MTAD in endodontics: an update review

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The major objective in endodontic therapy is to achieve complete chemomechanical debridement of the entire root canal system. This can be accomplished with biomechanical instrumentation and chemical irrigation. Various endodontic irrigants, such as sodium hypochlorite, chlorhexidine, and iodine potassium iodide, are available, each having its own advantages with some limitations. MTAD, a new endodontic irrigant, has been introduced to fulfill these limitations. MTAD is a mixture of doxycycline, citric acid, and a detergent (Tween 80). Since its introduction, it is a material that has been researched extensively for its properties. This article presents a review on the numerous properties of MTAD, such as antimicrobial activity, smear layer- and pulp-dissolving capability, effect on dentin and adhesion, and biocompatibility. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:e70-e76)

The purpose of endodontic treatment is to achieve thorough debridement of root canals. Microorganisms considered to be responsible for all pulpal and periapical pathology are present not only in the root canals but also invade the dentinal tubules up to varying depths. Irregularities in canal systems, narrow isthmis, and apical deltas prevent complete debridement by mechanical instrumentation alone. Thus, chemical disinfection through irrigation becomes a critical adjunct. For clinical usage, an ideal irrigant should have certain properties, such as ability to flush out loose debris, to lubricate the dentinal walls, to dissolve organic matter in the canal, and to have antimicrobial effects.

A wide range of irrigating solutions is available for endodontic use, such as NaOCl, EDTA, chlorhexidine (CHX), and iodine potassium iodide (IKI). However, none of these irrigants is able to meet all the ideal requirements, with each having its own advantages and disadvantages. Varying concentrations of NaOCl have been in use for many decades. The main advantages of NaOCl are (1) its ability to dissolve necrotic tissues, (2) its antibacterial properties against most microorganisms, and (3) its ability to disrupt biofilms associated with most microorganisms. The disadvantages of NaOCl are its unpleasant taste, high toxicity, and inability to remove smear layer when used alone. EDTA chelates with calcium and removes the mineralized portion of the smear layer, but has to be used with a proteolytic agent (NaOCl) to remove the organic component. EDTA itself does not possess disinfecting ability and also has been shown to inactivate chlorine, the active agent in NaOCl. CHX is reported to have good antibacterial properties but does not possess tissue-dissolving capabilities. IKI has a wide antibacterial spectrum but has the disadvantage of possibly producing an allergic reaction in some patients.

Considering these limitations, a new irrigant was introduced that could fulfill all the ideal requirements. Since its introduction, MTAD (a mixture of doxycycline, citric acid, and a detergent [Tween 80]; Dentsply, Tulsa, OK) has been the focus of attention as an alternative root canal irrigant. MTAD, introduced by Torabinejad and Johnson at the Loma Linda University in 2003, is an aqueous solution of 3% doxycycline, a broad-spectrum antibiotic; 4.25% citric acid, a demineralizing agent; and 0.5% polysorbate 80 detergent (Tween 80). In this product, doxycycline hyclate is used instead of its free-base doxycycline monohydrate, to increase the water solubility. It is commercially available as a 2-part mixture (Biopure MTAD; Dentsply). It is considered to be clinically effective and a biocompatible endodontic irrigant. This article discusses various parameters of this root canal irrigant.

REVIEW OF LITERATURE

Antimicrobial efficacy

Investigations have confirmed the importance of microorganisms in the pathogenesis of pulpal and periapical diseases. Other investigations have reported a...
significantly higher success rate of root canal treated teeth with negative bacterial cultures at the time of obturation to those that had positive cultures.24–26 *Enterococcus faecalis*, primarily a facultative gram-positive anaerobe, is predominantly associated with persistent periapical infections in endodontically treated teeth and is extremely resistant to current treatment modalities.26–28 MTAD must have the capability to eradicate even the most resistant microorganisms to be considered effective.

Earlier in vitro research on MTAD proved its antimicrobial efficacy over conventional irrigants.29–33 In an in vitro study by Torabinejad et al.,29 MTAD was effective in killing *E. faecalis* up to 200× dilution; NaOCl ceased to exert its antibacterial activity beyond 32× dilution, whereas EDTA did not exhibit any antibacterial activity. Only MTAD was able to kill *E. faecalis* after an exposure of 2 or 5 minutes. Portenier et al.30 found that full concentration (100%) of MTAD and 0.2% CHX rapidly killed both strains of *E. faecalis* and the presence of dentine or bovine serum albumin caused a marked delay in killing by both medicaments. Shabahang and Torabinejad31 showed that the combination of 1.3% NaOCl as a root canal irrigant and MTAD as a final rinse was significantly more effective against *E. faecalis* than the other regimens. Newberry et al.32 showed that MTAD in conjunction with 1.3% NaOCl was effective in completely eliminating growth in 7 of 8 strains of *E. faecalis*. The minimum inhibitory concentration/minimum lethal concentration (MIC/MLC) tests showed that MTAD inhibited most strains of *E. faecalis* growth when diluted 1:8192 times and killed most strains of *E. faecalis* when diluted 1:512 times. Similar to these results, Davis et al.33 found that MTAD showed significantly more zones of microbial inhibition for *E. faecalis* than NaOCl, CHX, and Dermacyn (a superoxidized water; Oculus Innovative Sciences, Petaluma, CA).

