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Review Article

Mixture tetracycline citric acid and detergent – A root canal irrigant. A review

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ARTICLE INFO

Article history:

Received 16 May 2012

Accepted 9 September 2012

Keywords:

MTAD

Sodium hypochlorite (NaOCl)

Ethylene diamine tetra acetic acid (EDTA)

Hydrogen peroxide

Root/intra canal irrigants

ABSTRACT

Background: Root canal irrigants play an indispensable role for the complete disinfection of the root canal system, in particular those areas of the root canal that are not accessible for instrumentation. Sodium hypochlorite, ethylene diamine tetra acetic acid, hydrogen peroxide and chlorhexidine are the most commonly used root canal irrigants in endodontic practice, but they do not satisfy all the properties of an ideal root canal irrigant. Mixture tetracycline, citric acid and detergent, a root canal irrigant, is commercially available as BioPure MTAD (Dentsply, Tulsa Dental, Tulsa, OK).

Methodology: The literature was searched for root canal irrigants used in the last 3 decades in PubMed. Data showed 83 relevant articles, of which 24 were found most suitable on the basis of description of properties, advantages and disadvantages of MTAD, hence were included. The aim of this study was to evaluate the properties of MTAD for its antibacterial efficiency, biocompatibility, chelating action with removal of endodontic smear layer and compare it with other commonly used root canal irrigants like sodium hypochlorite, ethylene diamine tetra acetic acid, hydrogen peroxide, chlorhexidine.

Results: MTAD was found to be highly effective intracanal irrigant compared to other commonly used root canal irrigants with excellent disinfection of the entire root canal system.

Conclusion: MTAD is biocompatible with superior antimicrobial efficiency compared to other commonly used root canal irrigants.

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1. Introduction

Root canal system becomes a privileged site for microorganisms and its by-products.¹ As the irregularities in the root

canal systems, narrow isthmi and apical deltas prevent complete debridement by mechanical instrumentation alone. Thus chemical disinfection through irrigation becomes a critical adjunct.²

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<http://dx.doi.org/10.1016/j.jobcr.2012.09.001>

A root canal irrigant needs to have certain properties like antibacterial activity, ability to dissolve organic tissues, smear layer removal, should be non-toxic to the periapical tissues, biocompatible and should aid for complete debridement of the root canal system.³

2. Materials and methods

The key words searched were MTAD composition (6 articles), MTAD manipulation (5 articles), MTAD antibacterial efficiency (38 articles), MTAD ability to remove smear layer (14 articles) and MTAD biocompatibility (20 articles).

3. Composition of MTAD⁴

BioPure MTAD is commercially available as powder–liquid system.

Part A is liquid supplied in syringes (single dose, 5 ml and multiple dose, 20 ml). The liquid contains 4.25% citric acid and 0.5% polysorbate 80 detergent (Tween 80). Antimicrobial action of citric acid is not known, but it helps in the removal of smear layer. Tween 80 is known to decrease the surface tension and increase the antimicrobial effect of various root canal irrigants.⁴

Part B is powder supplied in bottles (single dose, 150 mg and multiple dose, 600 mg). It contains 3% doxycycline hyclate. Being a bacteriostatic antibiotic, does not kill bacteria but prevents multiplication of many susceptible bacteria. The bacteriostatic property is advantageous as in the absence of bacterial cell lysis, antigenic by-products (endotoxins) are not released.⁴ Single doses are used in teeth with single canal and multiple doses are used in teeth with multiple canals. BioPure MTAD is highly effective as an intracanal irrigant only when used in full dosage that is 5 ml per root canal.⁴

4. Manipulation of MTAD⁴

Depending upon the number of root canals to be irrigated with BioPure MTAD single or multiple doses should be selected. The nozzles of the syringe containing liquid and the bottle containing powder are snugly fit. Slowly and steadily the entire liquid from the syringe should be injected into the bottle containing powder. With the syringe still attached to the bottle, gently shake the combination back and forth upto 60 s for the complete assimilation of powder and liquid.

Never vigorously shake the combination as it may cause bubble formation which may hinder the BioPure MTAD to reach into the entire root canal space.

Now withdraw the mixed component from the bottle into the syringe slowly. And if we notice any powder particles suspended in the liquid, then the solution is injected back into the bottle and is shaken gently back and forth for 30 s until the entire powder particles gets completely dissolved in the liquid and now the final solution which is obtained appears yellowish in colour.

Now the syringe is separated from the bottle and a 28 gauge needle with side vented bore which comes along with BioPure

MTAD is fixed to the nozzle of the syringe. The solution should be passively injected into the canal space depositing upto 1 ml of the BioPure MTAD close to the apex. Now agitate the solution with a no:15 k-file for 5 min after which the entire solution is suctioned out followed by irrigating the canal space with the remaining 4 ml of the BioPure MTAD for 5 min.

