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Chelating Agents In Endodontics :An Overview

[1]Farheen Akhtar , [2]Bonny Paul , [3]Mantri Shivkumar , [2]Kavita Dube , [4]Charu Kapur [1]Ankita, [1]Niharika Singh

[1]Post Graduate, Department of Conservative dentistry and Endodontics, Hitkarini Dental College, Jabalpur, M.P, India.

[2] Professor, Department of Conservative dentistry and Endodontics, Hitkarini Dental College, Jabalpur, M.P, India.

[3]Professor and Head, Department of Conservative dentistry and Endodontics, Hitkarini Dental College, Jabalpur, M.P, India.

[4]Senior Lecturer, Department of Conservative dentistry and Endodontics, Hitkarini Dental College, Jabalpur, M.P, India.

Corresponding Author: Dr Bonny Paul, Professor, Department of Conservative dentistry and Endodontics, Hitkarini Dental College, Jabalpur, M.P, India

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Abstract

Chelating agents were developed in endodontics as an aid for preparation of narrow and calcified root canals. Clinically chelating agents are used along with irrigating solutions to facilitate root canal instrumentation and to remove the smear layer. The main purpose for removal of the smear layer is to eliminate the micro-organisms from the root canal and disinfect the open dentinal tubules. Various chelating agents like EDTA , chitosan, peracetic acid, maleic acid, citric acid and etidronate have potential to maximize root canal disinfection. This article presents an overview of chelating agents and focusing on its relevance in endodontics.

Keywords: Chelating agents, Chitosan, Citric acid Ethylenediaminetetraacetic acid, Etidronate, Maleic acid, Peracetic acid , Phytic acid.

Introduction

Endodontic treatment depends on access opening, cleaning and shaping , disinfection and sealing of the root canal.[1] Biomechanical preparation is an important aid for successful endodontic treatment and it is based on the use of chelating agent, irrigating solutions and proper root canal instrumentation.[2] An amorphous ,irregular and granular layer is produced during biomechanical preparation. This layer is termed as "smear layer" which contains inorganic debris, organic material like pulp tissue , necrotic debris, odontoblastic process , coagulated proteins, blood cells, nerve fibers, collagen, tissue fluid, microorganisms and their byproducts. Presence of smear layer causes microleakage, acts as a barrier between canal walls and filling materials and reduces dentinal permeability.[3] There are many reasons for use of chelating agents along with irrigating solutions during biomechanical preparation such as removal of debris and inorganic phase of smear layer , difficulty of penetration of the instruments in calcified root canal, prepared in a dentinal walls for better adhesion of filling materials etc .[1] The efficiency of chelating agent depends on various factors such as root canal

length ,pH , hardness of the dentin ,duration of application and concentration of chelating agents.[4]

Several chelating agents has been introduced such as ethylenediaminetetraacetic acid (EDTA), peracetic acid, etidronic, citric acid, maelic acid,phytic acid, chitosan .

History of Development Of Chelators

In 1951, Hahn & Reygadas , Screebny & Nikiforuk were the first who reported the demineralizing effect of EDTA on dental hard tissues. In 1957, Nygaard-Ostby were the first who introduced in endodontics and who suggested the use of 15% EDTA solution (pH 7.3) with following composition

- Disodium salt of EDTA (17.00g)
- Aqua dest.(100.00 ml)
- 5M sodium hydroxide (9.25 ml)

After a fews years detergent was added to increase cleaning and bactericidal capability of EDTA solution . In 1963 Von der Fehr & Nygaard-Ostby introduced EDTAC. EDTAC is developed when EDTA is mixed with 0.84g of quarternary ammonium compound (Cetavlon; Goldberg Abramovich ,1977) and the aim of this addition is to reduce surface tension of the irrigant, facilitate wetting of root canal and increase ability to penetrate chelators in dentine.