In contrast to the previously mentioned studies, later research displayed less than optimal antimicrobial activity of MTAD.34–37 Kho and Baumgartner34 demonstrated no difference in antimicrobial efficacy for irrigation with 5.25% NaOCl/15% EDTA versus irrigation with 1.3% NaOCl/MTAD in the apical 5 mm of roots infected with *E. faecalis*. Dunavant et al.35 found that 6% and 1% NaOCl were significantly more efficient in eliminating *E. faecalis* biofilms than other irrigants such as 2% CHX, MTAD, and commercial preparations of EDTA (REDTA; Roths International Ltd., Chicago, IL, and Smear Clear; SybronEndo, Orange, CA). A study by Baumgartner et al.36 found no growth of *E. faecalis* in root canals irrigated with 5.25% NaOCl/15% EDTA, whereas 50% of the canals irrigated with 1.3% NaOCl/MTAD demonstrated growth of *E. faecalis*. Giardino et al.37 compared the antimicrobial efficacy of 5.25% NaOCl, MTAD, and Tetraclean (a mixture of doxycycline hyclate, an acid, and detergent; Ogna Laboratori Farmaceutici, Milano, Italy) against *E. faecalis* biofilm and found that only 5.25% NaOCl could disgregate and remove the biofilm each time; treatment with Tetraclean caused a higher degree of biofilm disgregation in each considered time interval as compared with MTAD.

On comparing the antifungal activity of the 3 irrigant solutions, Mohammadi38 found greater substantivity of MTAD over 1.3% NaOCl and 2% CHX. The antifungal substantivity of MTAD was retained in root canal dentin for at least 28 days. Ruff et al.39 showed that 6% NaOCl and 2% CHX were equally effective and superior to MTAD and 17% EDTA with regard to antifungal activity.

**Smear layer removal and tissue-dissolving action of MTAD**

The smear layer, first described in endodontics by McComb and Smith,9 is a thin layer that occludes the orifices of the dentinal tubules. It contains inorganic and organic substances that include fragments of odontoblastic processes, microorganisms, and necrotic materials.40 The smear layer itself may be infected and also may protect bacteria already present in the dentinal tubules from the action of an antimicrobial agent.9,41,42 Its removal from infected root canals allows deeper penetration of intracanal medications into the dentinal tubules for more effective disinfection of the root canal system.43

The effect of MTAD on smear layer has been evaluated in various studies.44–49 Use of MTAD has been reported to be more efficient in removing smear layer as compared with the use of EDTA and NaOCl, especially from the apical third.44–46 Torabinejad et al.44 showed that MTAD effectively removed smear layer and did not significantly change the structure of the dentinal tubules when used after NaOCl (5.25%) as compared with irrigation with EDTA and 5.25% NaOCl. Park et al.47 evaluated the effect of smear-layer removal using MTAD on coronal leakage of obturated root canals and found that teeth treated with MTAD yielded significantly less leakage than samples treated with NaOCl. Although the teeth treated with EDTA showed more coronal leakage compared with those treated with MTAD, the difference was not significant. Ghoddusi et al.48 found no difference in bacterial leakage in teeth when smear layer was removed either by MTAD or EDTA. In a recent investigation, De-Deus et al.49 reported significantly faster dissolution of inorganic material by both 5% citric acid and MTAD as compared with 17% EDTA.
Another aspect of effective irrigation is the dissolution of remaining pulp tissue. Beltz et al. found 5.25% and 2.60% NaOCl to be effective pulp solubilizers. EDTA was capable of solubilizing both organic and inorganic material in dentin and organic material in pulp. It could dissolve more than 70% of the dentin and more than 51% of the pulp. In this study, MTAD showed similar properties to EDTA.

