

Primljen/ Recived on: 21.12..2013.
 Revidiran/ Revised on: 28.12..2013.
 Prihvaćen/ Accepted on: 10.01.2013.

INFORMATIVNI RAD
 INFORMATIVE ARTICLE
 doi: 10.5937/asn1469373G

ISPRAVLJEN I PONOVO ŠTAMPAN RAD
 CORRECTED AND REPUBLISHED ARTICLE :

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 CORRECTIONS OF THE ROOT CANAL IRRIGATION PROTOCOL-PRIMUM NON NOCERE

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Acta Stomatologica Naissi 2013; vol. 29(68): 1289 – 1297.

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Sažetak

Endodontski irigansi imaju važnu ulogu u eliminaciji mikroorganizama iz kanalnog sistema zuba, rastvaranju organskih tkiva, uklanjanju debrisa i razmaznog sloja. Natrijum hipohlorit (NaOCl) predstavlja snažno antiseptično sredstvo koje rastvara organski deo dentina, razgrađuje vitalno i nekrotično tkivo i neutrališe toksične produkte. Njegov antibakterijski efekat raste sa povećanjem koncentracije. Zbog neadekvatnog površinskog napona, NaOCl ima ograničen pristup uskim i akcesornim kanalčićima. Hlorheksidin (CHX) ima sličan spektar delovanja, ali može ispoljiti aktivnost i prema NaOCl rezistentnim sojevima bakterija. Postiže efikasnu dezinfekciju kanala zbog osobine supstantivnosti, tj. postepenog i prolongiranog dejstva na mikroorganizme. Za razliku od NaOCl, CHX nije u stanju da rastvori organski material unutar kanala korena. Etilen-diamin-tetraacetat (EDTA) uklanja neorganski deo dentinskog zida olakšavajući prolaz endodontskim instrumenatima. Ovaj irigans ne deluje na organski deo razmaznog sloja i ne poseduje antimikrobna svojstva. Izgleda da ni jedan irigans nije u stanju da sam ispunji sve potrebne zahteve, zbog čega je neophodna njihova kombinovana upotreba. Istraživanja su pokazala da između pojedinih iriganasa postoje interakcije koje su nepoželjne i mogu kompromitovati endodontsku terapiju.

Mešavina NaOCl i CHX dovodi do prebojavanja zuba i stvaranja narandžasto-braon precipitata koji ostaje na dentinskom zidu ili prelazi u periapeksno tkivo. Kombinacija CHX i EDTA takođe stvara talog. Ovaj precipitat smanjuje permeabilnost, remeti hermetičku opturaciju kanala i može delovati kao hemijski razmazni sloj. Ustanovljeno je da se sastoji od para-hloranilina, za koga je eksperimentalno dokazano da ima toksično dejstvo na tkiva oko vrha korena zuba. Jednostavne korekcije u protokolu irigacije kanala korena zuba mogu sprečiti pojavu neželjenih reakcija između endodontskih iriganasa.

ključne reči: endodontski irigansi, interakcije, precipitat

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Abstract

Endodontic irrigant play an important role in the elimination of microorganisms from the root canal system, dissolving organic tissue, removing of debris and the smear layer. Sodium hypochlorite (NaOCl) is a powerful antiseptic agent which dissolves the organic part of dentin, vital and necrotic tissue and neutralizes toxic products. Its antibacterial effect increases with increasing concentration. Due to inadequate surface tension, NaOCl has restricted access to narrow and accessory canals. Chlorhexidine (CHX) has an antibacterial efficacy comparable to NaOCl, while being effective against certain NaOCl resistant bacterial strains. Effective root canal disinfection is achieved due to substantivity, i.e. continued and prolonged antimicrobial effect. Unlike NaOCl, it's not able to dissolve organic material within the root canal. Ethylene-diamine-tetra-acetate (EDTA) removes the inorganic part of the dentinal wall facilitating the passage of endodontic instruments. It doesn't act on the organic smear layer and hasn't antimicrobial properties. It seems that not all irrigants not able to fulfill all the necessary requirements, so their combined use is necessary. Studies have shown that there are interactions between some irrigants, which are undesirable and may compromise endodontic therapy. A mixture of NaOCl and CHX leads to staining of the teeth and the creation of an orange-brown precipitate, which either remains in the dentinal wall or exceeds to the periapical tissues. CHX and EDTA combination also produces a precipitate. This precipitate reduces permeability, disrupts hermetic obturation and can act as a chemical smear layer. It was found that the precipitate consist of the para-chloroaniline, which has been experimentally shown to have toxic effects on the tissue around the root apex. Simple adjustments in the irrigation protocol can prevent the occurrence of adverse reactions between endodontic irrigants.

Key words: endodontic irrigants, interactions, precipitate

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Uvod

Endodontski irigansi imaju važnu ulogu u eliminaciji mikroorganizama iz kanalnog sistema zuba, rastvaranju organskih tkiva, uklanjanju debrisa i razmaznog sloja^{1,2,3,4}.

