MTA) as a pulpotomy medicament. Most of these reports do not offer a critical assessment on the data quality. Therefore, this review evaluated whether the currently available evidence is of an appropriate quality to support the long-term effectiveness of MTA as a pulpotomy medicament in primary molars using a standardized assessment criterion. A comprehensive literature search of human clinical outcome studies, which employed MTA as a pulpotomy medicament in primary teeth, was conducted using the MEDLINE database. Two independent observers rated these articles using the standardized assessment criteria. Furthermore, based on the initial sample mentioned in the individual studies and the sample included for the final analysis, the drop-out rates were calculated. Twenty-two studies were included for quality assessment with an excellent interobserver agreement. None of the 22 studies obtained grade A, four studies attained grade B1, five were graded B2 and 13 received grade C. Based on the assessment criteria employed, there was no evidence that MTA was better than present materials and techniques as a pulpotomy medicament. Furthermore, given the low quality of data, it is highly desirable to establish standard requisites for conducting and reporting on pulp therapy studies in primary teeth so as to benefit both researchers and clinicians to produce high-quality studies that are comparable and to prevent the misuse of clinical material and resources.

Keywords: children, mineral trioxide aggregate, primary teeth, pulpotomy.

Introduction
Mineral trioxide aggregate (MTA), which has been classified as ‘hydraulic silicate cements’ (Darvell & Wu 2011), was introduced to seal communications between roots and external surfaces of teeth (Lee et al. 1993). Subsequently, it has been advocated for other uses such as, direct pulp capping, root-end filling, apexogenesis and apexification in immature teeth with necrotic pulp, filling of root canals, treatment of horizontal root fractures, internal and external resorption, and repair of perforations. In primary teeth, MTA is predominantly used for direct pulp capping and pulpotomy procedures. The major benefits of MTA are that it is biocompatible, bactericidal (high pH, 12.5) and able to stimulate cementum-like formation, osteoblastic adherence and bone regeneration. Moreover, its sealing, mineralizing, dentinogenic and osteogenic potentials make it the preferred choice for numerous clinical applications (Parirokh & Torabinejad 2011).
As is common for any new material, MTA is now claimed to be superior to all existing materials. To date, narrative (Srinivasan et al. 2009) and systematic reviews (Simancas-Pallares et al. 2010), meta-analyses (Peng et al. 2006) and evidence-based assessments (Ng & Messer 2008) have all been published to illustrate the effectiveness of MTA as a pulpotomy medicament in comparison with formocresol, which is considered as the ‘gold standard’. However, these reports do not offer a critical assessment on the data quality. Furthermore, in the current era of evidence-based dentistry, it is essential that any clinical material should possess sound evidence to support its efficacy and safety. Therefore, the purpose of this review was to evaluate whether the currently available evidence is of an appropriate quality to support the long-term effectiveness of MTA as a pulpotomy medicament in primary molars using the modified version (Fuks & Papagiannoulis 2006) of the standard criteria (Curzon & Toumba 2006).

Materials and methods
In May 2012, a comprehensive literature search of studies that have employed MTA as a pulpotomy medicament in primary teeth catalogued in MEDLINE was performed using the keywords: pulpotomy, primary teeth, deciduous teeth, mineral trioxide aggregate, MTA, gray MTA, grey MTA, white MTA, GMTA and WMTA. Only human clinical outcome studies that evaluated the efficacy of MTA as a pulpotomy medicament in primary molars using the modified version (Fuks & Papagiannoulis 2006) of the standard criteria (Curzon & Toumba 2006) were selected. Papers not published in the English language, abstracts, observational studies (Caicedo et al. 2006) and case reports were excluded.

All the articles were assessed and graded, by two examiners (RPA & NMK), using the modified standard assessment criteria, for pulpotomy in primary teeth, as proposed by Fuks & Papagiannoulis (2006). Based on this criterion, a paper could be awarded a maximum score of 42, as the assessment sheet had 17 criteria with a weighting of two points and eight criteria with a weighting of one point. The assessment criteria included such as (i) power calculation to determine the sample size, (ii) inclusion criteria, (iii) exclusion criteria, (iv) tooth selection criteria, (v) criteria for the control group (age, sex, race), (vi) sample stratification or convenience sample recorded, (vii) details of the operators and their experience, (viii) training and calibration of the examiners, (ix) randomization of the subjects by an acceptable system, (x) outcomes recorded, after at least a 2-year period, (xi) clinical and radiographic assessment, (xii) postoperative assessment criteria, (xiii) postoperative assessment in a blinded manner, (xiv) postoperative assessment examiner(s) calibration, (xv) kappa scores or equivalent for the examiners reliability, (xvi) appropriate statistical test and (xvii) reporting outcomes based on the results. The assessment criteria weighting one point included (i) type of study, (ii) carries status recorded as dmft/dmfs, (iii) mandibular teeth used for pulp therapy, (iv) preoperative and postoperative radiographs taken by a standardized method, (v) time to pulp therapy failure or replacement recorded at intervals up to 2 years, (vi) published in a peer review journal, (vii) sponsors of the trial reported and (viii) fluoride background of the subjects. Furthermore, based on the initial sample mentioned by the authors and the sample included for the final analysis, the drop-out rates were calculated, which should be used as an approximate, because the intention was to illustrate the limitations of the published data only. Moreover, given the poor quality of some of the data in the studies that attained grade C, it was considered inappropriate to extrapolate their findings.

