Will mineral trioxide aggregate replace calcium hydroxide in treating pulpal and periodontal healing complications subsequent to dental trauma? A review

REVIEW ARTICLE

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Abstract – Mineral trioxide aggregate (MTA) has over the last two decades begun to take the place of calcium hydroxide (CH) in the treatment of a variety of pulpal and periodontal healing complications following dental trauma. These conditions include teeth with: (i) exposed pulps, (ii) immature roots and pulp necrosis, (iii) root fractures and pulp necrosis located in the coronal part of the pulps, and (iv) external infection-related (inflammatory) root resorption. The main reasons for replacing CH with MTA in these situations have generally been the delayed effect when using CH to induce hard tissues, the quality of such induced hard tissues, and finally the dentin weakening effect of CH, which in some instances lead to cervical root fractures in immature teeth. MTA appears, from a relatively few clinical studies, to overcome these shortcomings of CH. The lack of long-term clinical studies, however, may warrant a certain reservation in an unrestricted replacement of CH with MTA. A definite need for randomized clinical studies comparing CH and MTA in trauma healing situations is urgently needed.

Calcium hydroxide (CH) has for many decades been the main material used to treat a variety of pulpal healing complications in dental traumatology, such as in teeth with exposed pulps (pulp capping, pulpotomy), in teeth with incomplete root formation and pulp necrosis (apexification), in teeth with root fractures and pulp necrosis located in the coronal part of the pulps, and in teeth with infection-related external root resorption (1). In spite of its successful outcome in many of the above-mentioned trauma healing complications, a number of shortcomings have been noted with respect to its use in dental traumatology. These problems can be summarized as follows:

1 *Length of time for induction of coronal or apical hard tissue barriers.* This typically ranges from 2–3 months in the case of pulp capping (2) and 6–18 months in the case of apexification procedures (3–5) with an average of 9 months for the latter (6). Such lengths of time, apart from delaying completion of treatment, also represent a risk of failure in patient compliance with subsequent appointments.

2 *Induction of initial zones of sterile pulp necrosis.* These zones represent the contact area between calcium hydroxide and vital pulp tissue; they may become infected at a later time through micro-leakage under restorations, leading to pulpitis and subsequent pulp necrosis (7).

3 *Incomplete coronal and apical hard tissue barriers because of vascular inclusions.* This is a phenomenon that may allow bacterial invasion through such vascular tunnels (8, 9).

4 *CH-related changes in the physical structure of dentin.* These changes are related to the loss of inorganic and organic components of the dentin (10–18). Such changes have been found to lead rather frequently to cervical root fractures (5, 19, 20).

In 1993, a new endodontic material, mineral trioxide aggregate (MTA) was developed by Torabinejad and co-workers, primarily for the purpose of making a bacteria tight and biocompatible material to, among other applications, seal accidental perforations of the root canal (21). Subsequently, the material was shown to also be ideal as root-end filling material and a material for use in pulp capping and pulpotomy cases (22–27). Later, MTA found its way into treatment of traumatized immature teeth with pulp necrosis (apexification), as some of the shortcomings of CH seemed to be overcome with the use of MTA (28).

Comparison of treatment modalities: CH and MTA

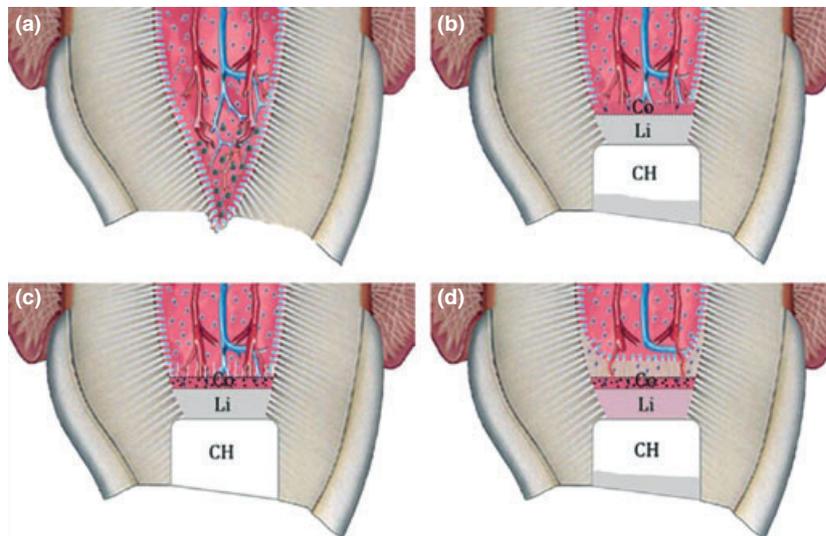In an effort to compare the use of CH and MTA, the reported effects of these two materials on pulp, dentin,