Mnoga istraživanja su pokazala da između pojedinih iriganasa postoje interakcije koje su nepoželjne i mogu kompromitovati endodontsku terapiju^{5,6}. Cilj ovog istraživanja je razmatranje literaturnih podataka o interakcijama koje nastaju kada se natrijum hipohlorit, hlorheksidin, etilen-diamin-tetraacetat i limunska (ili maleinska) kiselina koriste zajedno u toku endodontske terapije.

Za dobijanje informacija o interakcijama između endodontskih iriganasa, urađeno je pretraživanje literature preko PubMed baze podataka i ključnih reči: interakcija i endodontski irigansi, natrijum hipohlorit i hlorheksidin, natrijum hipohlorit i EDTA, hlorheksidin i EDTA, NaOCl i limunska (ili maleinska kiselina), helatni agens i hlorheksidin". Pretraživanje literature je urađeno u junu 2013. godine.

Irigansi u endodonciji

Najčešće korišćen irigans je **natrijum hipohlorit (NaOCl)** koji predstavlja snažno antiseptično sredstvo sa sposobnošću rastvaranja organskog dela dentina, razgradnje vitalnog i nekrotičnog tkiva, neutralizacije toksičnih produkata i lubrikacije^{1,2}. Uklanjajući debris, ovaj irigans sprečava "zatrpavanje" apeksnog dela kanala strugotinama dentina i ostacima mekih tkiva, kao i istiskivanje inficiranog materijala u periapeksni prostor^{1,2,3}.

Svoje antimikrobno dejstvo NaOCl ostvaruje preko hipohlorne kiseline koja rastvara organsko tkivo i oslobađa hlor. Reakcijom između hlora i amino grupa formiraju se hloramini koji remete ćelijski metabolizam. Hlor ispoljava antimikrobno dejstvo tako što dovodi do ireverzibilne oksidacije SH grupa esencijalnih bakterijskih enzima^{4,7}.

Iako se u literaturi sreću podaci da se NaOCl u endodontskoj terapiji može koristiti u koncentracijama od 0,5%, 1%, 1,25%, 2,6% i 5,25%, još uvek ne postoji usaglašeno mišljenje u vezi ove teme. Činjenica je da antibakterijski efekat ovog irigansa raste sa povećanjem koncentracije, tako da je full-strength

Introduction

Endodontic irrigants play an important role in the elimination of microorganisms from the root canal system of the tooth, dissolving organic tissue, removing of debris and the smear layer^{1,2,3,4}.

Many studies have demonstrated certain irrigants interactions that are undesirable and may compromise endodontic therapy^{5,6}. The aim of this study was to consider the literature data on the interactions occurring when sodium hypochlorite, chlorhexidine, ethylene-diamine-tetraacetate and citric (or maleic) acid are used together during endodontic treatment.

In order to obtain information about the interactions among the endodontic irrigants, literature search was performed through PubMed, and key words: interaction and endodontic irrigants, sodium hypochlorite and chlorhexidine, sodium hypochlorite and EDTA, chlorhexidine and EDTA, NaOCl and citric (or maleic acid), chelating agents and chlorhexidine. Literature search was performed in June 2013.

Irrigating solutions in endodontics

The most commonly used irrigant is **sodium hypochlorite (NaOCl)**, which is a powerful antiseptic agent with the ability to dissolve organic part of dentine, decompose vital and necrotic tissue, neutralization of toxic products and lubrication^{1,2}. Removing debris, NaOCl prevents packing of the hard and soft tissue in the apical root canal and extrusion of infected material into the periapical area^{1,2,3}.

Antimicrobial effect of NaOCl is achieved through hypochloric acid which in contact with organic tissue acts as a solvent and releases chlorine. Reaction between chlorine and the amino group (NH) forms chloramines that interfere in cell metabolism. Chlorine has an antimicrobial action, leading to an irreversible oxidation of SH groups of essential bacterial enzymes^{4,7}.

Although the literature provides information that sodium hypochlorite in endodontic therapy can be used in concentrations of 0.5%, 1%, 1.25%, 2.6% and 5.25%, there is still no agreed opinion about this topic.

koncentracija (5,25%) izuzetno efikasna protiv mikroorganizama, ali, istovremeno i veoma toksična. S obzirom da je aktivnost NaOCl vezana za količinu slobodnog hloridnog anjona, smanjenje koncentracije može se kompenzovati povećavanjem volumena. To znači da je za redukciju bakterija u kanalnom sistemu mnogo važnija količina NaOCl nego njegova koncentracija. Takođe, zagrevanje i primena aparata sa ultrazvukom mogu povećati aktivnost rastvora^{1,2,8}.

Literaturni podaci ukazuju na značajno manju antimikrobnu aktivnost NaOCl u *in vivo* uslovima. Pretpostavlja se da je razlog tome neadekvatan površinski napon što ograničava pristup lateralnim i apeksnim ramifikacijama, uskim i akcesornim kanalićima koji ostaju slabo ili nedovoljno tretirani. Pored toga, prisustvo organskih materija (ostaci tkiva, zapaljenjski eksudat, dentinski kolagen, mikroba biomasa) troši NaOCl i slabi njegovo dejstvo¹.

Imajući u vidu toksičnost visokih koncentracija NaOCl, nemogućnost pristupa svim delovima kanalnog sistema, redukciju aktivnosti *in vivo*, izgleda da ne postoji opravdanje za korišćenje NaOCl kao endodontskog irrigansa u koncentraciji višoj od 1%².

Hlorheksidin (CHX) ima sličan spektar delovanja, s tim što može ispoljiti aktivnost i prema NaOCl rezistentnim sojevima bakterija (*E. Faecalis*, *C. Albicans*). Antimikrobni mehanizam dejstva CHX je vezan za katjonsku strukturu njegovih molekula, zbog čega ovaj irrigans ima jak afinitet prema negativno naelektrisanim fosfatnim grupama ćelijskog zida, povećavajući permeabilnost i mogućnost prodiranja sredstva u bakteriju⁹. Hlorheksidin na niskim koncentracijama (0,2%) ima bakteriostatski efekat. Više koncentracije (2%) su baktericidne i uslovljavaju gubitak ćelijskih elemenata, precipitaciju i koagulaciju citoplazme, a promene koje nastaju na ćelijskom zidu bakterije imaju ireverzibilan karakter^{9,10}.

Ovaj irrigans postiže efikasnu dezinfekciju kanala korena zbog osobine supstantivnosti, tj. postepenog i prolongiranog dejstva na mikroorganizme^{10,11}. Međutim, za razliku od NaOCl, nije u stanju da rastvori organski material unutar kanala korena, što predstavlja jedan od glavnih nedostataka CHX^{1,9}.

The fact that the antibacterial effect of irrigant increases with increasing concentration, so that the full-strength concentration (5.25%) is extremely effective against microorganisms, but also very toxic. Since the activity of NaOCl related to the amount of free chloride anions, reducing the concentration can be compensated by increasing the volume. So, for bacteria reduction in the canal system, the NaOCl quantity is more important than its concentration. Also, a rise in temperature and use of ultrasonic agitation increased the effectiveness of the solution^{1,2,8}.

Literature data indicate significantly lower *in vivo* antimicrobial NaOCl activity. It is assumed that the reason for this inadequate surface tension, which restricts access to the lateral and apical ramifications, narrow and accessory canals that remain poorly or insufficiently treated. Additionally, the presence of organic matter (tissue remnants, inflammatory exudate, dentine collagen, microbial biomass) consumes NaOCl and weakens its effect¹.

Due to the toxicity of high concentrations of NaOCl solution, lack of access to all parts of the canal system, and the reduction of activity *in vivo*, it appears that there is no rationale for using hypochlorite solution, as an endodontic irrigant, at a concentration higher than 1%².

Chlorhexidine (CHX) at concentrations of 0.2-2% has a similar spectrum of activity, but the activity can be manifested and the NaOCl-resistant strains of bacteria (*E. faecalis*, *C. albicans*). Antimicrobial mechanism of CHX action is related to cationic structure of its molecules, making the irrigant has a strong affinity for the cell wall of microorganisms, interacting with the negatively charged phosphate groups and increasing permeability and the possibility of penetration irrigants into bacteria⁹. Chlorhexidine in low concentrations (0,2%), has a bacteriostatic effect. Higher concentrations have a bactericidal effect and influence on the loss of cellular elements, precipitation and coagulation of the cytoplasm, and the changes that occur in the cell wall of bacteria have an irreversible character^{9,10}.

This irrigants provides effective disinfection of the root canal due to characteristics of substantivity, ie. gradual and prolonged effects on microorganisms^{10,11}.

S obzirom da i NaOCl i CHX imaju niz prednosti i mana, mnogi autori su preporučili da se ova dva irigansa koriste zajedno u cilju poboljšanja antimikrobne aktivnosti u kanalu korena¹². Kuruvilla i Kamath (1998) su testirali naizmeničnu primenu 2,5% NaOCl i 0,2% CHX i ustanovili sinergizam antibakterijskog delovanja oba preparata i bolju razgradnju organskog tkiva nego kada se ovi irigansi koriste posebno¹³.

Etilen-diamin-tetraacetat (EDTA) uklanja neorganski deo dentinskog zida olakšavajući prolaz endodontskim instrumenatima. Koristi se u koncentracijama od 15-20%. Ovo organsko jedinjenje sa metalnim katjonima (kalcijum, magnezijum) iz dentina stvara helatne komplekse i time demineralizuje dentin. Etilen-diamin-tetraacetat može da odvoji adheriran biofilm sa zidova kanala korena, što ga čini relativno uspešnim u redukciji mikroorganizama, uprkos njegovom ograničenom antiseptičnom kapacitetu^{1,2}. S obzirom da ne deluje na organski deo razmaznog sloja i ne poseduje antimikrobna svojstva, EDTA treba koristiti sa nekom proteolitičkom komponentom. Preporučeno vreme za uklanjanje razmaznog sloja pomoću EDTA je jedan minut. Duže izlaganje dovodi do erozije sa značajnim uklanjanjem peritubularnog i intratubularnog dentina^{14,15}.

Limunska kiselina je slaba organska kiselina koja, u koncentraciji od 10%, efikasno eliminiše razmazni sloj i neutrališe aktivnost anarobnih bakterija uklanjajući bakterijske toksine sa zidova kanala korena¹⁶. *In vitro* studije su pokazale njenu citotoksičnost, ali u poređenju sa 17% EDTA, 10% limunska kiselina je značajno biokompatibilnija¹⁷.

Maleinska kiselina je nezasićena karbonska kiselina koja se uglavnom koristi kao kondicioner u adhezivnoj stomatologiji. Nedavno su objavljeni podaci da se ova kiselina može koristiti kao endodontski irigans koji, u koncentraciji od 7%, značajno bolje uklanja razmazni sloj u apeksnoj trećini od 17% EDTA¹⁸. Takođe je ustanovljeno da 7% MA pokazuje manji citotoksični efekat u poređenju sa 17% EDTA¹⁹.

However, unlike the sodium hypochlorite solution, it is not able to dissolve organic material within the root canal, and this is the main disadvantage of the CHX^{1,9}.

Given that NaOCl and CHX have a number of advantages and disadvantages, many authors have recommended that these two irrigants should be used together to enhance the antimicrobial activity of root canal¹². Kuruvilla and Kamath (1998) tested combination of 2.5% NaOCl and 0.2% CHX and found synergistic antibacterial activity and better decomposition of organic tissue than that of either agent used separately¹³.

Ethylene-diamine-tetra-acetate (EDTA) removes the inorganic part of the dentinal wall facilitating the passage of endodontic instruments. It is used in concentrations of 15-20%. This is an organic compound, and with the metal cations (calcium, magnesium) from dentin creates chelate complexes and thereby demineralised the dentin. Ethylene-diamine-tetra-acetate can separate adhered biofilm from the root canal walls, which makes it relatively successful in reducing microorganisms, despite its limited capacity antiseptic^{1,2}. Since there is no effect on the organic part of the smear layer and does not have antimicrobial properties, EDTA should be used with a proteolytic component. Recommended time to remove the smear layer with EDTA is one minute. Prolonged exposure leads to the erosion with significant removing of peritubular and intratubular dentin^{14,15}.

Citric acid (CA) is a weak organic acid, at a concentration of 10%, capable of eliminating the smear layer and neutralizing the activity of anaerobic bacteria removing bacterial toxins from the root canal walls¹⁶. *In vitro* studies have shown its cytotoxicity, but compared with 17% EDTA, 10% citric acid was significantly biocompatible¹⁷.

Maleic acid (MA) is unsaturated carboxylic acid used as an acid conditioner in adhesive dentistry. Recent study showed that 7% MA was significantly better than 17% EDTA in removing smear layer from the apical third of the root canal system¹⁸. Also, 7% MA was found to be less cytotoxic when compared with 17% EDTA¹⁹.

Interakcije između iriganasa

Interakcija između NaOCl i CHX:

Ustanovljena je interakcija između dva najčešće korišćena iriganasa u endodontskoj terapiji, NaOCl i CHX, koja se ogleda u prebojavanju dentina i stvaranju narandžasto-braon precipitata.

Basrani i sar. (2007) su dokazali da postoji trenutna reakcija koja se ogleda u promeni boje rastvora kada se 2% CHX pomeša čak i sa vrlo niskim koncentracijama NaOCl (0,023%)²⁰. Povećanje koncentracije NaOCl na samo 0,19%, dovodi i do formiranja vidljivog taloga čija se količina povećava sa koncentracijom NaOCl²⁰.

Slično tome i druga istraživanja su, u cilju ispitivanja interakcije između ovih iriganasa koristila kombinaciju 2% CHX i različitih koncentracija NaOCl^{21,22,23,24}. Međutim, nedavno je objavljen podatak da se precipitat formirao i u mešavini deset puta niže koncentracije CHX (0,2 %) i najniže, klinički prihvatljive koncentracije NaOCl (0,5%)²⁵. Uočena je promena boje rastvora od svetlo do tamno braon, pri čemu je najtamniju prebojenost pokazao rastvor sa najvećom koncentracijom NaOCl. Prisustvo precipitata u zamućenom rastvoru je zapaženo tek nakon centrifugiranja. Ova studija je ukazala da interakcija između NaOCl i CHX, kao i stvaranje precipitata, ne zavise samo od koncentracije NaOCl već i od koncentracije CHX²⁵.

Smatra se da precipitat nastaje kiselinsko-baznom reakcijom. Hlorheksidin ima kiselu reakciju (pH 5,5-6,0) i sposobnost da donira protone, dok je NaOCl baza i može da prihvati protone iz CHX^{9,20}. Rezultat ove razmene je formiranje nerastvorljivog taloga koji prebojava dentin vezujući se za zidove pristupnog kaviteta i kanala korena^{26,27}. Na taj način, precipitat se ponaša kao rezidualni film i hemijski razmazni sloj koji sprečava difuziju intrakanalnih medikamenata u dentin, remeti atheziju materijala za punjenja kanala i kompromituje koronarnu restauraciju^{22,23,28,29}. Osim toga, ustanovljeno je da se ovaj talog sastoji od para-hloranilina (PCA), za koga je dokazano da deluje toksično u eksperimentima subkutane implantacije kod pacova³⁰. Literaturni podaci ukazuju ne samo na toksičnost PCA, nego i na toksičnost njegovih degradacionih produkata^{31,32,33}. Para-hloranilin se inače koristi kao pesticid i može imati kancerogeno dejstvo³⁴.

Interactions between irrigating solutions

Interaction between NaOCl and CHX:

Interaction between the two most commonly used irrigant in endodontic therapy, NaOCl and CHX, which is reflected in the teeth staining of the teeth and forming an orange-brown precipitate was established.

Basrani et al. (2007) have proven that there was a reaction immediately when mixed 2% CHX even with very low concentrations of sodium hypochlorite solution (0.023%)²⁰. Increasing NaOCl concentrations only to 0.19%, results in the staining solution and the formation of visible precipitate whose amount increased with the concentration of NaOCl solution²⁰.

Similarly, and other studies, in order to investigate the interaction, have used a combination of 2% CHX and various concentrations of sodium hypochlorite solution^{21,22,23,24}. However, recently published data that the precipitate formed in the mixture ten times lower concentrations of CHX (0.2%) and the lowest, clinically acceptable concentrations of NaOCl solution (0.5%)²⁵. There was the change in color from light to dark brown, so that the darkest discoloration of the solution showed the highest concentration of NaOCl. The presence of precipitates in the turbid solution was observed after centrifugation. This study indicated that the interaction between NaOCl and CHX, as well as the formation of precipitate, depends not only on the concentration of NaOCl, but also on the concentration of CHX²⁵.

It is believed that the precipitate formed by the acid-base reaction. Chlorhexidine, a dicationic acid (pH 5.5 to 6.0) has the ability to donate protons, whilst NaOCl is alkaline and can accept protons from the dicationic acid^{9,20}. The result of this exchange is the formation of insoluble precipitate that can stain dentin, bonding to the walls of the access cavity and the root canal^{26,27}. In this way, a precipitate is acting as a residual film and the chemical smear layer that may compromise the diffusion of intracanal medicaments into the dentine, disrupt the adhesion of the root canal filling and favour coronal restoration breakdown^{22,23,28,29}. In addition, it was found that the precipitate consists of the para-chloroaniline (PCA),

Interakcija između NaOCl i EDTA: Ova dva irigansa imaju potpuno različite karakteristike i svaki od njih ima svoj zadatak u dezinfekciji kanalnog sistema. Iz tog razloga je postojala ranija preporuka da se u protokolu dezinfekcije kanala korena koristi njihova mešavina. Međutim, interakcija između ovih irigansa ipak postoji i ogleda se u naglom smanjenju količine slobodnog hlora odmah pri mešanju, što ima za posledicu gubitak aktivnosti NaOCl i nemogućnost rastvaranja mekog tkiva unutar kanala^{35,36}. Međutim, NaOCl nije u stanju da spreči demineralizujuće dejstvo EDTA na peritubularni i intertubularni dentin jer dovodi do veoma spore degradacije ovog helatora. Zbog toga se ne preporučuje kao finalni irigans neposredno posle EDTA³⁷.

Interakcija između NaOCl i limunske (ili maleinske kiseline): Hemijska reakcija između NaOCl i limunske kiseline ne stvara precipitat već rezultira stvaranjem i "ispuštanjem" mehurića iz novonastalog rastvora⁶. Literaturni podaci potvrđuju da sva helatna sredstva reaguju sa NaOCl, što ima za posledicu redukciju aktivnog jona hipohlorita i sledstveni pad aktivnosti NaOCl^{38,39}.

Interakcija između EDTA (i drugih helatora) i CHX: Pri mešanju EDTA i CHX dobija se nehomogeni rastvor sa mlečno belim precipitatom⁴⁰. Postoje dokazi da se ovaj precipitat ne sastoji od PCA već ga čine soli koje nastaju neutralizacijom katjionskog CHX i anjonskog EDTA. Iako netoksičan sa hemijskog aspekta, ovaj talog može biti utisnut u periapikalni prostor ili predstavljati smetnju definitivnom punjenju⁴⁰. Mešanjem limunske kiseline i CHX ne dolazi do hemijske reakcije^{6,41}.

Ustanovljeno je da je maleinska kiselina manje toksična, a efikasnija u uklanjanju smear layer od EDTA^{18,19} i može biti korišćena kao zamena za EDTA, dok kombinacija MA i CHX nije pokazala formiranje precipitata i diskoloraciju^{38,39}.

Korekcija protokola irigacije

Prema podacima iz literature, za irigacioni tretman kanala korena preporučuje se ispiranje sa NaOCl u cilju rastvaranja organskog sadržaja kanala, irigacija sa EDTA (limunska ili maleinska kiselina) u cilju eliminacije razmaznog sloja i završna irigacija sa CHX u cilju

which has been experimentally shown to have toxic effect in experiments of subcutaneous implantation in rats³⁰. Literature data indicate not only the toxicity of PCA, but also the toxicity of its degradation products^{31,32,33}. Para-chloroaniline is used as a pesticide and can have carcinogenic effect³⁴.

The interaction between NaOCl and EDTA: These two irrigant have completely different characteristics and each of them has its task in the root canal system disinfection. For this reason, there was a previous recommendation that there has been tempting to use them as a mixture. However, the interaction between these irrigant exists and is reflected in a sharp reduction in the amount of free chlorine immediately upon mixing, resulting in a loss of activity of NaOCl and inability dissolution of soft tissue inside the canal^{35,36}. However, NaOCl was not able to prevent the effect of EDTA on peritubular and intertubular dentin demineralisation, and it leads to a very slow degradation of the chelator. Therefore, it is not recommended as the final irrigant immediately after the EDTA³⁷.

The interaction between the citric and NaOCl (or maleic acid): The chemical reaction between the citric acid and NaOCl does not form a precipitate, and have resulted in the creation of "dropping" of the newly-formed bubbles solution⁶. Literature data indicate that all chelating agents react with NaOCl, which results in a reduction of the active hypochlorite ion and subsequent decline in NaOCl activity^{38,39}.

Interaction between EDTA (and other chelators) and CHX: During mixing EDTA and CHX homogeneous solution with a milky-white precipitate is obtained⁴⁰. There is no evidence that this precipitate consisted of PCA, but it consists of a salt formed by neutralization of the anionic EDTA and cationic CHX. Although non-toxic with chemical approaches, this residue can be embedded in the periapical area or impede obturation⁴⁰. Mixing citric acid and CHX does not give the chemical reaction^{6,41}. It has been found that maleic acid is less toxic and more effective in the removal of the smear layer compared to the EDTA^{18,19}, and may be used as substitutes for EDTA, while a combination of CHX and MA does not form a precipitate and does not cause discoloration^{38,39}.

povećanja antimikrobnog učinka i prolongiranja dezinficijentnog dejstva na zidove kanala korena^{2,9}.

Korišćenje CHX kao finalnog irigansa ima puno opravdanje zbog činjenice da se tada može najbolje iskoristiti: kanal korena je već očišćen od organskih ostataka i većine mikroorganizama (NaOCl) sa uklonjenim razmaznim slojem (helator) i mogućnošću da CHX u povoljnoj sredini ispolji osobinu supstantivnosti. Ovo je naročito značajno u slučajevima kada se endodontski tretman mora ponoviti i kada se očekuju gram pozitivne bakterije u kanalnom sistemu².

S obzirom da ni jedan irigans nije u stanju da sam ispuni sve potrebne zahteve, zbog čega je neophodna njihova kombinovana upotreba, i činjenice da oni pri kontaktu reaguju jedan sa drugim, jednostavne korekcije u protokolu irigacije kanala korena zuba mogu doprineti uspešnom okončanju endodontske terapije.

Da bi se sprečio nastanak precipitata i eventualno prebojavanje zuba, ne treba dozvoliti da NaOCl i CHX dođu u neposredan kontakt. Zaostali NaOCl posle ispiranja treba ukloniti destilovanom vodom i kanal korena osušiti papirnim poenima pre irigacije sa CHX^{5,22,23,27}. Neke laboratorijske studije su dokazale da alkohol i sirćetna kiselina mogu sprečiti stvaranje precipitata²¹. Do skora je i fiziološki rastvor bio predlagan kao pogodan međuirigans koji uspešno "razdvaja" rastvore za ispiranje kanala korena zuba²⁷. Međutim, izgleda da između CHX i fiziološkog rastvora može postojati interakcija koja se ogleda u stvaranju rastvorljivog beličastog taloga⁶.

Natrijum hipohlorit i EDTA takođe treba koristiti odvojeno: obilna irigacija omogućava da NaOCl ispolji svoje antimikrobno dejstvo, a posle ispiranja sa destilovanom vodom^{5,33} i sušenja kanala, moguće je upotrebiti EDTA za uklanjanje neorganskog debris³⁵.

Slično tome, može se predložiti ispiranje sa destilovanom vodom između EDTA i CHX, kao i sušenje kanala pre uvođenja CHX kao završnog irigansa⁵.

Zaključak

Interakcije između iriganasa u endodonciji i dalje su aktuelna tema i predstavljaju pravi izazov za istraživače. Još uvek je nedovoljno ispitan sastav i priroda produkata interak-

Correction of the irrigation protocol

According to the literature, the recommendation for root canal treatment before obturation is as follows: irrigation with NaOCl to dissolve the organic components, irrigation with EDTA in order to eliminate the smear layer and irrigation with CHX to increase the antimicrobial spectrum of activity and to impart substantivity^{2,9}.

The use of CHX as a final irrigant is fully justified since in this case can best employed: root canal has been cleaned of organic residues and most of the microorganisms (NaOCl), with removed the smear layer (helator) and the possibility that CHX in a favorable environment exhibits characteristic substantivity. This is particularly important in cases where endodontic treatment must be repeated when the expected gram-positive bacteria in canal system².

Since no single solution is able to fulfill these actions completely, therefore, their association is required, and the fact that they react in contact with each other, simple adjustments in the protocol of root canal irrigation can prevent the occurrence of adverse reactions between endodontic irrigants.

In order to prevent the formation of precipitates and possible tooth discoloration, the direct contact of NaOCl and CHX should be avoided. Residual NaOCl should be removed after rinsing with distilled water or saline solution and the root canal should be dried with paper points before irrigation with CHX^{5,22,23,27}. Some laboratory studies have shown that alcohol and acetic acid can prevent the formation of precipitate²¹. Until recently, the saline solution was proposed as a suitable inter-irrigant which successfully "separates" irrigation solutions²⁷. However, it seems that between the CHX and saline may be interaction, which is reflected in the creation of soluble whitish precipitate⁶.

NaOCl and EDTA should also be used separately: abundant irrigation allows NaOCl to demonstrate its antimicrobial activity, and after irrigation with distilled water^{5,35} and the root canal drying, EDTA should be used to remove inorganic debris³⁵.

Separate use of EDTA and CHX is also recommended. It is suggested to rinse the root canal with saline solution or distilled water after the use of EDTA, as well as to dry root canal before the introduction of CHX as a final irrigant⁵.

cije, kao i posledice koje bi ovaj toksičan supstrat mogao imati. Iako postoje preporuke koje uslovno mogu sprečiti stvaranje precipitata, dalja ispitivanja su neophodna da bi se ustanovio klinički prihvatljiv način njegovog uklanjanja u situacijama kada se on ipak formira. S tim u vezi, protokol irigacije podleže novom konceptu u cilju prevencije antagonističkih reakcija i, osim efikasne, omogućavanja i bezbedne irigacije kanalnog sistema zuba.

Conclusion

Interactions between irrigants in endodontics are interesting topic and a challenge for researchers. The nature and composition of precipitates are still not well understood, as well as the consequences that this toxic substrate could have. Although there are recommendations for conditional prevention of precipitate formation, further investigations are necessary to determine the clinically acceptable way to resolve them in situations where they have already formed. In this regard, the protocol subject to the new concept of irrigation in order to prevent antagonistic reactions and provides, except efficient, safe root canal irrigation.

LITERATURA / REFERENCES

- Haapasalo M, Shen Y, Qian W, Gao Y. Irrigation in endodontics. *Dent Clin North Am* 2010;54:291-312.
- Zehnder M. 2006. Root canal irrigants. *J Endod*; 32:389-398.
- Basrani B. Irrigation in endodontic treatment. *Alpha Omegan*. 2011;104:18-25.
- Kandaswamy D, Venkateshbabu N. Root canal irrigants. *J Conserv Dent*. 2010;13:256-264.
- Rossi-Fedele G, Dogramaci EJ, Guastalli AR, Steier L, de Figueiredo JA. Antagonistic interactions between sodium hypochlorite, chlorhexidine, EDTA, and citric acid. *J Endod*. 2012; 38:426-431.
- Prado M, Santos Junior HM, Rezende CM, et al. Interactions between irrigants commonly used in endodontic practice: a chemical analysis. *J Endod*. 2013, 39:505-510.
- Estrela C, Estrela CRA, Barbin EL, Spano JCE, Marchesan MA, Pecora JD. Mechanism of action of sodium hypochlorite. *Braz Dent J* 2002; 13:113-117.
- Stojicic S, Zivkovic S, Qian W, Zhang H, Haapasalo M. 2010. Tissue dissolution by sodium hypochlorite: effect of concentration, temperature, agitation, and surfactant. *J Endod*; 36:1558-1562.
- Mohammadi Z, Abbott PV. The properties and applications of chlorhexidine in endodontics. *Int Endod J* 2009; 42:288-302.
- Mohammadi Z, Abbott PV. Antimicrobial substantivity of root canal irrigants and medicaments: a review. *Aust Endod J* 2009; 35:131-139.
- Rosenthal S, Spangberg L, Safavi K. Chlorhexidine substantivity in root canal dentin. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 98:488-492.
- Kishen A, Sum CP, Mathew S, Lim CT. Influence of irrigation regimens on the adherence of *Enterococcus faecalis* to root canal dentin. *J Endod* 2008;34:850-854.
- Kuruville JP, Kamath P. Antimicrobial activity of 2.5% sodium hypochlorite and 0.2% chlorhexidine gluconate separately and combined, as endodontic irrigants. *J Endod* 1998; 24:472-476.
- Calt S, Serper A. Time-dependent effects of EDTA on dentin structures. *J Endod*. 2002;28:17- 19.
- Gašić J, Dačić-Simonović D, Radičević G, Mitić A, Stojilković G, Daković J. Skening electron mikrofgrafski izgled zidova kanala korena posle uklanjanja razmaznog sloja. *Stom Glas S* 2003;2:65-69.
- Herrera DR, Santos ZT, Tay LY, Silva EJ, Loguercio AD, Gomes BP. Efficacy of different final irrigant activation protocols on smear layer removal by EDTA and citric acid. *Microsc Res Tech* 2013;76:364-369.
- Malheiros CF, Marques MM, Gavini G. In vitro evaluation of the cytotoxic effects of acid solutions used as canal irrigants. *J Endod* 2005;31:746-748.
- Ballal NV, Kandian S, Mala K, Bhat KS, Acharya S. Comparison of the efficacy of maleic acid and ethylenediaminetetraacetic acid in smear layer removal from instrumented human root canal: a scanning electron microscopic study. *J Endod* 2009;35:1573-1576.
- Ballal NV, Kundabala M, Bhat S, Rao N, Rao BS. A comparative in vitro evaluation of cytotoxic effects of EDTA and maleic acid: root canal irrigants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;108:633-638.
- Basrani BR, Manek S, Sodhi RNS, Fillery E, Manzur A. Interaction between sodium hypochlorite and chlorhexidine gluconate. *J Endod* 2007; 33:966-969.
- Marchesan MA, Pasternak B Jr, Afonso MMF, Souza-Neto MD, Paschoalato C. Chemical analysis of the flocculate formed by the association of

- sodium hypochlorite and chlorhexidine. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; 103:e103–105.
22. Bui TB, Baumgartner JC, Mitchell JC. Evaluation of the interaction between sodium hypochlorite and chlorhexidine gluconate and its effect on root dentin. *J Endod* 2008; 34: 181–185.
 23. Akisue E, Tomita VS, Gavini G, Poli de Figueiredo JA. Effect of the combination of sodium hypochlorite and chlorhexidine on dentinal permeability and scanning electron microscopy precipitate observation. *J Endod* 2010;36:847-850.
 24. Basrani BR, Manek S, Matbers D, Fillery E, Sodhi RNS A. Determination of 4-chloroaniline and its derivatives formed in the interaction sodium hypochlorite and chlorhexidine by using gas chromatography. *J Endod* 2010;36:312-314.
 25. Gasic J, Popovic J, Zivkovic S, Petrovic A, Barac R, Nikolić M. Ultrastructural analysis of the root canal walls after simultaneous irrigation of different sodium hypochlorite concentration and 0.2% chlorhexidine gluconate. *Microsc Res Tech* 2012;75:1099-1103.
 26. Vivacqua-Gomes N, Ferraz CC, Gomes BP, Zaia AA, Teixeira FB, Souza-Filho FJ. Influence of irrigants on the coronal microleakage of laterally condensed gutta-percha root fillings. *Int Endod J* 2002; 35:791-795.
 27. Krisbnamurtby S, Sudbakaran S. Evaluation and prevention of the precipitate formed on interaction between sodium hypochlorite and chlorhexidine. *J Endod* 2010;36:1154-1157.
 28. Stratton R, Apicelle M, Mines P. A fluid filtration comparison of gutta-percha versus Resilon, a new soft resin endodontic obturation system. *J Endod* 2006;32(7):642-645.
 29. Prado M, Simao RA, Gomes BP. Evaluation of different irrigation protocols concerning the formation of chemical smear layer. *Microsc Res Tech* 2013;76(2):196-200.
 30. Cintra LT, Watanabe S, Samuel RO, et al. The use of NaOCl in combination with CHX produces cytotoxic product. *Clin Oral Investig* 2013; DOI 10.1007/s00784-013-1049-5.
 31. Matsumoto M, Aiso S, Senoh H, et al. Matsushima T. Carcinogenicity and chronic toxicity of parachloronitrobenzene in rats and mice by two-year feeding. *J Environ Pathol Toxicol Oncol* 2006; 25: 571–584.
 32. Thomas JE, Sem DS. An in vitro spectroscopic analysis to determine whether para-chloroaniline is produced from mixing sodium hypochlorite and chlorhexidine. *J Endod* 2010;36:315-317.
 33. Nowicki JB, Sem DS. An in vitro spectroscopic analysis to determine the chemical composition of the precipitate formed by mixing sodium hypochlorite and chlorhexidine. *J Endod* 2011;37:983-988.
 34. Chhabra RS, Huff JE, Haseman JK, Elwell MR, Peters AC. Carcinogenicity of p-chloroaniline in rats and mice. *Food Chem Toxicol* 1991;29:119–124.
 35. Grawehr M, Sener B, Waltimo T, Zehnder M. Interactions of ethylenediamine tetraacetic acid with sodium hypochlorite in aqueous solutions. *Int Endod J* 2003;36:411–415.
 36. Clarkson RM, Podlich HM, Moule AJ. Influence of ethylenediaminetetraacetic acid on the active chlorine content of sodium hypochlorite solutions when mixed in various proportions. *J Endod* 2011;37:538-543.
 37. Grande NM, Plotino G, Falanga A, et al. Interaction between EDTA and sodium hypochlorite: a nuclear magnetic resonance analysis. *J Endod* 2006;32:460–464.
 38. Ahmed HM, Abbott PV. Discolouration potential of endodontic procedures and materials: a review. *Int Endod J* 2012;45:883-897.
 39. Ballal NV, Moorkoth S, Mala K, Bhat KS, Hussien SS, Pathak S. Evaluation of chemical interactions of maleic acid with sodium hypochlorite and chlorhexidine gluconate. *J Endod* 2011; 37:1402-1405.
 40. Rasimick BJ, Nekich M, Hladek M, Musikant BL, Deutsch AS. Interaction between chlorhexidine digluconate and EDTA. *J Endod* 2008;34:1521–1523.
 41. Gonzalez LS, Camejo AD, Sanchez SP, Bolanos-CV. Effect of CHX on the decalcifying effect of 10% citric acid, 20% citric acid, or 17% EDTA. *J Endod* 2006; 32:781–784.