



REVIEW ARTICLE

Endodontic essay

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Keyword

Mineral Trioxide Aggregate.

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doi:10.1111/j.1747-4477.2011.00305.x

Set essay topic and abstract

“It has been said that Mineral Trioxide Aggregate is driving an endodontic revolution. Discuss this statement considering the biological and clinical attributes of this innovative material.”

Introduction

A recent development in the treatment of many endodontic conditions has involved the use of Mineral Trioxide Aggregate (MTA). This material is suggested to possess many advantageous properties over previously used materials and consequently, some consider this product to be driving a revolution in contemporary pulp therapy and endodontics. With many clinical indications having been identified for its use, MTA commands widespread acceptance within endodontics as a root end filling material, pulpotomy medicament, perforation repair material and in dental traumatology.

Background

MTA is a fine hydrophilic powder which shares many similarities in chemical composition with Portland cement. Although not exactly the same, both Portland cement and MTA consist of dicalcium silicate, tricalcium silicate, tricalcium aluminate, gypsum and tetracalcium aluminoferrite (1). The main differences between Portland cement and MTA is that bismuth oxide is added to the latter to give the material a greater degree of radiopacity (2). Similarly, MTA lacks trace amounts of heavy metal oxides and has approximately half the amount of gypsum than Portland cement (3). Hence, Portland cement is different to MTA and should not be used as an alternative.

MTA is currently available in two forms; as a grey or white preparation. These two types, although similar, have some slight differences in chemical composition (3), especially with regard to some of the trace minerals found in the compounds which some have suggested are responsible for the dark grey appearance of grey MTA (4). Clinical studies have subsequently found that these two forms of MTA can respond differently clinically, with the white preparation resulting in less tooth discolouration in anterior teeth (3). White MTA also has significantly less levels of tetracalcium aluminoferrite than the grey preparation (5), however, the significance of this is not currently known.

MTA sets in the presence of moisture, including fluids such as blood (2). When sterile water is added to MTA, the powder preparation forms a colloidal mixture which sets to form a hardened cement. Approximately three to four hours are required for an initial set (2), with MTA having been shown to slowly release calcium hydroxide for at least 3 months after initial mixing and placement (6) and it has been suggested, just as with the use of calcium hydroxide, that this material may activate the enzyme pyrophosphatase and interact with precapillary sphincters to reduce local blood flow to induce hard tissue formation as suggested by Heithersay (7,8). During the setting process, the pH of MTA dramatically increases from its initial pH of 10.2, to a pH of 12.5 due to the calcium hydroxide released from the setting material (1). It has been suggested that this high pH of the setting material, at least in part, is its therapeutic mechanism (9).

Micro-leakage properties

One of the ideal properties of an endodontic material is to minimize micro-leakage, and to a large degree the success of most endodontic procedures is highly dependent on this. Much research has been conducted to evaluate the sealing capacity of MTA and whether it is suitable for use in perforation repair and as a root end filling material. To date, this has been evaluated mostly using an *in vitro* dye or fluid filtration approach or an *in vitro* bacterial penetration method.

When comparing MTA with other materials that have been used in the past, it appears that there is little consensus within current research regarding which materials seal best. To date, there is a significant lack of *in vivo* research analysing this specific quality of MTA. Some studies using an *in vitro* dye or fluid filtration technique have reported no difference in leakage between MTA and zinc-oxide-eugenol (ZOE) containing materials (10,11). A similar observation between MTA and glass ionomer cements (GIC) where no difference between sealing ability has also been observed (12). In contrast, however, other similarly designed studies have reported that MTA has a superior sealing capacity to ZOE containing materials (13,14) and GIC materials (15) when used as a retrograde sealing material after root resection. In each of these studies, a different thickness of MTA material was used making comparisons between the reported findings difficult. The overall results, however, show that the weight of evidence supports MTA as a more biocompatible and better sealing material and that the greater the thickness of MTA placed in the canal, the better the seal (16).

In addition to *in vitro* dye or fluid filtration techniques, other investigations involving bacterial penetration methodology have been used to evaluate the sealing capacity of MTA. Similarly, there are inconsistencies in the research regarding which materials seal best. Some studies have shown that MTA has superior sealing capabilities to bacterial invasion than ZOE containing preparations and Amalgam (17,18) while other reports fail to show any statistical difference between these materials (19,20) in this regard. With each of these reports, however, the micro-organism used in the research varied and this makes comparing the results difficult.

Overall, most research points to MTA requiring a minimum thickness of 3mm for an optimal seal in fully developed teeth and a minimum layer of 5mm in teeth with immature apices, to gain an appropriate seal (12).