Fig. *1*. Calcium hydroxide induced pulp changes after pulptomy. (a) Exposed pulp. (b) Pulpotomy with application of CH. Because of its high pH effect on dentin, calcium hydroxide (CH) causes the release of a number of wound healing signals (growth factors), and for some time, the high pH also may prevent bacteria from entering the amputation site. The high pH of CH generates a zone of liquefaction necrosis (Li) and a zone of coagulation necrosis (Co) (approximately 1 mm combined width, in case of non-setting CH). In the case of hard setting CH cements (e.g., Dycal®), a very narrow or absent liquefraction zone is formed (9, 90, 91). (c) The coagulation zone seems to be an initiator of a wound healing response starting with spherical foci of calcification, which coalesce to form a calcification zone and next to that collagen is formed. (d) Bone-like tissue is deposited containing cells and vascular inclusions (67–69). After approximately 2–3 weeks, new odontoblast-like cells appear subjacent to the initial hard tissue bridge and normal dentin begins to be formed.

and periodontium in various applicable dental trauma situations are described.

Calcium hydroxide and its capacity to induce hard tissues in relation to pulp capping and pulpotomy

The effects of CH on pulpal and periapical tissues have been studied for many years (2, 7, 29, 30) (Fig. 1). The hard tissue eliciting effect on adjacent soft tissue appears to be related to a necrotizing effect of CH because of its high pH (pH = 12.5) (29, 31). This effect takes a few hours and results in a zone of liquefaction necrosis subjacent to the CH and a deeper zone of coagulation necrosis next to the vital pulp tissue. This latter zone appears to stimulate a bone-like hard tissue bridge formation between it and the vital pulpal tissue (29, 31).

Recently, it has been demonstrated that CH and MTA may solubilize growth factors sequestered in dentin during tooth development (35–37). The release of these factors and other bioactive cell signaling molecules may cause the recruitment of undifferentiated pulpal cells to the wound site leading to production of a hard tissue bridge.

It is thought that the release of wound healing signals (i.e., growth factors) activate progenitor cells in the pulp to proliferate and form the initial bridge (9, 38, 39). This bridge formation has been found in humans to take place in about 2–4 weeks in case of non-setting CH (7, 9, 29, 40). During this process vessels may become included in the bridge formation (7–9, 29, 31, 41, 42), a situation that later may become a problem if the sealing of the pulp capping or pulpotomy area is not optimal. Because of the

unavoidable *dissolution* of the CH, during which it loses its antibacterial effect and allows bacteria to use these vascular channels to enter the pulp, pulpitis may occur (8, 43–45).

A desirable feature of CH (at its normally high pH level) is its excellent antibacterial property (46, 47). This may establish a bacteria-free environment at the amputation site during the critical time when the hard tissue bridge is formed. Furthermore, its dissolving effect of necrotic tissue remnants (48, 49) promotes healing. The average healing rate in three clinical studies on the use of CH in pulpotomies is 95% (range 94–96%) (Table 1).

Mineral trioxide aggregate and its capacity to induce hard tissues in relation to pulp capping and pulpotomy

The effect of MTA on pulpal and periapical tissues has certain similarities to that produced by CH (Fig. 2). The mixture of MTA with water results in the formation of calcium hydroxide (50, 51). MTA is biocompatible and has antibacterial properties and an ability to induce the release of bioactive dentin matrix proteins (36). The initiation of hard tissue bridges (coronally or apically)

Table 1. Healing of the exposed pulp in crown-fractured teeth after pulpotomy with calcium hydroxide

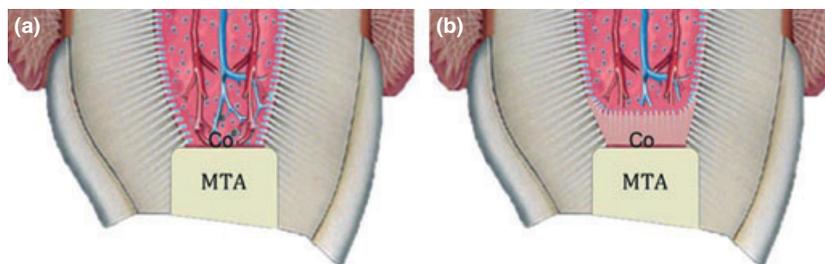| Authors	No of teeth	Healing (%)
Cvek (94)	60	58 (96)
Fuks et al. (95)	63	59 (94)
Cvek (96)	178	169 (95)
Total	301	286 (95)

Fig. 2. Mineral trioxide aggregate induced pulp changes after pulpotomy. (a) Mineral trioxide aggregate (MTA) induces, by its high pH an effect on dentin, a release of wound healing signals (growth factors) and a chemical bond between MTA and dentin (a layer of hydroxyapatite) that prevents or reduces oral bacterial penetration to the pulp amputation site. (b) MTA induces by its pH effect a very narrow zone of coagulation necrosis (Co). Next to that zone, a reparative dentinogenesis zone is found. (c) Subsequently, a dentinal bridge is formed faster than in case of CH and with fewer vascular inclusions (9, 39).

appears to be by stimulation of cell proliferation (32) and cell migration with subsequent differentiation (33, 34). The exact mechanism whereby MTA induces a hard tissue bridge is only partly understood. Tziafas et al. observed a homogenous zone of crystalline formed along the pulp-MTA interphase after 1 week; next to that zone, pulpal cells were arranged in close proximity to the crystals. A regular hard tissue barrier with cellular inclusion was seen after 2 weeks, and after 3 weeks, cellular dentin was formed (39). Apart from that, MTA forms a very tight seal where it contacts the dentin walls coronally and apically (22, 23, 52, 53), most likely due to a physical bond between MTA and dentin (a layer of hydroxyapatite is created as a link) (52). This seal prevents and reduces bacterial penetration to the pulp amputation site (54, 55).

Concerning leakage of MTA used as a coronal plug material, two bacterial leakage investigations comparing MTA and Fuji glass ionomer cement showed no difference between the two types of materials in regard to bacterial penetration (54, 55).

As can be expected, because of the recent introduction of MTA, there are relatively few studies in humans, on the hard tissue inducing effect of MTA when used for pulp capping and pulpotomy in permanent teeth (9, 56). During setting, a high pH (12.5) is created in the area next to the MTA and it will remain high for at least 8 weeks (57). As can be seen from these studies, there seems to be an effect because of the high pH of MTA during setting next to living pulp tissues (50). The hard tissue bridge appears to be formed earlier than under CH, with larger daily dentin increments and few vascular inclusions (9, 39, 58–60).

Only two clinical studies on pulpotomy have been published to date, both with a healing rate of 100%. However, only 10 of the 34 teeth included were pulps exposed by trauma and the rest were pulp exposed by caries (Table 2). A clinical report of MTA used in case of exclusively caries pulp exposures showed 98% outcome (61).

Calcium hydroxide and its capacity to induce hard tissues in immature teeth with pulp necrosis

A substantial amount of research exists on the effect of CH on apical healing events after pulp necrosis in young

Table 2. Healing of the pulp in carious and crown-fractured teeth after pulpotomy with mineral trioxide aggregate

Examiner	No of teeth	Healing (%)
El-Meligy and Avery (97)	15[1]	15 (100)
Witherspoon et al. (98)	19[2]	19 (100)
Total	34	34 (100)

[1]Only four trauma affected teeth.
[2]Only six trauma affected teeth.

teeth with immature roots (1, 62, 63) (Table 3) (Fig. 3). The essential features appear to be, as in the coronal use of CH, a bacteria-killing effect as well as a hard tissue inducing effect, the latter related to the initiation of zones of liquefaction and coagulation necrosis next to the apical vital tissue. This results in the development of hard tissue at the apex (apexification), usually as a cementum-like structure (63–71). The drawback of this hard tissue bridge is that numerous vascular channels, which could lead to bacterial invasion into these channels, perforate it (63). Three large clinical studies have shown an average healing rate of 95% (range 77–98%) (Table 3).

