Review article:

Mineral Trioxide Aggregate (MTA) and its application in Pediatric Dentistry: A review

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Abstract:
Background: The retention of pulpally involved deciduous teeth in a healthy state until the time of normal exfoliation and treatment of traumatized young permanent teeth remains to be of prime importance as far as pediatric dentistry is concerned. Several materials which have been popular pulpotomy medicaments are being used like formocresol, ferric sulphate, etc. Also materials like calcium hydroxide are extensively being used for apexogenesis and apexification procedures. Concerns have been raised about the toxicity and potential carcinogenicity of these materials, and alternatives have been proposed to maintain the partial pulp vitality, however no material has been accepted as an ideal agent for such procedures till date. Mineral trioxide aggregate (MTA) is a biocompatible material which provides a biological seal. MTA can preserve the pulpal vitality and promote regeneration of pulpal tissue. MTA has been proposed as a potential medicament for various pulpal procedures like pulp capping with reversible pulpitis, apexification, repair of root perforations and more recently as a pulpotomy agent.

Aims and objectives: This paper presents a narrative review of the present literature of MTA, with particular reference to be used as a healing agent in primary and young permanent teeth. This paper also reviews the literature on the constituents and biocompatibility of Mineral Trioxide Aggregate (MTA) in terms of periradicular and pulpal responses.

Conclusion: Collectively, all the studies related to MTA have shown that MTA is biocompatible. However, there has been a lack of knowledge and understanding about the constituents of the material and its interaction with the surrounding tissues. Recent studies on the material constituents have clarified that MTA is silicate cement rather than an oxide mixture.

Introduction:
Mineral trioxide aggregate (MTA) was developed at Loma Linda University in the 1990s primarily as a root-end filling material. It received acceptance by the US Federal Drug Administration and became commercially available as ProRoot MTA (Tulsa Dental Products, Tulsa, OK, USA). Until recently, two commercial forms of MTA have been available (ProRoot MTA) in either the grey or white forms. Recently MTA-Angelus (Angelus Soluç¸o˜es Odontolo´gicas, Londrina, Brazil) has become available. The use of MTA as a root-end filling material was identified because the material is hydrophilic cement that sets in the presence of water. Much work has been published on the biocompatibility of this material, but relatively little on its constituents. A literature review was thus undertaken to know its constituents and biocompatibility.

In a short time, MTA gained numerous clinical applications in endodontic procedures and was recommended for direct pulp protection in primary as well as permanent teeth. MTA demonstrated remarkable success compared with calcium...
hydroxide. MTA is formulated to have physical properties (1), setting requirements (2) and characteristics necessary for an ideal repair and medicament materials (3-5). MTA with an excellent long term prognosis, relative ease at which it can be used and with its numerous clinical applications promises to be one of the most versatile materials in the field of dentistry. MTA is a potential medicament for pulpotomy procedures as well as capping of pulps with reversible pulpitis (4-7).

Constituents:
MTA consists of 50–75% calcium oxide and 15–25% silicon dioxide. These two components together comprise 70–95% of the cement. When these raw materials are blended they produce tricalcium silicate, dicalcium silicate, tricalcium aluminate and tetracalcium aluminoferrite. On addition of water the cement hydrates to form silicate hydrate gel. MTA is a Type 1 ordinary Portland cement (American Society for Testing Materials), with a fineness in the range of 4500–4600 cm² g. A radiopacifier (bismuth oxide) is added to the cement for dental radiologic diagnosis (Torabinejad & White 1995) (8). Although MTA is essentially ordinary Portland cement, few studies have been conducted on the comparative constituents of Portland cement and MTA.

The first research paper on the chemistry of Portland cement that had potential for dental use demonstrating the similarity of grey MTA to Portland cement was published in 2000 (Estrela et al. 2000) (9). A study comparing white MTA (White MTA, Dentsply; Tulsa Dental Products) to white Portland cement showed the cements to have similar constituent elements except for the bismuth oxide in the MTA (Asgary et al. 2004) (10). Investigations of the chemical and physical, surface and bulk material properties of Portland cement and MTA have shown that MTA had less gypsum. Decreased gypsum causes a reduction in setting time of the cement (Lea 1998) (11). Other findings included a higher level of toxic heavy metals and aluminium in Portland cement. Portland cement exhibited a wide range of sizes whereas MTA showed a uniform and smaller particle size. Thus, MTA cannot be substituted by a cheaper Portland cement (Dammaschke et al. 2005) (12). Both MTA (Pro- Root) and Portland cement (Quikrete, Columbus, OH, USA) had similar physical, chemical and biological properties, and the biocompatibility of both materials was due to the similarity in constituents (Saidon et al. 2003) (13). The production of calcium hydroxide as a byproduct of the hydration reaction of MTA has been published (Camilleri et al. 2005a) (14). The biological response to MTA has been linked to that of calcium hydroxide and it was postulated that the mechanisms of action were similar. It has been reported that MTA (MTA Angelus), released calcium ions and promoted an alkaline pH (Duarte et al. 2003) (15). The physicochemical basis for the biological properties of MTA (ProRoot), had recently been attributed to the production of hydroxyapatite when the calcium ions released by the MTA came into contact with tissue fluid (Sarkar et al. 2005) (16). Although the release of calcium ions has been reported, none of the publications demonstrated the origin of the calcium ions. On hydration, both MTA and Portland cement would produce calcium silicate hydrate gel and calcium hydroxide. This would explain the similar mode of tissue reaction to MTA and calcium hydroxide.