Results

Literature search
Of the 108 citations indexed in MEDLINE, only 23 publications had evaluated the efficacy of MTA for pulpotomy in primary teeth. The preliminary study by Eidelman et al. (2001) was excluded as it was considered appropriate to include the long-term report of this study made by Holan et al. (2005). This resulted in 22 studies that were included for quality assessment and grading. Seventeen studies compared MTA with formocresol, whilst 4 studies compared MTA with calcium hydroxide, ferric sulphate, Portland cement, calcium-enriched mixture cement (CEM), and one study compared white MTA with grey MTA.

Assessment and grading
None of the 22 studies obtained grade A. Amongst the 17 studies that compared MTA with formocresol as one of the groups, two studies attained grade B1, three were graded B2 and 12 received grade C. Furthermore, amongst the five studies that compared MTA with medicaments other than formocresol as
one of the groups, two studies attained grade B1, two were graded B2 and one study received grade C (Table 1). The interobserver agreement was found to be excellent with a score of 1.00 (kappa).

Studies comparing MTA with formocresol

Amongst the two studies that obtained grade B1, both MTA and formocresol exhibited similar success rates (Table 2). Although MTA demonstrated a higher success rate compared with formocresol, this did not reach statistical significance. Similarly, amongst the studies that attained grade B2, two studies reported no statistical differences between the two medicaments, whilst one study exhibited a significant difference with MTA being superior to formocresol.

Studies comparing MTA with medicaments other than formocresol

Amongst the two studies that obtained grade B1, one study reported a higher success rate for MTA when compared with ferric sulphate, whilst the other study reported similar success rates for both MTA and Portland cement (Table 3). Amongst the two studies that obtained grade B2, similar success rates were evident for (i) MTA and CEM and (ii) both white MTA and grey MTA.

Discussion

The overall success rates for MTA as a pulpotomy medicament in primary molar teeth ranges from 94% to 100%, and these figures have been the basis upon which meta-analyses (Peng et al. 2006) and evidence-based assessments (Ng & Messer 2008) have concluded that the efficacy of MTA is superior to formocresol. However, most often, these analyses and assessments only focus on the success rates/raw data and fail to comment on the quality of the data on

Table 1 Scores and grades according to the standard assessment criteria, and the frequency of occurrence amongst the 22 published studies that were evaluated

<table>
<thead>
<tr>
<th>Score/points</th>
<th>Percentage (%)</th>
<th>Grade</th>
<th>FC vs MTA</th>
<th>MTA vs medicaments other than FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>38-42</td>
<td>90-100</td>
<td>A</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>32-37</td>
<td>75-89</td>
<td>B1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>25-31</td>
<td>60-74</td>
<td>B2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>≤ 24</td>
<td>≤59</td>
<td>C</td>
<td>12</td>
<td>1</td>
</tr>
</tbody>
</table>

FC, formocresol; MTA, mineral trioxide aggregate.

Table 2 Papers that evaluated the efficacy of mineral trioxide aggregate (MTA) with formocresol (FC) for pulpotomies in primary teeth and the grades obtained based on the standard assessment criteria (Fuks & Papagiannoulis 2006)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Author (year)</th>
<th>Country</th>
<th>Age of patients (years)</th>
<th>No. of teeth used for analysis</th>
<th>Follow-up period (months)</th>
<th>Drop-out rate (%)</th>
<th>Treatment outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>Zealand et al. (2010)</td>
<td>USA</td>
<td>2½-10</td>
<td>103</td>
<td>6</td>
<td>19</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>Holan et al. (2005)</td>
<td>Israel</td>
<td>4-12</td>
<td>29</td>
<td>4 to 74</td>
<td>-3</td>
<td>24</td>
</tr>
<tr>
<td>B2</td>
<td>Saltzman et al. (2005)</td>
<td>Canada</td>
<td>3-8</td>
<td>24</td>
<td>16.7 ± 3.0</td>
<td>-6</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Ainehchi et al. (2007)</td>
<td>Iran</td>
<td>5-9</td>
<td>57</td>
<td>6</td>
<td>-21</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>Moretti et al. (2008)</td>
<td>Brazil</td>
<td>5-9</td>
<td>15</td>
<td>14</td>
<td>-6</td>
<td>11</td>
</tr>
<tr>
<td>C</td>
<td>Agamy et al. (2004)</td>
<td>Egypt</td>
<td>4-8</td>
<td>20</td>
<td>12</td>
<td>-17</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Jabbarifar et al. (2004)</td>
<td>Iran</td>
<td>5-8</td>
<td>32</td>
<td>12</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Farsi et al. (2005)</td>
<td>Saudi Arabia</td>
<td>3-8</td>
<td>36</td>
<td>24</td>
<td>-38</td>
<td>31</td>
</tr>
</tbody>
</table>