Mineral trioxide aggregate and its capacity to induce hard tissues in immature teeth with pulp necrosis

MTA has been shown to be a very biocompatible material, in fact more biocompatible than Super EBA and IRM (72) (Fig. 4). The success in use of this material

Table 3. Periapical healing following initial treatment with calcium hydroxide and subsequent gutta-percha root filling in teeth with pulp necrosis and immature roots

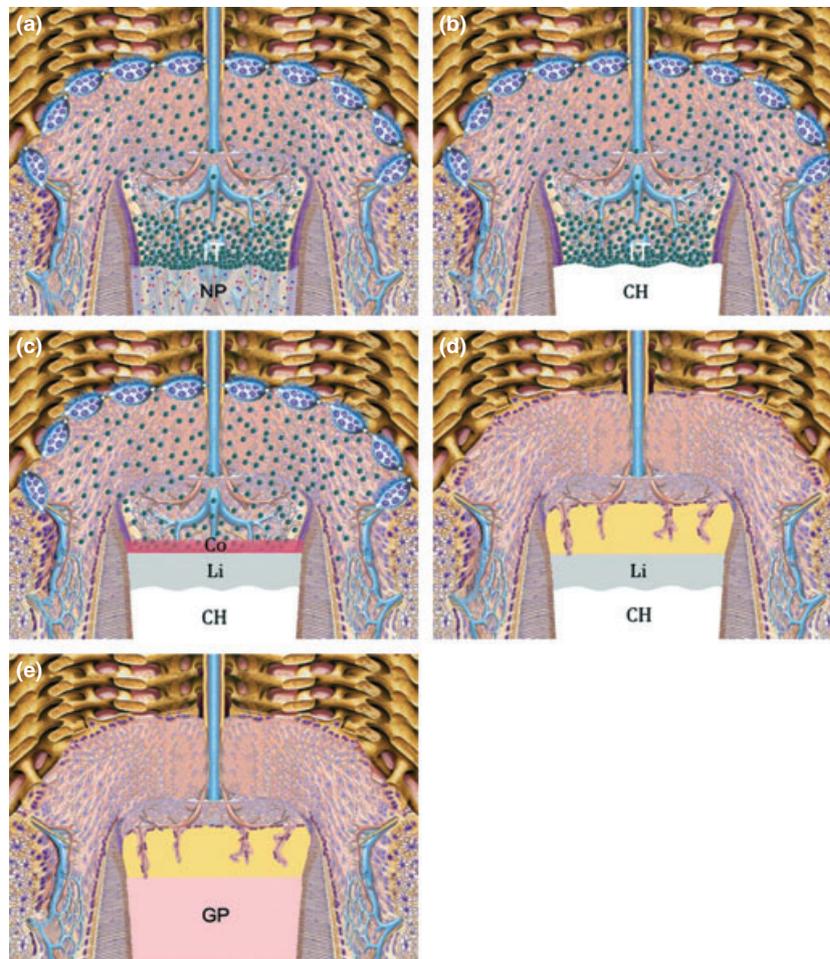| Examiner	No of teeth	Healing (%)
Kerekes et al. (99)	66	62 (94)
Vojinovic (100)	100	98 (98)
Mackie et al. (3)	112	108 (96)
Yates (4)	48	37 (77)
Merglova (101)	33	31 (94)
Cvek (5)	328	314 (96)
Total	687	650 (95)

Fig. 3. Calcium hydroxide induced apexification changes after pulp necrosis. (a) Infected pulp necrosis (NP) plus inflammation (IT) in the apical part of the root canal. (b) Dressing with calcium hydroxide (CH). (c) Because of its high pH effect upon dentin, calcium hydroxide (CH) causes the release of a number of wound healing signals (growth factors), and for some time, the high pH also may prevent bacteria from entering the wound healing site. CH induces by its high pH effect apical liquefaction (Li) and a coagulation zones (Co) of necrosis. (d). The response to the coagulation necrosis appears to be recruitment of new hard tissue forming cells from the apical tissues, these are usually of cementoblastic origin, but may also be osteoblasts. During this process, vascular inclusions may occur. After 6–18 month, a hard tissue barrier is formed. (e) Status after root filling with gutta-percha (GP).

