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Calcium Hydroxide as an Intracanal Medicament –A Review

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Abstract: *The ultimate goal of endodontic therapy is to eradicate the microbes residing in the root canal system.Calcium hydroxide has been included in antimicrobial formulations that are used in several treatment modalities in endodontics, one such application as an inter-appointment intracanal medicament.The purpose of this article was to review mechanisms and the properties of calcium hydroxide in endodonticsas a medicament. Calcium hydroxide has a high alkaline pH and the lethal effects of calcium hydroxideon bacterial cells are due to protein denaturation and damage to DNA and cytoplasmic membranes.Calcium hydroxide is effective against common endodontic pathogens but is less effective against.Enterococcus faecalis and Candida albicans.Calcium hydroxide is also a valuable growth anti-endotoxin agent.However, its effect on microbial biofilms remainscontroversial.*

Keywords: *Calcium hydroxide, intracanal medicament,antimicrobial.*

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I. Introduction

Intracanal medicament is an antimicrobial agent placed inside the root canal between treatment appointments to destroyremainingmicroorganismsandpreventreinfection[1].Theyareusedtokillbacteria,reduceinflammation and pain,eliminatesapical exudate, control inflammatory root resorption [2].Endodontic treatment requires the use of intracanal medicaments in addition to instrumentation that simultaneously eliminate bacteria, prevent their,stop their ingress and cut off their nutrient supply[2].Calcium hydroxide is most commonly used as an intracanal medicament for disinfection of the root canals since its introduction by Herman in1920.

II. CalciumHydroxide

A white odorless powder with low solubility in water , which decreases as the temperature rises. The dissociation coefficient of calcium hydroxide $Ca(OH)_2$ permits a slow, controlled release of both calcium and hydroxyl ions,the low solubility to become soluble in tissue fluids when in direct contact with vital tissues[2].A high pH (about 12.5-12.8), insoluble in alcohol, and is a strong base.

It is used in endodontics like inter-appointment intracanal medicaments, pulp-capping agents, root canal sealers, treatment of root perforations, root fractures,rootresorptions, tooth avulsion and luxation injuries[3].Thisreviewhighlightsthemechanismofactionofcalciumhydroxide,variouspropertiesofcalcium hydroxide as an intracanal medicament in endodontics,placement andretrival.

2.1.Mechanism of action ofCalcium Hydroxide

The application of calcium hydroxide paste at intervals of at least 7 days is able to eliminate or reduce the number of bacteria surviving even after biomechanical preparation.The main actions of calcium hydroxide come from the ionic dissociation of $Ca^{2+}$and OH^- ions, and the action of these ions on vital tissue and bacteria generates the induction of hard tissue deposition and the antibacterial effect[4]. However, when Ca^{2+} ions come into contact with carbondioxide (Co_2) or carbonate ions (Co^{3-}) in tissue, calcium carbonate is formed which alters the mineralization process by the overall consumption of the Ca^{2+}ions.

The high pH and the ionic activity in healing process, diffusion through dentinal tubules, influence on apical microleakage and placement within the root canal, interim flare-ups, the importance of periodic follow-up,redressingandinter-appointmentrestoration[4].Thehydroxylions presentprovideanalkalineenvironment, highly oxidant free radicals which helps in early healing and has an antimicrobialaction[5].

The lethal effect of calcium hydroxide is caused by damage to bacterial cytoplasmic membrane,proteindenaturation and DNA damage,Co2 adsorption,mineralization and neutralization of acids following inflammatory process.

III. Propertiesof Calcium Hydroxide as IntracanalMedicament

3.1Anti-bacterial activity

Calcium hydroxide will exert an antibacterial effect in the root canal system as long as a high pH is maintained[6]. Lin *et al.* reported that treatment with electrophoresis was significantly more effective than pure $Ca(OH)_2$ up to depths of 200–500μm. Specimens treated with electrophoretically activated $Ca(OH)_2$ revealed no viable bacteria in dentinal tubules to a depth of 500 μmfrom the root canal space within days[7].
Waltimo*et al.* found that a $Ca(OH)_2$ dressing between appointments did not have the expected effect in terms of disinfection of the root canal system nor the treatment outcome[8].$Ca(OH)_2$ against E. *faecalis*is aeffective medicament[14] when used in combination of Sodium hypochlorite (NaOCl) or Chlorhexidine(CHX).
The lethal effects of hydroxyl ions on bacterial cells are probably due to the following mechanisms[9]

3.1.1 Damage to bacterial cytoplasmicmembrane
Hydroxylionsinducelipidperoxidationresultingindestructionofphospholipidstructureofcellularmembrane, removehydrogenatomsfromunsaturatedfattyacidgeneratingfreelipidradicalreactswithoxygenresultingin formation of lipid peroxide radical which removes another hydrogen atom from a second fatty acid generating another lipid peroxide. These act as free radicals initiating an autocatalytic chain reaction resulting in further loss of unsaturated fatty acids and extensivedamage.