~ represents approximate value.

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which their conclusions have been drawn, which is essential if they are to be valid.

For instance, of the five studies included by Ng & Messer (2008), for their evidence-based assessment, three of them (Agamy et al. 2004, Jabbarifar et al. 2004, Farsi et al. 2005) obtained a grade C, one study (Holan et al. 2005) was grade B1, yet did not report a statistical significant difference, whilst the other study (Cuisia et al. 2001) could not be graded as it was published only as an abstract. Therefore, based on these studies, it is inappropriate to conclude that MTA provides significantly higher clinical and radiographic success rates compared with formocresol. Furthermore, in the meta-analysis by Peng et al. (2006), there are some questionable interpretations of the studies included because inconsistencies existed between the stated inclusion and exclusion criteria and the presented data. Furthermore, the treatment outcomes were unclear as were details of the data extraction procedure, and also, there was a lack of clarity in the follow-up periods of the individual studies and failure to employ sensitivity analysis, which could have demonstrated whether their results altered due to the inclusion of different end-points. In addition, they failed to follow standard guidelines such as QUOROM, for reporting such analyses. Therefore, the conclusions in both these reports (Peng et al. 2006, Ng & Messer 2008) can be disputable based on the quality of the data from the individual studies.

Amongst the four studies that obtained grade B1, two studies used a coin toss (Holan et al. 2005, Sakai et al. 2009), whilst one used an envelope draw (Zeuland et al. 2010) and the other study used a computer-generated random numbers table (Doyle et al. 2010) as the randomization method to assign the subjects. Amongst the five studies that attained grade B2, four studies (Saltzman et al. 2005, Moretti et al. 2008, Cardoso-Silva et al. 2011, Malekafzali et al. 2011) did not even mention the randomization methods, whilst only the study by Aeinehchi et al. (2007) stated the use of a random number system to assign the subjects. Most of the studies that were graded C failed to mention the method of randomization. It is difficult to understand why investigators did not employ accepted standards in their methodology, such as using random number tables to generate randomization and to also clearly report the method of randomization that was employed in their studies.

Hickel et al. (2005) in their evaluation of the published literature reported that pre-formed metal crowns (PMCs) exhibited lower annual failure rates than any other restorative materials used in primary molars; hence, stainless steel crowns are considered to be an appropriate restoration after pulp therapy in primary teeth. The choice of restoration after pulp therapy is another area of concern in many of the studies in which the investigators used amalgam, glass–ionomer cements or composite resin restorations instead of PMCs. This is a critical confounding variable for the evaluation of success rates after pulp therapy which many investigators failed to consider or discuss. However, it was interesting to note that the only study (Aeinehchi et al. 2007) to report a significant higher success rates for MTA compared with formocresol (grade B2) used amalgam and glass–ionomer cements as the restorative materials after pulp

### Table 3

Papers that evaluated the efficacy of mineral trioxide aggregate (MTA) with medicaments (M) other than formocresol for pulpotomies in primary teeth and the grades obtained based on the standard assessment criteria (Fuks & Papagiannoulis 2006)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Author (year)</th>
<th>Country</th>
<th>Age of patients (years)</th>
<th>No. of teeth used for analysis</th>
<th>Follow-up period (months)</th>
<th>Drop-out rate (%)</th>
<th>Treatment outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade B1</td>
<td>Sakai et al. (2009)</td>
<td>Brazil</td>
<td>5–9</td>
<td>PC 12, MTA 12</td>
<td>24</td>
<td>–1</td>
<td>Success 9/9</td>
</tr>
<tr>
<td>Grade B2</td>
<td>Cardoso-Silva et al. (2011)</td>
<td>Spain</td>
<td>–</td>
<td>74 GMTA, WMTA 136</td>
<td>6–84</td>
<td>–10</td>
<td>Success 74/130</td>
</tr>
<tr>
<td></td>
<td>Malekafzali et al. (2011)</td>
<td>Iran</td>
<td>4–8</td>
<td>CEM 35, MTA 35</td>
<td>24</td>
<td>–17.5</td>
<td>Failure 34/32</td>
</tr>
<tr>
<td>Grade C</td>
<td>Percinoto et al. (2006)</td>
<td>Brazil</td>
<td>3–8</td>
<td>45 CH, MTA 45</td>
<td>12</td>
<td>–18</td>
<td>Failure 39/43</td>
</tr>
</tbody>
</table>