Initially liquid chelator were used as irrigation during biomechanical preparation of root canal. In 1969, Stewart et al introduced paste type chelating agent i.e RC-Prep(premier Dental ; Philadelphia, PA, USA).[5]

Ethylenediaminetetraacetic Acid (EDTA)

EDTA is a polyaminocarboxylic acid. The chemical formula of EDTA is $(HO_2CCH_2)_2NCH_2CH_2N(CH_2CO_2H)$. The properties of EDTA is self limiting , non toxic ,colorless , biocompatible and water soluble solid . It acts as a lubricant,chelator and decalcifying agent . It helps in bypassing of broken instrument . EDTA binds to metals with four carboxylate and two amine groups and forms strong complexes with Mn(II),Cu(II),Fe(III) and Co(III). EDTA is the most effective chelating agent in endodontic therapy.15-17% EDTA solution is recommended for final irrigation of the root canal.[11] 17% EDTA is the most common concentration used for endodontic therapy. EDTA causes necrosis of pulp remnants ,inflammatory reaction of periapical tissue and erosion of peritubular and intertubular dentin .[5]

Endodontic smear layer has been formed during biomechanical preparation.The smear layer plays an important role in adhesion of root canal sealer and gutta percha to the root canal walls and apical leakage .In 1963,Nygaard-Ostby et al reported that EDTA decalcified dentin to a depth of 20-30 micrometer in 5min. Gin Chen et al in 2011 recommended liquid EDTA to be used as a final flushing solution during root canal preparation because it provides better smear layer removal before obturation.[19] SemraCalt et al suggested that EGTA be used as an alternative chelating agent. Based on the findings 10ml of 17% EDTA would completely remove the smear layer and EGTA was somewhat effective in removing the smear layer but the results indicated that EDTA action is stronger than that of EGTA. Hengameh Ashraf et al in 2014 compared effectiveness of 17% EDTA with 18% etidronate and Er: YAG in the removal of smear layer. Findings revealed that 17% EDTA was effective in

removal of smear layer than Er: YAG laser and 18% etidronate.[16]

Combination of EDTA and NaOCl was recommended for effective removal of both organic and inorganic components of smear layer[4]. Baumgartner and Mader et al revealed EDTA and NaOCl caused progressive dissolution of peritubular and intertubular dentin , so the diameter of tubular orifices were enlarged to2.5 to 4µm.Yamada et al suggested EDTA and NaOCl should be applied in 10ml of volume.[18] Teixeria et al compared the combination of EDTA and NaOCl in 1, 3 and 5 min application times and it was concluded that 1 min application time of EDTA and NaOCl is sufficient.[17] EDTA maintained its ability to chelate calcium in presence of NaOCl whereas tissue dissolution property of NaOCl was reduced. When EDTA was added to NaOCl solution the content of free chlorine was reduced from 0.50-0.06% ,so the authors concluded EDTA and NaOCl were to be used separately during instrumentation.[5]

Chitosan

Chitosan is a natural polysaccharide. It was obtained by acetylation of chitin, which was found in shells of crabs and shrimps (Kurita 1998). Chitosan is a derivative of chitin and produced by deacetylation of chitin in high alkaline conditions .[15] It is a linear polymer of α(1→4)-linked 2-amino-2-deoxy- β -D-glucopyranose. It is derived from N-deacetylation and characterized by the degree of deacetylation and copolymer of N-acetylglucosamine and glucosamine. Glycol chitin and a partial *o*-hydroxyethylated chitin were the first derivatives of chitosan. Chitosan is produced from crustacean shells and this crustacean shells contain quantities of astaxanthin and carotenoid. Crustacean shells involves the removal of proteins and dissolution of calcium carbonate . Chitosan have excellent properties such as biodegradability ,biocompatible ,non-toxicity and adsorption .Chemical modifications, graft reactions ,ionic interactions have been made to prepare functional derivatives of chitosan . Chitosan is only soluble in aqueous solutions of such some acids and selective N-alkylidinations and N –acylation.Four steps has been needed to produce chitosan from crustacean shells:

1. Deproteinization
2. Demineralization
3. Decolouration
4. Deacetylation

Chemically chitosan are linear polymine. They have reactive amino and hydroxyl groups and chelates many transitional metal ions .Biologically chitosan are biocompatible and binds to mammalian and microbial cells aggressively. They have regenerative effect on connective gum tissue and accelerates the formation of osteoblast responsible for bone formation. They also are hemostatic, fungistatic , spermicidal, antitumor, anticholesteremic, immunoadjuvant and central nervous system depressant.

The applications for chitosan are as follows-

1. Medicine and pharmaceuticals (antibacterial and antitumour agent ,drug carrier ,wound healing accelerator)
2. Biotechnology (enzyme and cell carrier ,chromatography resin)
3. Environment (water treatment)
4. Agriculture (seed preparation)
5. Cosmetics and food(iron and calcium absorption accelerator ,fibre source)[6]

Etidronate

Bisphosphonate have a calcium chelating property and have similar structure with pyrophosphate. The structure of pyrophosphate can chelate the divalent cations (Ca^{+2}).It has strong remodelling bone affinity.The bone remodeling perform at three levels .