Biocompatibility

Cytological investigations

Assessment of MTA's biocompatibility has been undertaken using numerous tissues and techniques. Typically, cell expression/growth and direct placement of the material in subcutaneous, intra-osseous settings or with dental pulp tissues *in vivo* have been used to analyse such interactions. Each evaluation technique has its advantages and disadvantages. For example, *in vitro* cellular studies are good in evaluating the toxicity of a substance but cannot examine the complex interactions between materials and a host, while *in vivo* trials are opposite with this regard.

With respect to cytological investigations, the type of cells used, the duration with which they are in contact with the material and assessment criteria of the degree of biocompatibility vary between the reported studies. Most studies have suggested that MTA is very biocompatible, with a layer of viable cells being deposited/attached to its surface by the host (21,22,23). In contrast, it has been reported by Haglund *et al.* (24) that MTA may have cytotoxic activity on macrophages and fibroblasts. The duration of time over which the material was in contact with the cells were generally less than ten days and as a result, the long-term effects are essentially unknown. Hence, this area presents as a current gap in knowledge.

Analysis of cellular responses and proliferation patterns in response to MTA placement as part of cytological investigations has generally involved the use of scanning electron microscopy (SEM). Some have suggested, however, that the extensive process required in preparing the material for SEM may alter the nature of the MTA material as well as the compounds it releases (25). Consequently, these reactions may produce inaccurate information gathering that will impact the results. An alternative to this technique involves the use of enzyme assays, which some have suggested is a more accurate method to assess cellular activity in this setting. This technique measures the biochemical processes of living cells and does not require the same degree of tissue preparation that would potentially interact with the MTA material or host cells (26). Both SEM and enzyme assay studies mostly show that MTA is very biocompatible (12).

Cytokine expression is another method by which to measure the health, activity, recruitment pattern and differentiation potential of cells in response to MTA. MTA has been shown to induce the expression of inflammatory interleukins which are considered beneficial in its integration and attachment with host cells (27). An increase in IL-4 and IL-10 production (28) and increases in IL-6 and IL-8, which is regarded as advantageous for good bone healing, have been demonstrated (29).

Likewise, MTA has been shown to increase IL-1 α , IL-1 β , IL-6 (30) and osteocalcin (31) release from osteoblasts. It has been postulated that MTA promotes secretion of these cytokines by attached osteoblasts, to recruit and develop osteoclasts to remodel localised hard tissues and thus, improve integration of this material (12). Alkaline phosphatase production and activity in both periodontal ligament and gingival fibroblasts have also been demonstrated with MTA (32). In contrast to these cellular reactions to MTA, controls and other comparison materials such as GIC, Amalgam and ZOE containing materials do not produce a similarly large immune response (12).

Subcutaneous and intra-osseous implantation

Animal studies investigating the tissue reaction when MTA is implanted into a living host have provided a valuable insight regarding host responses to this foreign material. Reports have been published where MTA has been deposited subcutaneously and intra-osseously. MTA initially elicits a severe immune reaction with subsequent coagulation necrosis in the nearby environment when placed subcutaneously in a rat model, which is said to relate to the calcium hydroxide release during the setting reaction (33). This necrotic area is later cleared with the initial reaction subsequently subsiding (34). Intra-osseously, MTA reacts less severely, with the tissue reaction spanning a period of up to twelve weeks (34,35). Likewise, similar results were found in guinea pig models (36). MTA has also been shown to not adversely impact the microcirculation of surrounding connective tissue, hence maintaining a healthy blood supply to the healing tissues after MTA placement (37).

Periradicular tissue reactions

Although amalgam materials have been used routinely for many years as a retrograde root end filling material, the introduction of MTA commands widespread approval by the dental profession and consequently, MTA has revolutionised this aspect of endodontics. MTA, when used as a root end filling material *in vivo*, has been shown to produce less periradicular inflammation than amalgam (38). Additionally, cementum has been shown to develop over the surface of this material, allowing for the potential of a viable periodontal ligament to attach to its surface (39). This has particularly been documented in cases of non-infected teeth, where there is an almost complete regeneration of the periodontium over the material (40). Initial stages of healing when MTA has been placed in the periodontium involve hard tissue deposition on the MTA surface that is exposed to the underlying connective

tissue. As with other areas of MTA research, the degree to which this material is superior regarding its periapical response compared to other materials is not consistent across the literature. For example, MTA has been shown to produce a more favourable periapical tissue response ahead of amalgam and GIC material (39), however, other reports have failed to find any significant difference between MTA and traditionally used materials (41). In each of the studies, different assessment criteria were used to evaluate what was considered a favourable or minimally inflammatory response, thus making comparisons between the studies difficult.