5. Mechanism of action of MTAD

The pH of BioPure MTAD is 2.15,⁵ so it contributes to its role as a calcium chelator, thereby causing enamel and root surface demineralization. The extent of dentin surface demineralization is comparable to that of citric acid, and it mainly removes the inorganic substances.^{6,7}

BioPure MTAD contains citric acid and Tween 80. Citric acid is a crystalline organic acid, antibacterial and helps in removal of smear layer in concentration of 10% and 25%, thus helping deeper penetration of doxycycline into the dentinal tubules and exerting its antibacterial action.⁸ Tween 80 (polyoxyethylene sorbitan monooleate) is a detergent present in MTAD and is a non-ionic surfactant. It helps in reducing the surface tension of distilled water, NaOCl, EDTA, thereby enhancing the flow and penetration of irrigating solutions deeper into the dentinal tubules and thus completely disinfecting the canal spaces. It has a pH of 7.0 and is a biologically acceptable material.^{9–11}

BioPure MTAD also contains doxycycline hyclate in powder form¹² and is a broad spectrum antibiotic effective against wide range of microorganisms. It is an isomer of tetracycline, a variation in structure but not in its composition. Tetracyclines act by inhibiting protein synthesis and reversibly binding to the 30s ribosomal subunits of susceptible microorganisms.

6. Antibacterial efficiency of MTAD

BioPure MTAD contains tetracycline which is bacteriostatic, as they prevent the growth of microorganisms. This property is advantageous as in the absence of bacterial cell lysis, antigenic by-products (endotoxins) are not released. Tetracycline also shows the property of substantivity as it can be absorbed and gradually released from tooth structures such as cementum and dentin, also shows anticollagenase activity.

Tay and Hiraishi⁴ demonstrated use of 1.3% NaOCl as an initial rinse followed by MTAD as final rinse, resulting in 30% reduction of the antimicrobial substantivity of MTAD. However, erosion of dentinal tubules was less when compared to that when MTAD was used as an initial rinse.

SEM (Scanning Electron Microscopic) examination of surfaces of the root canals treated first with MTAD followed by the use of various concentrations of NaOCl as final rinse, showed the presence of severe erosion of the dentinal tubules at all the levels of root canals. But it shows best antibacterial efficiency on *Enterococcus faecalis*.

Torabinejad et al¹³ studied the antimicrobial efficiency of MTAD by *in vitro* investigation to test its ability to kill *E. faecalis* and compare its efficacy to that of 2.5% NaOCl and ethylene diamine tetra acetic acid (EDTA). The zones of inhibition and

minimum inhibitory concentrations were measured for these root canal irrigants. EDTA demonstrated no antibacterial effects against *E. faecalis*, NaOCl and MTAD proved to be antibacterial to varying degrees. NaOCl continued to exert its efficacy up to 32× dilutions. On the other hand, MTAD was effective in killing *E. faecalis* up to 200× dilutions.

Although a 2 or 5 min exposure of *E. faecalis* to undiluted or 1:2 dilution of 2.5% NaOCl did not result in total killing of bacteria, exposure of the same bacterial species to undiluted or 1:2 diluted MTAD resulted in a completely negative culture after 2 and 5 min of exposure. The results showed that MTAD possessed superior antibacterial activity compared to 2.5% or 5% NaOCl or EDTA when tested against *E. faecalis*.

Newberry 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 tests showed that MTAD killed most strains of *E. faecalis* growth when diluted 1:512 times.¹⁴ Davis found MTAD to show significantly more zones of microbial inhibition of *E. faecalis* than NaOCl and chlorhexidine.¹⁵ Dunavant found that 6% and 1% NaOCl were significantly more efficient in eliminating *E. faecalis* biofilms than other irrigants such as 2% CHX, MTAD and EDTA.¹⁶ Baumgartner found no growth of *E. faecalis* in root canals irrigated with 5.25% NaOCl and 15% EDTA, where as 50% of the root canals irrigated with 1.3% NaOCl and MTAD demonstrated growth of *E. faecalis*.¹⁷

However, in contrast, Kho demonstrated no difference in antimicrobial efficacy for irrigation with 5.25% NaOCl and 15% EDTA verses irrigation with 1.3% NaOCl and MTAD in the apical 5 mm of roots infected with *E. faecalis*.¹⁸ In contrary, Ruff showed that 6% NaOCl and 2% CHX were equally effective and superior to MTAD and 17% EDTA with regard to antifungal activity.¹⁹

7. Effect of MTAD on smear layer

Torabinejad and Cho⁵ studied the effect of various concentrations of sodium hypochlorite on the ability of MTAD to remove the smear layer, to investigate the effectiveness as an intracanal irrigant before final rinse with BioPure MTAD. The results showed that MTAD removed most of the smear layer when used as an intracanal irrigant, however, some remnants of the organic component of the smear layer remained scattered on the surface of the root canal walls. They noticed that effectiveness of MTAD to completely remove the endodontic smear layer was enhanced when low concentrations of sodium hypochlorite were used as an intracanal irrigant before final rinse with MTAD. Also, the regimen did not seem to significantly change the structure of dentinal tubules. They concluded that MTAD could remove smear layer much more effectively than various concentrations of sodium hypochlorite.

