Metaanalysis of filler materials in periapical surgery

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Abstract
Objective: To evaluate the success and failure, apical sealing and biocompatibility of silver amalgam, IRM®, SuperEBA® and MTA as retrograde filler materials.

Study design: A metaanalysis is made of filler materials in periapical surgery, evaluating a total of 30 articles published in recent years.

Results: Percentage success with silver amalgam was 76.5% and slightly inferior to that afforded by IRM®. Performance in turn increased considerably when the materials used were SuperEBA® or MTA. As regards marginal leakage, MTA with a mean leakage time of 65.5 days afforded the best results, followed by SuperEBA®, IRM® and silver amalgam. MTA was the most biocompatible of the materials studied, with practically no inflammatory response, while inflammation proved mild or moderate with SuperEBA®, mild with IRM®, and moderate to severe in the case of silver amalgam. Tissue regeneration was only observed with MTA, in the same way as cement appositioning. Bone neoformation was observed with all four filler materials.

Conclusions: MTA appears to be an ideal material, though the results obtained require confirmation by in vivo studies.

Key words: Periapical surgery, apicoectomy, retrograde filler materials, apical sealing, silver amalgam, SuperEBA®, IRM®, MTA.

Introduction
Periapical surgery is defined as surgery of the periapical tissues and tooth apex, with the purpose of eliminating diseased tissues and ensuring good root canal sealing, with the avoidance of leakage and the penetration of bacteria and toxins from the tooth towards the surrounding tissues. A key consideration for the success of periapical surgery is filling of the root canal, to ensure good sealing and avoid leakage.

The lack of an ideal material for effective and lasting sealing of the root canal system has led to the constant search and evaluation of new materials. Indeed, this search focuses much of current research in periapical surgery (1).

It has always been claimed that “there is no ideal material”, though it is also true that the many studies and analytical approaches used contribute little to define the usefulness of one material with respect to the rest. In effect, a great many studies have compared the same materials using different research methods; as a result of such methodological differences, conflicting results have been obtained with the same materials (2). In vitro studies are carried out under conditions that differ from those found in actual surgical practice. Histocompatibility studies have limited clinical significance, because they are not carried out under the conditions found in the real-life biological environment in which the study materials are required to perform their
function. In turn, animal studies offer results that can only be extrapolated to the human setting with great caution, while clinical trials involve protocols and designs with numerous variables that make comparative evaluation with routine clinical practice almost impossible. The lack of a working model thus slows the development of an ideal or first choice retrograde filler material (3). The aim of the present study is to offer an update on the periapical surgical success and failure criteria, based on the most widely used retrograde filler materials, with an evaluation of apical sealing, leakage and marginal adaptation of silver amalgam, IRM®, SuperEBA® and MTA, and the biocompatibility and cytotoxicity of these materials.

Material and Methods
A metaanalysis has been made of the results of a PubMed literature search. The data from the selected articles have been subjected to a descriptive statistical study, evaluating the following parameters:

- Success, failure and healing: Treatment success was defined as a functional tooth without symptoms or clinical evidence of infection. Radiological follow-up was required to confirm bone healing, with a normal (or tending towards normal) periodontal ligament. Healing was considered to be complete in the absence of symptoms, and with full bone regeneration or a radiotransparency of less than 1 mm in size. Incomplete healing was defined as the absence of symptoms and a radiopaque image smaller than at baseline. Uncertain healing corresponded to vague or sporadic symptoms and a radiotransparent image smaller than at baseline. Finally, unsatisfactory healing was considered in the presence of symptoms and with either no change or an increase in rarefaction (5).

- Marginal leakage considered the percentage of samples with leakage, the depth of leakage in millimeters, and the time required by certain microorganisms to penetrate through the material.

- Biocompatibility was evaluated on the basis of tissue regeneration, cement appositioning, bone neoformation, the cells present, toxicity and inflammatory response.

Results
1. Success, failure
Following the analysis of 2689 cases, the mean percentage success rate of treatment with silver amalgam was found to be 76.5%, with a failure rate of 22.6%, after a minimum control period of three months. In most cases follow-up extended to over one year. The complete, unsatisfactory and uncertain healing rates were 58.16%, 25.6% and 12%, respectively. In the case of IRM®, the success rate was slightly greater than in the case of silver amalgam (77.77%), though the study sample in this case was also significantly smaller. The complete healing rate with this filler material was 53.99%. This percentage was seen to increase with the duration of follow-up.

On examining SuperEBA® the success rate was seen to increase considerably (95.62% for a mean control period of 55.8 months). These results were also seen to be quite homogeneous among the different authors consulted. The complete healing rate with SuperEBA® was found to be 72.2% in our study. The results obtained with MTA are very encouraging, with a success rate of 91.8% and a complete healing rate of 73.77% after two years. However, these results must be regarded with caution, since very few in vivo studies were found in the literature search (Figure 1).