Two forms of MTA (Dentsply) are commercially available in the market, grey and white. The difference between them has been reported to be in the concentrations of aluminium, magnesium and...
iron compounds. The white MTA lacks the aluminoferrite phase that imparts the grey color to grey MTA.

Biocompatibility:
The biocompatibility of MTA has been investigated in a number of ways, using cell expression and growth, and direct contact with dental tissues (periapical and pulpal) in vivo.

Cytological investigation of biocompatibility:
Most of the cell studies showed good cell growth over MTA with the formation of a cell monolayer over the material. Cell studies test the cytotoxicity in vitro but cannot examine the complex interactions between materials and host. Contact time was generally less than 7 days. Only one study evaluated biocompatibility of MTA 28 days following its setting. The most commonly used method for evaluation of cell proliferation was scanning electron microscopy (SEM) followed by enzyme assay. Calcium hydroxide which is a by-product of calcium silicate hydration reacted with phosphate-buffered solutions producing calcium phosphate crystals over the material surface.

Few studies have been published on the material extracts of MTA and this may reflect an incomplete understanding of the chemical constitution of the material. As MTA is calcium silicate cement, its biocompatibility may be questioned due to the presence of silicate ions. The observed biocompatibility of MTA could arise from reaction by-products. Good cell growth was demonstrated on material extracts when tested using methyltetrazolium (MTT) assay (Keiser et al. 2000)\(^{(17)}\).

MTA induced expression of inflammatory cytokines from bone cells and exhibited good cell attachment. MTA (ProRoot) caused an increase in IL-4 and IL-10 expression. Increase in IL-6 and IL-8, with no increase in levels of IL-1a and IL-1b was demonstrated in the presence of MTA (Loma Linda University). Conversely, Koh et al. (1997, 1998)\(^{(18)}\) showed a rise of both IL-1a and IL-1b together with IL-6 after the cells were in contact with the material for 6 days. Osteocalcin levels were also increased in the presence of MTA (ProRoot; Thomson et al. 2003)\(^{(19)}\). There was a negligible increase in levels of cytokines with the other materials used as controls. MTA (ProRoot) also preferentially induced alkaline phosphatase expression and activity in both periodontal ligament and gingival fibroblasts (Bonson et al. 2004)\(^{(20)}\). In short, it can be said that MTA elicited an inflammatory cytokine response in order to promote healing.

Periradicular tissue reactions:
When MTA has been used as a root-end filling material in vivo, less periradicular inflammation was reported compared with amalgam (Torabinejad et al. 1995d)\(^{(21)}\). In addition, the presence of cementum on the surface of MTA was a frequent finding. It induced apical hard tissue formation with significantly greater consistency, but not quantity, in a study of three materials, although the degree of inflammation was not significantly different between the groups (Shabahang et al. 1999)\(^{(22)}\). Again, MTA (ProRoot) supported almost complete regeneration of the periradicular periodontium when used as a root-end filling material on non-infected teeth. Early tissue healing events after MTA root-end filling were characterized by hard tissue formation, activated progressively from the peripheral root walls along the MTA–soft tissue interface (Economides et al. 2003)\(^{(23)}\). Both fresh and set MTA (ProRoot) caused cementum deposition at the root-end when used after apical surgery (Apaydin et al. 2004)\(^{(24)}\).
Pulpal reactions:
MTA used for pulp capping or partial pulpotomy stimulates reparative dentine formation. MTA-capped pulps showed complete bridge formation with no signs of inflammation (Pitt Ford et al. 1996, Faraco & Holland 2004)\(^{25, 26}\). The same results were obtained when MTA was placed over pulp stumps following pulpotomy (Holland et al. 2001b)\(^{27}\). The incidence of dentine bridge formation was shown to be higher with MTA than with calcium hydroxide. Clinical use of MTA has demonstrated their applicability in wet environments, preventing bacterial microleakage and alkalinizing the medium. On account of the predominant presence of calcium oxide in its formula (Camilleri & Pitt Ford 2006)\(^{28}\), its biological properties show similarity to those of calcium hydroxide, making it useful for tissue healing. However, little evidence is available on the bonding of composites and other materials to MTA.

White MTA was introduced as a low-iron, non-staining formula. Despite this, in case of inflammatory internal root resorption, the cement discoloured the tooth perhaps as a result of oxidation of iron in the product formulation: tetracalcium aluminoferrite (Camilleri & Pitt Ford 2006)\(^{28}\). This has not been reported before and warrants further investigation.

Conclusion:
It can be concluded that many studies have shown that MTA is biocompatible. However, there has been a lack of knowledge and understanding regarding the constituents of the material and its interaction with the surrounding tissues. Recent studies on the material constituents have clarified that MTA is silicate cement rather than an oxide mixture. Hence further studies regarding its composition and biocompatibility are required to be carried out.

References: