CONTINUOUS CHELATION – A BIOLOGICAL AND CLINICAL UPGRADE OF ROOT CANAL TREATMENT STRATEGY IN ORAL REHABILITATION

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ABSTRACT

In current endodontic practice the root canal irrigation by using sodium hypochlorite as primary irrigant of choice coupled subsequently with a chelating agent, usually EDTA, is a crucial mean of cleaning and disinfection of endodontic system. Continuous chelation is a new paradigm relied on the increased role and efficacy of irrigation in root canal treatment. This novel approach of irrigation replaces the alternative use of irrigants according to present accepted treatment protocols by sole irrrigant flushing with a chair side mixture of sodium hypochlorite and a weak chelator, mainly etidronate (Dual Rinse HEDP). Continuous chelation is not inferior to the antimicrobial activity of sodium hypochlorite, allows the dissolution of pulp remnants and removal of smear layer and shortens the time required for chemomechanical treatment of the root canals.

Key words: root canal treatment, continuous chelation, Dual Rinse HEDP

INTRODUCTION

Presently when discussing the concept of chemomechanical treatment in endodontics we understand that the instrumental enlarging of root canals is only the way to provide a better access of irrigants to the apical foramina of the teeth aiming to result in an optimal cleaning and disinfection of entire endodontic system [1].

In current clinical practice the root canal irrigation, as a crucial mean of cleaning and disinfection, entails the use of sodium hypochlorite and a chelator, mainly EDTA, in the following somehow standard sequence hypochlorite/EDTA/hypochlorite. This usual operative protocol aims to accomplish the final goal of the root canal treatment that is the removal of the residual biofilm, by using sodium hypochlorite as primary irrigant of choice coupled subsequently with a chelating agent [1,2].

Despite the real technological improvement in Ni-Ti rotary

instruments, to enlarging the root canals and to providing an increased access of irrigants in the apical area of endodontic system, the biomechanical treatment is still far to directly contact a large portion of the root canal. Actually contemporary endodontic treatment is still facing with inappropriate debridement and disinfection mainly in its anatomic irregularities such as apical delta, isthmuses, lateral canals, and fins that remain inaccessible [1-3].

Accordingly, for a better outcome of endodontic treatment in infected root canals irrigation is called to play a key role in achieving this goal by cleaning and disinfecting the mechanically untouched areas above mentioned that harbor resting bacterial biofilms [1-3].

CURRENT IRRIGANTS IN ROOT CANAL TREATMENT

Sodium hypochlorite is beyond a doubt the most common irrigant used since round hundred years in endodontic therapy. Presently is recommended as the primary irrigant of choice due to its antimicrobial efficacy against microorganisms forming biofilms, by strongly reducing the pathogenic effect of endotoxins and lipoteichoic acids and to its high dissolving potential of pulp tissue remnants and biofilm matrix [1,4,5].

According to literature sodium hypochlorite may be used to irrigating the root canals in concentrations between 0.5-8.25%, which cover its antimicrobial window of efficiency, without to be still established a consensus [6-10]. Though it was thought that as higher the concentration as better the efficiency it seems that clinical outcome in root canal treatment of chronic apical periodontitis does not depend on this issue but on appropriate full approach both biomechanical and chemical [6,7,11].

Moreover, when used in operative sequence with EDTA as a final rinse, by dissolving collagen fibrils, sodium hypochlorite may adversely affect some basic properties pf the dentin matrix such as Young modulus and its tensile and flexural strength as well, resulting in decrease of resistance to vertical root fractures [1].

Though a matter of concern, the apical extrusion of sodium hypochlorite during root canal irrigation did not prove that the clinical severity of such accident was concentration depending as it was observed also at 1% value [1]. Higher concentrations of sodium hypochlorite were not culpable neither for inter-appointment pain in case of two visits nor in single visit endodontic treatment [10].

Unfortunately though a frequent exchange of sodium hypochlorite solution during root canal treatment is strongly recommended there is still no consensus regarding the necessary volume, solution concentration, exchange frequency and delivery time as the anatomy of the endodontic system and mainly its internal milieu are extremely versatile [1].

Another issue of increasing the efficacy of irrigant solution, mainly of

low concentrated sodium hypochlorite, in order to avoiding the associated clinical risks of apical extrusion while improving the antimicrobial and dissolution beneficial properties, was thought to be its preheating between 50^{o}C and 60^{o}C [1].

However, after the introduction into the root canal the temperature is abruptly reducing approximately at body temperature (37^{o}C) so that the hope to an increased strength of preheated irrigant reaction with organic pulp remnants is soon lost [12].

As previously mentioned the root canal irrigation relies on sodium hypochlorite and a chelator, mainly EDTA, though some other biocompatible chelators such as citric acid and maleic acid may also be used [1,2,13].

Typically in endodontic treatment is used as irrigant Na_2EDTA that has a pH within a moderately alkaline range [14]. Though EDTA solutions might be slightly alkaline or pH neutral, as a rule EDTA 15-17% (etylenediamine tetraacetic acid) is currently indicated as irrigant for removal of inorganic component of the smear layer and hard-tissue debris produced during biomechanical treatment of the root canal regardless the endodontic instruments used handy or rotatory [1,2,15,16].

Its disodium salt is neutral or slightly alkaline and in 15-17% solution may easy dissolve the hard-tissue debris and smear layer generated during root canal enlargement [1,2,17,18]. Furthermore, EDTA may disrupt the bacterial biofilm matrix despite its pretty week direct antimicrobial effect [3,5,6,18]. Similar to EDTA the antimicrobial activity of citric acid is reduced unlike maleic acid that demonstrated the ability to deadly damage the bacteria hosted in biofilms of infected root canals [1].

It has to be underlined that EDTA irrigation raises some concern in generating the dentinal erosions by demineralizing the peritubular dentine especially while using in clinical sequence of irrigation sodium hypochlorite-EDTA-hypochlorite [19].

Another disadvantage of this alternative irrigation is that consumes the free available chlorine (FAC) due to the chemical reaction between sodium hypochlorite and EDTA [20]. The other two less used aforementioned chelators, citric and maleic acids, are also in charge with the fast lost of free available chlorine, based on same chemical reaction with sodium hypochlorite [1,13].

All mixtures of sodium hypochlorite and EDTA solutions in proportion of respectively 9:1, 5.5:2.5, and 1:1 demonstrated an abrupt loss in FAC having a dramatic treatment outcome [20].

An important issue that unfortunately the endodontists underestimate the necessity of completely remove the first irrigant when are using alternate irrigation of the root canal since the second irrigant may chemically interact with the former

[4,13,20]. Even a small proportion of EDTA, as in mixture of 9:1, results in FAC drop to 75% of its initial activity [20].

Looking at the clinical relevance of aforementioned proportion, especially in case of 1:1 mixture, which can be rather frequent encountered during root canal irrigation during flushing interchange of sodium hypochlorite and EDTA it has to carefully avoid the simultaneous presence of these irrigants in root canal [20].

In addition to continuous loss of active chlorine, the prolonged presence of sodium hypochlorite and calcium complexing agent may also develop in the apical part of the root canal dentin erosions as both are still active for a while. To some extent some, similar to EDTA, initial erosions were also observed in case of mixture with weak chelators as etidronate (HEDP) [4].

Accordingly strong recommendations support the aspiration of initial irrigant with devices such as Endovac or the maneuver of root canal drying with common paper points before to introduce the other solution of irrigation [4,13].

Moreover, mainly in the apical area of narrow root canals a special attention has to be done to this issue because the tooth anatomy facilitates the stratification of irrigants and practical changes their relative proportion into canal lumen. If uncontrolled this unwanted outcome diminishes or even abolishes the aim of a successful irrigation [20].

During past decades in stratification are also involved gel formulations containing EDTA that are simultaneously used with rotary Ni Ti instruments to enlarging the root canals. Obviously any gel formulation is more difficult to be displaced from root compared to common 17% EDTA irrigation solution so that its inefficient removal negatively might affect the treatment outcome [20].

FREE AVAILABLE CHLORINE (FAC)

Free available chlorine (FAC) consists of hypochlorite and hypochlorous acid, which are strong oxidizers and orchestrate both main treatment activities, antibacterial and pulp remnants dissolution [20].

The relative proportion of hypochlorite and hypochlorous acid depends on pH. The fresh normal solution of unbuffered sodium hypochlorite has a pH of 11-12 [1]. If the pH of sodium hypochlorite solution shifts to acid zone the outcome will be a higher proportion of hypochlorous acid, which is in charge with increased antibacterial efficacy of irrigant. Nevertheless, such pH decrease is a disadvantage as the solution stability is highly compromised [1,13].

Though initially the fresh mixture of 7% 1-hydroxyethylidene-1, 1-biphosphonate solution (HEPB, Zschimmer & Schwarz) with sodium hypochlorite keeps 100% of its FAC one hour after mixing is recorded some drop,

which proved to be dose dependent after a while [13].

Unlike the sodium hypochlorite that has no influence on calcium-binding action of chelators, the decalcifying solutions such as 15% aminotrismethylenephosphonic acid (ATM, Merck) or citric acid after admixing with sodium hypochlorite caused almost complete lost of FAC in less than 1 minute [13].

The mixture of sodium hypochlorite with a weak decalcifying agent, as it happens by continuous chelation, confers a higher chemical stability of the irrigating solution based on less consumption of FAC [21].

Heating sodium hypochlorite alone does not interfere with its FAC content. Conversely, heating the mixtures of sodium hypochlorite with etidronate or alkaline tetrasodium EDTA results in a significant drop of FAC [22].

CONTINUOUS CHELATION

Continuous chelation is definitely the consequence of the paradigm shift in endodontic treatment relying on the increased role of irrigation. As definition, continuous chelation is a novel concept introduced by Zehnder and Wright, which aims to simplify the currently accepted irrigation protocol used in biomechanical root canal treatment [2,13]. Actually throughout the whole root canal mechanical enlargement a sole irrrigant is flushing the endodontic system without the alternative use of irrigants recommended by present accepted treatment protocols [1,4,5,23].

The irrigation technique is based on a freshly prepared mixture of sodium hypochlorite with a weak nontoxic chelator, mainly etidronate (1-hydroxyethylidene-1, 1-biphosphonate) but also clodronate or tetrasodium EDTA [2,4,13,15,16].

Pivotal is that this one irrigant-mixture preserves both main antibacterial [5,15] and tissue-dissolving properties of sodium hypochlorite [4,17,24,25]. Moreover, this soft chelating protocol of irrigation results in efficient hard-tissue debris [16,26,27] and smear layer removal [16,28]. Accordingly, this already reduced chemical reactivity of sodium hypochlorite facilitates less consumption of FAC [21].

All the above mentioned high treatment benefits demonstrated by continuous chelation rely on its ability to chemically guarantee a stable liquid mixture of its components, sodium hypochlorite and chelating agents, characterized by a minimal loss of FAC in order to ensure as much as possible a prolonged action [13,2,15,16,23].

On the other hand it was also observed that during the process of continuous chelation the chemical reaction that develops between sodium hypochlorite and etidronate is increasing to the same extent as the chelator concentration is higher [23].

To achieving a proper therapeutic window in continuing chelation it is mandatory that the chelating agent to

prove a high stability when admixed with sodium hypochlorite. That means to be chemically compatible with the proteolytic agent in order to preserve the ability of binding calcium ions during chelation and its alkalinity, which is crucial to avoiding the premature loss of FAC from sodium hypochlorite [13].

A noticeable clinical advantage of using continuous chelation is also the hampering of inducing the smear layer during instrumental enlargement of the root canal due to immediate involvement of decalcifying agent [4,28].

WEAK CHELATORS

The principal weak chelator used in continuous chelation procedure is etidronate that is delivered for endodontic practice as Dual Rinse HEDP [29]. Actually is tetrasodium etidronate (Na_4HEDP) that proved noticeable efficacy in removal of dentinal debris in conjunction with significant antibacterial effects and compatibility regarding dental materials [2,5,26,27].

Unfortunately, the simultaneous use of sodium hypochlorite and etidronate as irrigation mixture is chemically instable and in a couple of hours is loosing its FAC [29]. It was observed that at room temperature the mixture of 5% sodium hypochlorite and 18% etidronate is maintaining the activity one hour [23] as compared to the mixture of 2.5% sodium hypochlorite and 9 % Dual Rinse HEDP that has an active life prolonged to 2 hours [29].

The advantage of tetrasodium salt of HEDP is the chemical compatibility with sodium hypochlorite that allows its direct dissolution by mixing. Nevertheless, compared to weaker effect of alkaline solutions of EDTA in removing the smear layer the HEDP did not show a similarity [14].

However, these two mixtures of 9% or 18% etidronate already used in continuous chelation have a longer active life than the mixture of 5% alkaline tetrasodium EDTA (Na_4EDTA) and 2.5% sodium hypochlorite, which is active only 30 minutes [23].

The sodium hypochlorite mixtures either with clodronate or CDTA (cyclohexanediaminetetraacetic acid) are more compatible than with alkaline EDTA or etidronate [13].

Related to FAC, 0.5 mol L^{-1} clodronate mixed with 10% sodium hypochlorite preserved unchanged the use life at least 18 hours as compared to the 15% sodium hypochlorite mixture with CDTA that kept FAC unchanged only round one hour [13].

Some other chelators such as EGTA (egtazic acid), DTPA (pentetic acid), ATMP (aminotrimethylene phosphonic acid), HPAA (hydroxyphosphonoacetic acid) that were studied for the potential ability to form a mixture with sodium hypochlorite in order to be used in continuous chelation procedures lost quickly their use life. The weakest hope was HPAA (hydroxyphosphonoacetic acid), which lost its FAC in one minute [13].

Though all the analogues of EDTA such as EGTA (egtazic acid), CDTA (cyclohexanediaminetetraacetic acid), and DTPA (pentetic acid) demonstrated high constants of stability, some of them (EGTA and CDTA) recorded even more elevated values than EDTA [13].

The lack or reaction of CDTA and clodronate with sodium hypochlorite may be explained in case of CDTA by stereochemical restrictions as its chemical formula contains a cyclic hexane group. Regarding clodronate is sufficient to remind that is the final product of a chemical synthesis where is involved sodium hypochlorite [13].

Clodronate is also efficient in root canal irrigation especially in chronic apical periodontitis due to antiinflammatory, antiosteoclastic, and antimicrobial activity. However, before use is recommended to guarantee an appropriate time-depending stability by controlling the pH and storage temperature [13].

Though less proficient calcium-binding agent as compared to 10% citric acid, 7-10% HEPB solution when admixed chair-side with sodium hypochlorite might also be promising as weak calcium sequestrating chemical means as respects the stability constant of chelator-calcium complex [13].

The solution of etidronate (18% HEDP) is less aggressive compared to EDTA since as final flush needs 5 minutes to completely remove the smear layer [17]. Nevertheless this weak chelator proved to efficiently avoid smear layer formation and diminishing hard-tissue debris accumulation in anatomical irregularities of the root canal. Not of less importance is that it allows to be safely mixed with sodium hypochlorite without to hamper its antibacterial activity [13,4,26,28].

It might be conclude that in case of using etidronate admixed with sodium hypochlorite for irrigation in continuous chelation the pulp remnants will be dissolved, the antimicrobial activity will be preserved and smear layer has no condition to be formed. Accordingly the time required by root canal enlargement will be reduced as the final flush would not be necessary [4].

SMEAR LAYER REMOVAL

The removal of smear layer, as compulsory outcome of the biomechanical treatment of root canals, is highly endorsed due to its content in microorganism and nutrients supporting their growth in addition to the obstruction of dentinal tubules, which hampers the disinfection and sealer penetration during the maneuvers of root canal filling [2,13,15,16,18].

Since the sodium hypochlorite is not able to dissolve the inorganic component of smear layer the use of an additional decalcifying agent is highly asked [4,20]. Usually in clinical practice this agent is EDTA which is introduced into the root canal either alternately with sodium hypochlorite or as final irrigant [4].

Though the simultaneous use of proteolytic agent such as sodium hypochlorite and a chelating agent

during continuous chelation may raise the risk of peritubular erosions in dentin, it was proved that some weak chelators such as clodronate and etidronate admixed with sodium hypochlorite when used in root canal irrigation less than 15 minutes do not provoke dentin erosions. It seems that if the chelator pH is higher its ability to demineralize the dentin is coming down [13].

In mixture with sodium hypochlorite, clodronate proved to have the ability of removing the smear layer. Additionally, as compared to Na_4EDTA and Na_4etidronate, it seems that clodronate showed a better stability when admixed with sodium hypochlorite [13].

Calcium sequestrating solutions have different impact in removing the smear layer. It was demonstrated that compared to HEPB solution, 10% citric acid is five times and 17% EDTA three times stronger [13]. Moreover, a mixture of 2.5% sodium hypochlorite and 9% HEPB has an excellent ability of smear layer removal regardless its amount on root canal walls [21].

It was proved that the removal of smear layer do the implication of chemical mechanism relying on calcium chelation for both decalcifying agents, EDTA and HEDP is highly dependent on pH value. For both of them their tetrasodium salts increase the pH of irrigating solution while the disodium salts have a dropping outcome that is in charge with a stronger chelation [14].

It is not worthless to remember that the continuous chelation is also a preventive means to reducing the smear layer formation during mechanical enlargement of the root canal as well as the amount of resulting hard tissue debris [21].

Heating the mixture of sodium hypochlorite with HEDP before using as endodontic irrigant expands its capacity of removing the smear layer though it requires frequent refreshment due to inherent reduction in FAC [22].

ANTIMICROBIAL PROPERTIES

Obviously the antimicrobial irrigants exert a maximum of activity as deep as they penetrate inside dentin tubules. During root canal irrigation the main obstacle that reduces their therapeutic effect is the presence of smear layer [21].

Once it was proved that the continuous chelation results in final removal of smear layer it was also important to find out to which extent the weak chelator used in the mixture with sodium hypochlorite may affect or not the antimicrobial activity of hypochlorite [21]. One study proved that the mixture of sodium hypochlorite with HEDP killed 50% of free culturable microbiota as compared to only 40% that succeeded a pure irrigation with sodium hypochlorite [30].

Antibacterial activity of sodium hypochlorite is related to its free available chlorine. Regarding the disinfection abilities HEPB has no impact on bacterial viability. EDTA can affect bacterial growth until a 1:10 dilution but not beyond. Neither citric

acid can kill bacteria further down than 1:1 dilution [13].

The antibacterial activity of 2.5% sodium hypochlorite was not reduced when mixed with 9% HEPB, proving that the hypochlorite penetrated in dentin tubule due to the previous removal of smear layer by added decalcifying agent [21]. Conversely, if the smear layer was not removed by using 2.5% sodium hypochlorite alone, the irrigant lost about 50% of its killing ability against root canal pathogen microbiota [21].

SOFT TISSUE-DISSOLVING PROPERTIES

Soft tissues dissolving properties of irrigant solutions used in continuous chelation are related to various parameters, such as chemical structure, concentration, volume, renewal frequency, action time, temperature, and kind of associated agitation [4,31].

It is notorious that the FAC of sodium hypochlorite is guiding its soft tissues dissolution capacity, based on hypochlorite ion (OCl^-), respectively the antimicrobial power, related to hypochlorous acid (HOCl) [1,4]. Therefore a mixture of sodium hypochlorite with EDTA at pH of 7.4 hinders the pulp remnants dissolution as consequence of hypochlorite ion reduction unlike the mixture with HEDP at pH of 11.2 that afford a maximum value of dissolution [4]. An additional factor to reducing the mixture ability of dissolution is the chlorine gas loss due to the drop in FAC [4].

Similar to beneficial outcome of increasing the removal of smear layer by heating either the sodium hypochlorite alone at 60^{o}C or the mixture of sodium hypochlorite with HEDP at 37^{o}C, an obvious simultaneous effect was observed in dissolution of organic debris accumulated after root canal enlargement if care was taken for proper refreshment of irrigating solution [22].

CONCLUSIONS

Continuous chelation is a new paradigm relied on the increased role and efficacy of irrigation in root canal treatment. This novel approach of irrigation replaces the alternative use of irrigants according to present accepted treatment protocols by sole irrrigant flushing with a chair side mixture of sodium hypochlorite and a weak chelator, mainly etidronate (Dual Rinse HEDP). The antimicrobial activity, dissolution of pulp remnants and removal of smear layer by continuous chelation are similar to alternative use of sodium hypochlorite and chelators. However, the continuous chelation has a clinical advantage as it shortens the time required for chemomechanical treatment of the root canals.

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