**Effect of MTAD on bond strength to enamel and dentin**

The creation of a reliable endodontic-restorative continuum is one of the significant factors that determines the overall success of endodontic treatment. Some authors indicated that irrigants may have the capacity to change the structure of dentin and subsequently the bonding procedures. CHX has been reported to significantly increase the bond strength, whereas NaOCl, H2O2, and their combination adversely affect the tensile bond strength to superficial dentin. EDTA was capable of solubilizing both organic and inorganic material in dentin and organic material in pulp. It could dissolve more than 70% of the dentin and more than 51% of the pulp. In this study, MTAD showed similar properties to EDTA.

**Biocompatibility of MTAD**

The materials that are used for endodontic treatment are often placed in intimate contact with the periapical tissues. Therefore, it is essential that the root canal irrigant should be nontoxic and biocompatible with its surrounding host tissues.

As stated earlier, MTAD has been found to be less cytotoxic and more biocompatible than other irrigant solutions. In an in vivo study, Torabinejad et al. reported that the clinical protocol for removal of smear layer and disinfection of the root canal system using 1.3% NaOCl and MTAD does not result in an increased incidence of postoperative pain as compared with 5.25% NaOCl and 17% EDTA.

Pulp regenerative techniques hold the future for endodontics. To accomplish regenerative endodontic therapy, it is necessary to stimulate dental pulp stem cells (DPSC) for attachment to the root canal dentin after treatment. In a recent study by Ring et al., the cytotoxicity of NaOCl/MTAD was found to be slightly less than NaOCl and NaOCl/EDTA, indicating that MTAD is more biocompatible than NaOCl. Although the highest average numbers of DPSCs attached to the root canal were seen after irrigation with AquatineEC (Sterilox, Puricore, Malvern, PA), a product with hypochlorous acid as the active ingredient, and EDTA, and the lowest average number of cells attached to dentin were seen after irrigation with NaOCl and MTAD, still some cells remained viable after treatment with MTAD that could have a potential role in regenerative therapy.

**DISCUSSION**

The preceding discussion puts light on different aspects of MTAD as an endodontic irrigant. MTAD was expected to fulfill the requirements of an ideal irrigant, one requirement being the antimicrobial property. The exact antimicrobial action of MTAD has not been fully understood. Doxycycline, being a bacteriostatic antibiotic, does not kill bacteria; it prevents the multiplication of susceptible bacteria. The bacteriostatic property may be advantageous because in the absence of bacterial cell lysis, antigenic by-products (endotoxins) are not released. We speculate that these residual bacteria may resume growth when appropriate conditions are restored and cause reinfection. But doxycycline has substantive to dentin that can provide prolonged antibacterial effect. The antimicrobial action of citric acid is not known. Tween 80 is known to increase the antibacterial effect of various substances, but in itself might have some antibacterial activity.

The initial studies conducted on MTAD showed good antimicrobial activity against E. faecalis, but later studies that tried to simulate clinical conditions showed a lesser antimicrobial effect of MTAD. The lesser antimicrobial activity of MTAD in the study by Dunavant et al. could be because of the difference in the study model. In their study, the microorganisms were grown as a biofilm, whereas Torabinejad et al.
used planktonic bacteria and showed greater antimicrobial action for MTAD. In the study by Baumgartner et al., the lesser antibacterial effect of MTAD as compared with the study by Shabahang and Torabinejad could be because of the difference in methodology and microbial sampling procedures. Baumgartner et al. evaluated the samples immediately after debridement, whereas Shabahang and Torabinejad assessed turbidity in growth media after 1-week incubation. Also, Shabahang and Torabinejad soaked the entire tooth in the test irrigant for 5 minutes after debridement, whereas Baumgartner et al. excluded this step to simulate clinical settings.

The antimicrobial action of MTAD is believed to be because of the presence of doxycycline. However, the results of the study by Giardino et al. were surprising, as MTAD contains 3 times the concentration of doxycycline as compared with Tetraclean, but showed lower efficacy in removing bacterial biofilm as opposed to Tetraclean.

Regarding the removal of the smear layer, Barkhordar et al. and Haznedarooglu and Ersev recommended the use of tetracycline HCl on instrumented canals and root-end cavity preparations. It has a low pH and acts as a calcium chelator and causes enamel and root surface demineralization. Its surface demineralization of dentin is comparable to that seen using citric acid. MTAD can also be expected to remove smear layer, as it contains both doxycycline and citric acid. Because of the low surface tension of MTAD (34.5 mJ/m²), the intimate contact of irrigant solutions with the dentinal walls might increase, which may permit deeper penetration for effective smear layer removal and thereby disinfection.