in immature teeth with pulp necrosis is possibly related to two features:

1 The extraordinary cementum and PDL-inducing potential of MTA.

2 The bacteria tight sealing capacity of MTA when placed in the apical part of the root canal.

This combination of a bacteria tight seal in the apical foramen of the root canal and formation of new cementum and PDL makes this technique a very biologically acceptable method for closing a root canal with an open apex (44). In a recent review article, on the mechanism of action of MTA on pulpal and periodontal tissues, the following actions are described: when placed, MTA immediately releases calcium ions activating cell attachment and proliferation, and at the same time, the high pH creates an antibacterial environment. Furthermore, MTA modulates cytokine production and encourages differentiation and migration of hard tissue producing cells whereby hydroxyapatite is formed on the MTA surface, and a biologic seal is created (59).

When MTA is used as an apical plug in cases of pulp necrosis, studies in dogs and monkeys where apical osteitis was induced showed that MTA can form a biologic seal and the MTA becomes covered with cementum and a normal PDL attachment (28, 73–75). Several studies have shown that when used as a root-end filling material MTA demonstrates a good resistance to bacterial penetration as well as to endotoxin (76). In eight *clinical studies*, an average healing rate of 89% was found (range 77–100%) (Table 4).

Based on the available information, one can state that MTA is suitable for induction of an apical hard tissue barrier in immature incompletely developed teeth with pulp necrosis.

Calcium hydroxide and its ability to induce hard tissue in root fractures with coronal pulp necrosis

The methodology was first described by Cvek (77) and consisted of placing CH in the coronal part of the pulp in
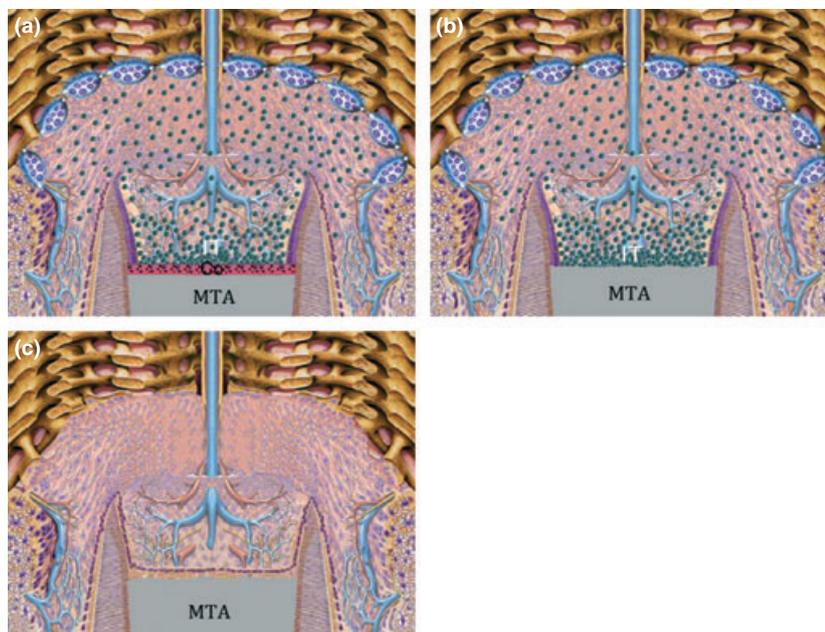
Fig. 4. Mineral trioxide aggregate induced apexification changes after pulp necrosis. (a) Mineral trioxide aggregate (MTA) induces, by its high pH effect upon dentin, a release of wound healing signals (growth factors). Subsequent to this a physical bond between MTA and dentin provides a barrier against bacterial penetration (22, 23, 72, 92, 93). MTA induces by its high pH effect a very narrow zone of coagulation necrosis (Co). Next to that zone, a reparative cementum zone is formed. (c) Subsequently, the hard tissue barrier is associated with formation of normal PDL attachment to the cementum layer. MTA should not be placed directly against an area with inflammatory tissue fluid as the low pH will prevent setting of the MTA. If fluid is present, it makes sense to place CH for a short period of time to 'dry' the area before placing the MTA.