Tay and Hiraishi⁴ reported that when MTAD was used as an initial rinse followed by use of various concentrations of NaOCl (2.6%, 5.25%) as final rinses in or without light, brownish discolouration was noticed at the point of contact of these two solutions on teeth. It was suggested to be caused by the dentinal absorption and release of doxycycline present in MTAD solution. Bench top reproductions of the phenomenon

revealed that the reaction between MTAD and NaOCl is a redox reaction. A mechanism of this observed pigmentation has also been proposed earlier when photo-oxidation of tetracycline resulted in the formation of red purple degradation product, with high affinity for hydroxyapatite.⁴ Tay and Mazzoni²⁰ concluded that addition of tetracycline to hydroxyapatite resulted in stronger affinity of the two components, producing a pale yellow powder which under ultraviolet light showed a bright yellow fluorescence.

Torabinejad and Cho⁵ reported that effectiveness of MTAD to completely remove the smear layer was enhanced when low concentrations of NaOCl were used as intracanal irrigant during instrumentation followed by use of MTAD as final rinse. This combination and sequence do not significantly change the structure of the dentinal tubules and caused minimal erosion of dentinal tubules. Torabinejad and Khademi¹² concluded that combination of 1.3% NaOCl as a root canal irrigant with MTAD as a final rinse was more effective against *E. faecalis* than 5.25% NaOCl with 17% EDTA.

8. Effect of BioPure MTAD on tooth structure

Machnick et al²¹ studied the effect of MTAD on flexural strength and modulus of elasticity of dentin. Based on the results, they concluded that clinical use of BioPure MTAD as intracanal irrigant caused no adverse effects on the physical properties of the exposed dentin.

Tay and Pashley²² investigated the structure of mechanically instrumented intraradicular dentin after irrigation. They determined that both EDTA and MTAD created a zone of demineralized collagen matrices in eroded dentin and around the dentinal tubules, with the mildly acidic MTAD being more aggressive than EDTA.²²

9. Biocompatibility of BioPure MTAD

In choosing a root canal irrigant, biocompatibility should be a major consideration. Zhung and Torabinejad²³ studied the cytotoxicity of MTAD, 3% H₂O₂, and 5.25% NaOCl and demonstrated that 5.25% NaOCl was about 195 times more cytotoxic than MTAD and 3% H₂O₂ was 50 times more cytotoxic than MTAD. They concluded that the cytotoxicity of MTAD was very minimal as evaluated by MTT-Tetrazolium assay. Ring found that the cytotoxicity of MTAD was slightly less than NaOCl, indicating the biocompatibility of MTAD.²⁴

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.²⁴ This suggests that, presently MTAD cannot be considered as the root canal irrigant of choice in pulp revascularization techniques.

10. Instructions for use of BioPure MTAD¹²

Unmixed powder and liquid should always be stored at room temperature away from direct sunlight. Mixed solution can be stored for 48 h if refrigerated. After the liquid (syringe) is

injected into bottle (powder), without removing the syringe from the nozzle of the bottle the combination has to be gently moved back and forth for not more than 60 s, do not vigorously shake the powder and liquid together. For a single canal disinfection always the full dose that is 5 ml of MTAD has to be used, failure to do so reduces its efficiency as a root canal irrigant. MTAD should never be washed out but only suctioned out from the root canal. It should always be the last irrigant to be used in the canal space. It is contraindicated in pregnancy and in children below 8 years of age. It is also contraindicated in patients who are sensitive to doxycycline.

11. Advantages

MTAD is a most biocompatible material with least cytotoxicity and strongest antimicrobial activity. It was found to be highly effective against *E. faecalis* in refractory root canal infections. It does not cause any irritation to the periapical tissues even if it is extruded into periapical area. It is the most effective in the removal of endodontic smear layer with minimal erosion of dentinal tubules.¹² It helps in the simultaneous removal of endodontic smear layers and disinfection of root canals and clinically effective.

12. Disadvantages

MTAD a tetracycline derivative has the ability to intrinsically stain teeth during odontogenesis, can chelate calcium ions and can get incorporated into teeth, resulting in discolouration of both primary and permanent dentitions.¹¹ It is contraindicated in pregnancy. It is expensive than other commonly used root canal irrigants. MTAD (once the liquid component is mixed with powder) has a short shelf life and has to be used within 48 h even if refrigerated. It demonstrates lesser compatibility to dental pulp cells for revascularization procedures.

13. Results

MTAD is a biocompatible material, found to be highly effective for removal of endodontic smear layer, has potential antibacterial efficiency to completely disinfect the root canal system.

14. Conclusion

MTAD is a highly efficient, biocompatible substance with potential antibacterial efficiency and represents an innovative approach for simultaneous removal of endodontic smear layer and disinfection of root canals. It is particularly effective against *E. faecalis* in refractory root canal infections. It can be concluded that MTAD is a promising root canal irrigant, but still further clinical studies are required to establish it as an ideal irrigant.

Conflicts of interest

All authors have none to declare.

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