2. Marginal leakage, sealing capacity
Marginal leakage is considered to account for 60% of all failures in periapical surgery. In this context, MTA was seen to offer the best performance in terms of marginal leakage.

- In the studies that evaluate the time required by certain microorganisms to penetrate 3 mm of retrograde filler material, the differences of MTA with respect to the rest of materials is seen to be considerable. Thus, the mean time after which MTA begins to show leakage was 65.5 days, versus 31.75 days for silver amalgam, 44.75 days in the case of IRM®, and 48.66 days for SuperEBA®.

- On considering the mean leakage depth in millimeters associated with each material, MTA continued to show the best performance, with an average of 0.46 mm after a control period of 41 days. In comparison, silver amalgam showed an average leakage depth of 2.32 mm after a follow-up period of 60.94 days - though the study sample in this case was larger (655 cases). SuperEBA® in turn showed a leakage depth of 1.18 mm, with a control period far longer than that of the silver amalgam series. Lastly, IRM® showed a leakage depth of 1.75 mm after 70 days - though the sample size in this case was comparatively smaller (Figure 2).

- In relation to the percentage of teeth showing no leakage with each filler material, the best results once again corresponded to MTA (78.47%). The performance of SuperEBA® came very close to that of MTA (73.45%). In the case of IRM®, 39.1% of the teeth showed no leakage - this figure being slightly greater than in the silver amalgam group (35.02%). However, as with the rest of the results, both the control time and sample size were significantly smaller (Figure 3).

3. Biocompatibility
The inflammatory response induced by MTA at periapical tissue level was found by almost all authors to be practically inexistent. SuperEBA® induced mild or moderate inflammation after placement. Most authors considered silver amalgam to induce moderate to severe inflammation. Lastly, IRM® induced a mild inflammatory response.

- As refers to tissue regeneration, only MTA was seen to generate areas of calcification that induce tissue regeneration. Silver amalgam and SuperEBA® induce fibrous cicatricial tissue, dense connective tissue and granulation tissue.
Fig. 1. Percentage success rates afforded by the different filler materials.

![Bar chart showing success rates for different filler materials.]

Fig. 2. Mean marginal leakage depths recorded with the different retrograde filler materials (in mm).

![Bar chart showing mean marginal leakage depths.]

Fig. 3. Percentage leakage of the different retrograde filler materials.

![Pie charts showing percentage leakage for different filler materials.]

<table>
<thead>
<tr>
<th>Materials</th>
<th>Amalgama</th>
<th>IRM®</th>
<th>SuperEBA®</th>
<th>MTA</th>
</tr>
</thead>
<tbody>
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<td>% no filtration</td>
<td>35%</td>
<td>39%</td>
<td>27%</td>
<td>22%</td>
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<tr>
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<td>61%</td>
<td>73%</td>
<td>78%</td>
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- Cement appositioning, of great importance for periodontal ligament neoformation, was observed in most cases when using MTA as retrograde filler material. In contrast, no such appositioning was reported with IRM®, SuperEBA® or silver amalgam.

- Bone neoformation was observed in the different studies with MTA, amalgam and SuperEBA®. However, bone formation proved more significant when MTA was used as filler material, since it creates a biological substrate for bone tissue production and induces the secretion of interleukin-1 and cytokines involved in bone formation.

- As regards to cell response, the use of MTA appears to favor osteoblast response. With fresh MTA, the cells appear rounded, non-adherent to the surface and with a low cellular density. Once the material has set, the cells are seen to flatten and appear firmly bonded to the root surface, with adoption of their normal morphology. The persistence of rounded cells may be indicative of material toxicity. The cell response to the rest of materials was seen to be less apparent and with greater cellular dispersion.