Investigations have reported the good smear layer removal capability of MTAD, especially in the apical third, and lesser amount of dentinal erosions as compared with EDTA. The occurrence of dentinal erosions can be harmful when they are located on the apical third, especially in teeth with cemental and dentinal erosions. The erosion promoted by the irrigant can reach external resorption areas. The erosion can reduce the dentin microhardness, consequently causing root fragility. Machnick et al. reported no significant difference in flexural strength and modulus of elasticity of dentin when exposed to saline or MTAD.

Park et al. revealed that the teeth treated with EDTA showed more coronal leakage compared with those treated with MTAD. This might have been because of the dentinal erosion caused by EDTA. The reduced amount of leakage in absence of smear layer with MTAD was attributed to improved mechanical locking of the sealer into dentinal tubules and better adhesion of sealers into canal walls. In this regard, the lesser amount of dentinal erosions caused by MTAD seems to favor its use as an irrigant.

The only investigation showing reduced smear layer removal from the apical third by MTAD, in contrast to the results of Torabinejad et al., could be because of the use of 1 mL of the final irrigant for 1 minute, whereas Torabinejad et al. followed the manufacturer’s instruction using a total of 5 mL of the testing solution (1 mL for 5 minutes and then a flush with 4 mL).

MTAD has been reported to solubilize pulp tissue. It was found to have a pulp dissolution property similar to that of EDTA.

Regarding the effect of MTAD on adhesive procedures, Sayın et al. showed that MTAD extracted the least amount of Ca²⁺ at 5 minutes. This may favor the usage of MTAD, as the presence of calcium plays an important role in the binding of adhesives. However, the results of the study by Yurdaguven et al. do not support this theory because MTAD caused a significant decrease in the bond strength in the self-etch adhesive group. According to Yurdaguven et al., MTAD caused a significant decrease in the bond strength in the self-etch adhesive group. According to Yurdaguven et al., MTAD caused a significant decrease in the bond strength in the self-etch adhesive group. According to Yurdaguven et al., MTAD could be regarded as a positive sign from a clinical point of view because smear layer removal is faster and efficient. Also revealed by this investigation was the full saturation of the demineralizing ability of MTAD after 30 seconds. This self-limiting activity might produce lesser erosive effects on dentin.

In the study by De-Deus et al., the greater bond strength values of etidronate were attributed to its lower chelating ability, which could provide larger intertubular dentin area for hybridization. Use of 17% EDTA and MTAD solutions displayed intermediate values, which could have been because of the greater depths of dentin demineralization causing collapse of the collagen network, which did not allow effective adhesive infiltration.

It has been suggested that teeth endodontically treated with the MTAD protocol for clinical use may not need any additional conditioning before the application of a dentin adhesive.

The biocompatibility of MTAD has been found to be better than other conventional irrigants. However, in spite of good biocompatibility, MTAD revealed the least number of viable dental pulp cells attached to
the root canal wall that could have a role in pulpal regeneration.\textsuperscript{61} This suggests that, at present, MTAD cannot be considered as the irrigant of choice in pulp revascularization techniques, especially when there are reports of successful pulpal revascularization with much less expensive and more easily available irrigants like NaOCl.\textsuperscript{76}

As per the manufacturer’s recommendations, MTAD being a 2-part mix needs to be freshly prepared just before its use. Once mixed, it has a shelf life of about 48 hours, which is shorter than other irrigants.\textsuperscript{77,78}

The points that favor the use of MTAD as an irrigant as opposed to other solutions can be summarized as follows:

- reasonable antimicrobial property
- better smear layer removal
- lesser adverse effects on dentinal structure
- better at promoting adhesion to dentin
- good biocompatibility

The shortcomings can be listed as follows:

- less than optimal antimicrobial activity
- lesser compatibility to dental pulp cells for revascularization procedures
- high cost
- reduced shelf life

CONCLUSIONS

The discussion for the use of MTAD as an irrigant can be summarized as follows.

1. Bench-top studies have proved the efficacy of MTAD as an effective antimicrobial agent, but the studies that simulated clinical settings demonstrated lesser antibacterial ability. Thus, it can be concluded that MTAD has less than optimal antimicrobial efficacy.

2. MTAD represents an effective solution for removal of the smear layer from instrumented root canals when used along with NaOCl. Its use also seems advantageous considering its ability to dissolve pulpal tissue.

3. MTAD favors adhesive restorative procedures.

4. MTAD is biocompatible and does not adversely affect the physical properties of the tooth.

It can be concluded that MTAD is a promising irrigating solution but still further clinical studies are required to establish MTAD as an ideal irrigant.

REFERENCES


23. Möller AJ, Fabricius L, Dahlen G, Ohman AE, Heyden G. Influence on periapical tissues of indigenous oral bacteria and


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