Pulpal reactions

MTA has been advocated by many in the treatment of pulpal exposures as encountered in pulp capping therapy and pulpotomy procedures. In such settings, this material has been observed to stimulate reparative dentine so as to create a complete bridge over the exposure with minimal signs of inflammation (12). It has been reported that the success rates of dentine bridge development is superior with MTA than calcium hydroxide which has been traditionally used in this clinical setting for many years (41).

Clinical applications

Traumatology

Trauma to a developing dentition can occur at any age and considering that the majority of injuries occur within the 5–10 year age bracket (42), it is inevitable that teeth which have not completed apexogenesis will be traumatised and consequently cease root development (43). Where apexogenesis is not possible, the process of apexification is desirable and assists the clinician in successfully treating the tooth endodontically (43). Calcium hydroxide and more recently MTA have been suggested to treat such teeth.

For many years calcium hydroxide, with its ability to induce hard tissue formation and its high pH (~12.5) acting as an anti-bacterial agent, has been used to induce apexification when root development has been arrested (43). Calcium hydroxide enjoys very high success rates with few teeth becoming infected. However, the use of calcium hydroxide has some drawbacks (43). Calcium hydroxide has been repeatedly shown to make dental hard tissues increasingly brittle (44). Consequently, when used to induce apexification in a tooth that is already weak due to lack of root development, this medicament may increase the likelihood of root fracture. In addition to this, the process of apexification may take many months and this not only prolongs the exposure of the tooth to

this agent, but also sustains the treatment process over a long period of time (45). These issues have led some to consider alternatives in treating teeth requiring apexification and one recent material that has shown good success rates is MTA (43).

The use of MTA in dental traumatology is relatively new and consequently, there are many areas regarding the specifics of its therapeutic mechanisms that are currently unknown. Currently, it is recommended that the material be placed at the time of pulp removal to form a foundation upon which the tooth can be endodontically filled (43). As MTA requires three hours to form an initial set, this means that a traumatized tooth can potentially be root filled the same day the necrotic pulp tissue is removed, eliminating the need for periodic redressings and months of monitoring when using calcium hydroxide medicaments to induce apexification. After MTA is placed, the process of apexification occurs subsequent to root filling placement.

Another advantage of using MTA over calcium hydroxide is that it provides an apical barrier which seals better than calcium hydroxide and the hard tissue barrier it induces (7). As some species of bacteria can survive the high pH of calcium hydroxide medicaments, tissue fluid seepage through a porous barrier into an unfilled canal raises the possibility that the canal may become infected (7). Similarly, the presence of bacteria in an unfilled canal has been shown to impede the host's ability to generate a hard tissue barrier, hence potentially drawing out the apexification process for longer than necessary when using calcium hydroxide (43). The advantages of this material over the calcium hydroxide initially used are numerous, and on this basis, it could be argued that MTA is driving an endodontic revolution in dentistry.

Pulpotomies and pulp capping

Animal and human studies have both shown that MTA is very successful as a pulp capping material (12). Most of these studies have involved comparisons with calcium hydroxide medicaments and these have all indicated that MTA is either equally or more successful in pulp capping, producing much less adjacent tissue inflammation (12). MTA has been found to produce a dentine bridge which is thicker in a shorter period of time than calcium hydroxide (12). In a 3rd molar split-mouth human study, it was found that cases treated with calcium hydroxide resulted in a layer of tissue inflammation, then a layer of pulp tissue necrosis then followed by a 0.15mm thick hard tissue bridge after 6 months (46). In comparison, MTA treated teeth showed tissue reactions that were very subdued initially and at 6 months, the teeth had on

average a 0.43mm thick hard tissue bridge with no pulp tissue inflammation evident (46).

The use of MTA as a pulpotomy material has been suggested by some. Most reports indicate that MTA is equally as successful as formocresol in this clinical setting (12). Despite there being little difference with success rates between these materials, MTA is by far more biocompatible than formocresol with the latter having been suggested to be potentially carcinogenic (12).

Perforations and root end filling materials

To date, there is much research lacking in this area. Most research has involved case studies or trials of the material that have not been compared to other materials. Currently, it appears that MTA is useful and successful in perforation repair or as a root end filling material. Although there is evidence lacking, the advantageous properties of MTA such as its sealing capacity and biocompatibility highly suggest that it would perform well in this environment and research, to date, indicates this to be the case (12).

Conclusion

The clinical uses for MTA are varied and current research indicates that it may be advantageous to substitute this material for the myriad of other materials used in the past to treat various conditions. MTA has now emerged as an excellent treatment choice for many pulpal/endodontic conditions and consequently, this has driven a revolution in endodontics. As this product is relatively new, however, the amount of evidence currently available is lacking in most areas. Consequently, more research needs to be completed regarding this material's therapeutic mechanisms, appropriate case selection criteria, as well as how this material could be further improved.

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