Table 4. Periapical healing following treatment with mineral trioxide aggregate (MTA) in teeth with pulp necrosis and immature roots

Examiner	No of teeth	Healing (%)
El-Meligy and Avery (102, 103)	15	15 (100)
Pradhan et al. (104)	10	10 (100)
Pace et al. (105)	11	10 (91)
Simon et al. (106)	57	46 (81)
Sarris et al. (107)	17	13 (77)
Holden et al. (108)	20	17 (85)
Witherspoon et al. (109)	116	106 (92)
Moore et al. (110)	22	21 (96)
Total	268	238 (89)

root-fractured teeth until a hard tissue bridge was formed at the fracture site. It was later shown in a large clinical study of 68 root fractures to result in healing in 86% of the cases (78). A drawback of this treatment scenario appears to be the relatively long treatment time it takes to induce a hard tissue barrier at the fracture site, typically around 6 months.

Mineral trioxide aggregate and its ability to induce hard tissue in root fractures with coronal pulp necrosis

The use of MTA in root fractures has only been described in a few case reports (79–84). Therefore, it is too early to make a comparison of MTA as an alternative to CH and gutta-percha.

Calcium hydroxide and its effect on external infection-related root resorption

This effect of CH external infection-related root resorption was first described in 1971 by Andreasen (85), and this observation has since been supported by a number of clinical studies demonstrating that CH is able to arrest 98% of infection-related resorptions in luxated teeth and 90% in avulsed and later replanted teeth (85–87). The drawback of this method has been the weakening effect of CH on the dentin, leading to the risk of cervical root fractures (5, 20).

MTA and its effect on external infection-related root resorption

This effect of MTA is not well known. Its use has only been described in a few case reports (88). One experimental study in monkeys shows that MTA used 1 week after intentional replantation could to a large extent prevent infection-related resorption (89). It is still too early to evaluate whether MTA can be considered a predictable replacement for CH in the management of infection-related root resorption.

Conclusion

The studies described may lead one to consider whether the time has come to replace CH with MTA in certain dental trauma situations such as pulp capping, pulpotomy, and apexification. Before reaching a conclusion in that regard, it is necessary to look at the amount of clinical data

related to the long-term outcomes of the two methods. In the case of CH, a number of long-term studies have demonstrated a healing rate of 95% for pulpotomy (Table 1) and 95% for apexification (Table 3). With respect to MTA, there are only a few clinical studies with relatively few subjects for either pulpotomy or apexification (Tables 2 and 4). That underscores that clinical MTA studies should be encouraged, optimally as randomized clinical studies (RCT), comparing CH and MTA. Until then, MTA should be used with the knowledge that it is a new material without a long-term usage background. This is particularly important with respect to its use in teeth with root fractures and coronal pulp necrosis and in teeth with infection-related external root resorption.

Particular problems regarding the use of MTA should be noted. One concern has to do with whether or not MTA exerts the same weakening effect upon dentin as CH. Two *in vitro* studies seem to indicate such a risk as MTA was found to maintain a high pH level in the root canal for many months, and the structural strength of dentin appeared to be weakened (12, 17). On the other hand, Hatibović-Kofman et al. (16) showed that the use of MTA did not seem to weaken dentin over a 3-month to 1-year period. Both additional *in vitro* and *in vivo* studies should be performed to determine whether such a risk is actually present.

Another problem has been an apparent staining effect of MTA when used for pulp capping, pulpotomy, and apexification in anterior teeth (59). That question needs to be addressed as MTA is increasingly being used for anterior tooth pulpotomies. The frequency and severity of this effect is presently unknown.

It may be concluded from this review that MTA appears to be a promising successor to CH for a variety of pulpal and periodontal healing complications after trauma. There is, however, presently a definitive lack of long-term clinical studies to demonstrate the safety and effectiveness of this new procedure. Randomized clinical studies need to be carried out to compare CH and MTA in the treatment of pulp and periodontal healing complications after trauma.

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