1. At tissue level – It decreases bone resorption and number of formation of bone cells .So it can leads to decrease in bone activity.So, positive bone balance is maintained.
2. At cellular level –It decreases osteoclast in recruitment , increases the osteoclast apoptosis ,decreased osteoclast adhesion , decrease in depth of resorption site, decreased in release of cytokines by the macrophages and increase the number of osteoblast and differentiation.
3. At molecular level – It inhibits the mevalonate pathway which is an important cellular metabolic pathway present in all higher eukaryotes and many bacteria.

Systemically bisphosphonates are administered in patients who are suffering from osteoclastic bone resorption , neoplastic disease , osteoporosis, Pagets disease , multiple myeloma ,breast cancer and prostate cancer. Now a days, it can be used as a chelating agent because of fewer adverse effects on root dentin . It is a weak chelating agent. Etidronate is not only used as a chelating agent ,but also can be used in household , personal products such as soap and toothpaste to control calculus formation. Zehnder et al was the first investigator who used etidronate for smear layer removal. Chelation effect of HEBP depends on concentration because it has constant calcium-binding capacity.[3][16] HEBP can be mixed chair side with NaOCl without fearing any loss of NaOCl activity.[7]

Citric Acid

Citric acid is another chelating agents which is used to eliminate smear layer after root canal preparation. 10-50% concentration of citric acid is used in endodontic therapy. Zehnder et al proved that 10% concentration citric acid was less toxic and effective for removal of smear layer. Citric acid is used along with NaOCl so, it reduces the availability of free chlorine and effect on bacteria and organic tissue.[10] Citric acid reacts with metal to form a nonionic soluble chelate. In operative dentistry citric acid has been proposed as a mild etchant for dental hard tissue, particularly for dentinal conditioning and enhanced smear layer and smear plug removal(Hennequin et al ,1994).[8] It is also used in periodontal therapy for conditioning dentin.[15] Citric acid is less cytotoxic. It is biocompatible to the tissue and helps in cemenum formation and periodontal tissue regeneration.[12] Citric acid is a weak organic acid .

Peracetic Acid

Peracetic acid has antibacterial, sporicidal, antifungal and antiviral properties. The explanation for antibacterial properties is its oxidizing action which leads to denaturation of protein, disruption of cell membrane, sulfhydryl oxidation and formation of sulfur bonds in proteins, enzymes and other metabolities.It has the potential to inactivate bacteria, fungi, yeast at low concentration etc. Peracetic acid can be clinically advantageous for bacteriocidal effect and the removal of smear layer. Peracetic acid remains in equilibrium with hydrogen peroxide, acetic acid and acetylhydroperoxide. Acetic acid is responsible for

removal of smear layer.2.25% Peracetic acid is effective in removal of smear layer. When PAA comes in contact with oral mucosa it may cause burn and irritation to oral mucosa . So,low concentration of PAA is better to use.[13]

Phytic Acid

Phytic acid is a major storage form of phosphorous(IP6 ,inositol hexakisphosphate) in plant seeds and bran that contributes to a wide variety of cellular functions . It also present in mammalian cells in concentration ranges from 10-100 mmol/L. Phytic acid has multiple negative charges ,making efficient chelating agent of multivalent cations such as Ca^{+2}, magnesium and iron. IP6 can be extracted with low cost from rice bran.[14]

Maelic Acid

Maleic acid is a mild organic acid which is used as an acid conditioner in adhesive dentistry.Maleic acid has ability to remove smear layer.It is also used as acid etchant in restorative dentistry.[9]

Conclusion

The effectiveness of chelating agent depends on application time , concentration, root canal wall surface area and amount of available chelating agent. Increased application time of chelating solution will leads to increased Ca^{2+} ions removal, more erosive effect of peritubular and intertubuar dentin, more dentin surface roughness , decreased dentin microhardness ,decreased bond strength between root canal sealers and dentinal wall. Some of the studies reported that EDTA , citric acid,peracetic acid , maleic acid are stronger chelating agents than etidronate.

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Abbreviations:

EDTA: Ethylenediaminetetraacetic acid , EDTAC : Ethylenediaminetetraacetic acid plus cetavlon , EGTA :Egtazic acid , Er:YAG : Erbium-doped yttrium aluminium garnet, HEBP :1- hydroxyethylidene-1, 1-biphosphonate , NaOCl: Sodium hypochlorite, PAA: Peracetic acid