Discussion
Considering the initial objectives of our study and the fact that most investigators continue to regard silver amalgam as the material of reference in their studies, the results obtained in the present metaanalysis can be described as follows:
The greatest success and healing rates correspond to MTA as retrograde filler material (6). In effect, the results obtained are very encouraging, with a success rate of 91.8% and a complete healing rate of 73.77%. However, while apparently very good, these results must be regarded with caution, since few in vivo studies were found in the literature search.
SuperEBA® likewise offered very good results, with a healing rate very close to that of MTA (7). The findings are quite homogeneous among the consulted authors, such as Méndez-Blanco (8) or Dorn and Gartner (cited by the previous investigators), with a reported 94% success rate (8). However, Niederman et al. (9) reported comparatively poorer performance (75% success rate). The complete healing rate with SuperEBA® was found to be 72.2% in our study. Maddalone and Gagliani (10) in turn reported even better performance (78.3%). According to Pautschev et al., however, the complete healing rate with this material is only 57% (8).
IRM® appears to offer better results than silver amalgam (6,8,11), though these results must be viewed with great caution, since few large series can be found in the literature. The best results with this filler material were obtained by Dorn (91% success rate)(8). Chong et al. (6) obtained results very similar to our own (76% success rate after 12 months). Values slightly lower than those recorded in our metaanalysis were published by Rapp et al. (71% success rate) and Vallecillo et al. (58.6% clinical success rate)(9,11). In relation to complete healing, authors such as Chong (6) have obtained results better than our own - with percentages of up to 70.68%. The data obtained by Vallecillo et al. (11) and Schwartz-Arad (5) are closer to our own, with complete healing rates of 55.2% and 50%, respectively.
Mean percentage success when using silver amalgam was very slightly inferior to that afforded by IRM®, with 76.5% - and this figure moreover improved on prolonging the duration of follow-up. Complete healing was recorded in 58.16% of the cases. However, it must be taken into account that silver amalgam was the material yielding the largest global sample size. The results obtained are slightly better than those published by Gregori-Sánchez et al. (72.8%)(12) and by Dorn and Gartner (75%) - this study involving the longest control period (8). The highest percentage success rate corresponds to Pérrarocho (93.7%) (13), and the lowest to Wesson (62%)(14). Other authors such as Martin (15), who conducted controls in different periods, have found the results to improve as the duration of follow-up is prolonged. The highest complete healing rates once again correspond to Pérrarocho (87.7% (13) and 90.4% (16)). Results similar to those of the present analysis were obtained by Wesson et al. (14), with a complete healing rate of 57%; Zetterqvist (17) with 54%; or Pautschev et al., with complete healing in 52% of cases (7). The poorest results correspond to Schwartz-Arad (5), with a complete healing rate of only 43.5% - though in this case the sample size was quite small in comparison with authors such as Pérrarocho.
MTA was seen to offer the best performance in terms of marginal leakage. With this filler material, the mean time to onset of leakage was 65.5 days. When considering these mean times, it must be taken into account that in the series published by Fischer, four of the 14 specimens examined did not show leakage for the full duration of the study (63 days)(18). Similar findings were published by Torabinejad, who observed no leakage in most of the specimens during the 90-day duration of the study. These observations imply that the mean time to leakage with MTA can be expected to increase in studies with longer durations of follow-up (19). In the case of SuperEBA®, the time to marginal leakage was between 36.7 to 48.66 days, while 44.75 days were recorded for IRM® and 31.75 days for silver amalgam.
On considering the mean leakage depth in millimeters, MTA showed an average of 0.46 mm after a control period of 41 days. The smallest depths correspond to Torabinejad (0.28 mm), and the largest to Martell (0.88 mm)(20,21). On considering these data, it must be taken into account that the study published by Martell involved the longest duration of follow-up (77 days). With SuperEBA® the mean leakage depth was found to be 1.18 mm. Authors such as Torabinejad, with a leakage depth of 0.60 mm, or Charles et al., who completed their study without ob-
serving leakage in their specimens, considerably improve upon these results (20,22). In contrast, other investigators such as Martell (21) report poorer results, with a mean leakage depth of 2.48 mm. The mean leakage depth with silver amalgam was 2.32 mm after a mean control period of 60.94 days. This figure practically doubles that recorded with SuperEBA®, and is similar to the depth reported by Vertucci and Beatty (23), with a mean value of 2.77 mm. Gregori et al. (12) obtained better results, with leakage depths of 1.74 mm and 1.99 mm over different follow-up periods. Lastly, IRM® showed a leakage depth of 1.75 mm after 70 days. According to authors such as Fayos (24), with a larger number of cases, leakage is practically the same as that recorded for amalgam, and although Martell (21) found performance to be better than with amalgam, we cannot affirm that IRM® is comparatively more effective in this sense.

In relation to the percentage of teeth showing no leakage with each filler material, the best results once again corresponded to MTA (78.47%). Similar figures were reported by Hong Ming Tang (73.9%) (25). According to Aqrabawi (26), performance with this material is much better, with no leakage in any of the samples studied. The performance of SuperEBA® came very close to that of MTA (73.45%). The poorest results with this material corresponded to Hong Ming Tang (56.5%) (25), and the best to Aqrabawi (26) - with no leakage in 80% of the specimens. Lastly, IRM® and silver amalgam showed no leakage in 39.1% and 35.02% of the samples, respectively. Finally, on evaluating filler material biocompatibility, most authors pointed to the toxicity of silver amalgam, while the best results once again corresponded to MTA. Although most authors considered the latter material to cause no inflammatory response, Ford detected severe inflammation in one of his samples, while Yaltirikm documented one case of moderate inflammation 7 days after retrograde filling (18,27). Although almost all authors considered silver amalgam to induce moderate to severe inflammation, Pertot (28) found inflammation with this material to be mild or moderate. There is no general agreement as to whether amalgam toxicity decreases over time or not. In the case of MTA, however, the associated toxicity does seem to decrease once the material has set (18). Similar observations apply to both SuperEBA® and IRM®, which exhibit moderate toxicity after setting (7,18,28-30).

References