PC, Portland cement; FS, ferric sulphate; GMTA, grey MTA; WMTA, white MTA; CEM, calcium-enriched cement material; CH, calcium hydroxide.
therapy. The investigators used either amalgam or glass-ionomer for subjects treated with formocresol, whilst the subjects in the MTA group had their access cavities restored with amalgam. Furthermore, the investigators did not account for the 21% drop-out rate and did not manage the clustering in their statistical analysis as their randomization was by child and not by tooth. It is worrying to observe that the follow-up radiographs demonstrate changes in the restoration surprisingly used in the MTA group [Figure 4 (b & c), pg. 265]; this could have certainly changed the quality of the seal of the restoration which may or may not have failed between reviews. Therefore, the author’s conclusion that MTA is superior to formocresol is disputable, and caution should be exercised when interpreting and extrapolating the findings of this study.

In the majority of the studies, there are several inconsistencies in the stated diagnostic, inclusion and exclusion criteria, and the use of restorative materials to seal the access cavities. In addition, investigators have failed to (i) employ power calculations to determine the sample size, (ii) assign subjects using an acceptable randomization system, (iii) record the caries status of the subjects, (iv) take radiographs using a standardized method, (v) provide details of the operators/examiners and their reliability scores, (vi) record long-term treatment outcome measures, (vii) include intention to treat analysis to account for drop-out subjects and (viii) appropriate statistical analysis to account for clustering, when randomization was by child and not by tooth. This illustrates the difficulties encountered when extrapolating the data from the published clinical studies.

Despite the fact that all studies, included in this review, used both clinical and radiographic evaluations to determine the treatment success, some of these studies (Naik & Hegde 2003, Godhi et al. 2011, Malekafzali et al. 2011) failed to mention the postoperative assessment criteria, and only a few studies (Zealand et al. 2010, Cardoso-Silva et al. 2011) provided a comprehensive list of the scoring criteria. There was a wide variation in the use of definitions for clinical and radiographic scoring amongst the included studies especially for tooth mobility, pain, periodontal pocket formation, internal root resorption, widened periodontal ligament and periapical or inter-radicular bone destruction. Furthermore, there were discrepancies in the number of items included to determine the success and failures amongst these studies, thus compelling the need for a standardized assessment criterion, which should be made mandatory for postoperative evaluation of treatment outcomes for primary molar pulp therapy studies.

The study that obtained the highest score of 36 was by Zealand et al. (2010), which compared MTA with diluted formocresol. Based on the standard assessment criteria, the only limitations of this study were (i) short-term study with 6-month follow-up, (ii) caries status of the subjects not recorded, (iii) use of both maxillary and mandibular molar teeth and (iv) the fluoride background of the subjects was not mentioned. Moreover, 13 studies obtained a grade C, which was alarming as one can appreciate the time and effort the investigators spend in carrying out their clinical studies. However, it appears that most investigators often overlook several factors when planning and conducting a study or they fail to report the exact methodology and findings, thus limiting extrapolation of the findings from which to draw definitive recommendations. Therefore, it is essential that authors of clinical trials follow a standard format for reporting such as CONSORT guidelines so as to facilitate complete and transparent reporting of their methodology and findings, thus aiding in their critical appraisal, interpretation and comparisons.

There is no consensus on the number of publications required to establish the efficacy of a material. It is not the quantity of the studies, but the quality which is critical. With 22 clinical studies published, that evaluated the efficacy of MTA, one could have made definitive recommendations if the available studies were of adequate quality. Therefore, it is highly desirable to establish standard requisites for conducting and reporting on pulp therapy studies in primary teeth so as to benefit both researchers and clinicians to produce high-quality studies that are comparable and to prevent the misuse of clinical material and resources.

No material is without limitations; therefore, given the questionable quality of the currently published data, there is no direct evidence to support the claim that MTA is superior to formocresol as a pulpotomy medicament in the primary teeth. In the future, meticulous implementation and reporting of well-designed clinical trials with standardized, comparable and patient-centred long-term outcomes are required before definitive recommendations can be made.

Conclusions

Based on the assessment criteria employed, there was no evidence that MTA was better than present materials and techniques as a pulpotomy medicament.
References