3.1.2 Protein denaturation and DNAdamage
Cellular metabolism is highly dependant on enzymatic activities. The alkaliniation provided by calcium hydroxide induces breakdown of ionic bond that maintains tertiary structure of proteins. These changes result in loss of biological activity of the enzyme and disruption of the cellular metabolism. Damage to the bacteria DNA and induce splitting of strands and replication inhibited.

3.2 Bactericidal property

$Ca(OH)_2$ is bactericidal on direct contact with most bacteria but not active against E faecalis and Pseudomonas aeruginosa. Asgary tested $Ca(OH)_2$ against P.aeruginosa,E. faecalis,Staphylococcusaureus and Escherichia coli and found it to inhibit growth of these bacteria[10].

3.3 Anti-endotoxinactivity

Endotoxin, part of cell wall of all gram-negative bacteria,composed of lipopolysaccharide(LPS),one of the concerns in endodontics is the treatment of teeth with necrotic pulps and periapicalpathosis because post-treatment disease persists more often than in cases without periapical disease[12].In chronic periapicallesions,greater prevalence of gram-negative anaerobic bacteria disseminated throughout the root canal system including apical bacterial biofilm because these areas are not reached by instrumentation, the use of a root canal medicament is recommended to aid in the elimination of these bacteria thus increasing clinical success[11].The procedures and medicaments used in root canal treatment should not only lead to bacterial death, but also to the inactivation of bacterial endotoxin.

Buck *et al*. (2001) found that long-term $Ca(OH)_2$ as well as 30-min exposure to an alkaline mixture of CHX, ethanol and sodium hypochlorite did detoxify LPS molecules by hydrolysis [12].

Tanomaru*et al*,evaluated the effect of biomechanical preparation using different irrigating solutions and a $Ca(OH)_2$ based root canal dressing containing endotoxin. Biomechanical preparation with only irrigating solutions did not inactivate the endotoxin but with the use of the $Ca(OH)_2$ dressing was effective in the inactivation of the toxic effects ofendotoxin.

Oliveira *et al* evaluated the effects of calcium hydroxide and polymyxinB on endotoxins in root canals.The calcium hydroxide and polymyxin Bintracanal medicaments detoxified endotoxin in root canals and altered the properties of LPS to stimulate the antibody production by B-Lymphocytes[13].

3.4 Antifungalactivity

Weckwerth*et al* (2012) determined the incidence of *C.albicans*in the oral cavity and the susceptibility of isolates to different pH values and saturated calcium hydroxide aqueous solution at pH 12.5 were tested [14]. In relation to time variables yeast viability was assessed by the Sabouraud's agar culture and Fluorescein diacetate and ethidium bromide fluorescent staining method[15].The yeasts became completely inviable after 48 h of contact with the calcium hydroxide solution when exposed to the alkaline culture broth, the yeasts were found to be viable at pH 9.5 and 10.5 for up to 7 days.*C. albicans*can only be completely inhibited by direct contact with saturated calcium hydroxide aqueous solution after 48 h of exposure.

Euchua*et al* (2014) investigated the antifungal activity of propolis, triple antibiotic paste (TAP), 2% chlorhexidinegel and calcium hydroxide with propylene glycol on Candida albicans-infected root canal dentinal tubules at two different depths (200 μmand 400 μm) and two time intervals (day 1 and 7) by culture method. It was concluded that calcium hydroxide with propylene glycol and 2% CHX gel against C.albicanson day 1 at 400 μmdeep inside the dentinal tubules, but equally effective after 7 days at both depths[16].

3.5 Anti-inflammatoryaction

The elevated pH of $Ca(OH)_2$ inhibits the substrate adherence capacity of macrophages and decreases or eliminates the amount of MMP-8, improving tissue circulation and controlling exudation as immunomodulatoryeffect.Endogenous inflammatory mediators like Interleukin- 1α and TNF-α play a role in regulation of inflammation, tissue destruction and denaturation of proinflammatory cytokines.[17].

3.6 Action againstbiofilm

In endodontics, the biofilm is on apex of teeth with necrotic and infected pulps or pulpless and infected rootcanal systemssuchbacterialaggregationshavebeenthoughttobethecauseoftherapy-resistantapicalperiodontitis[18] bacterial condensations on the walls of infected root canals have beenobserved[24].

Saber *et al* developed a mature biofilm of Enterococcus faecalis inside the root canal system and to test its susceptibility to amoxicillin + clavulanate, ciprofloxacin,clindamycin, doxycycline and calcium hydroxide as intracanal medications for 1 week. All the chemotherapeutic agents used were significantly better than calcium hydroxide in elimination of biofilm bacteria[19].

Athanassiadis*etal*(2010)hadtestedthepulpdentpaste,ledermixpaste,a50:50ledermixandpulpdentmixture, and a replica of ledermix paste. Bases included methyl cellulose with water, polyethylene glycol (peg), and peg with zinc oxide, calcium chloride and the other components (inactives) that make up the ledermix paste base.Results showed that calcium hydroxide containing preparations had greater potential for reducing the survival of *E.faecalis*in a biofilm[20].

3.7 Physicalbarrier

In addition to eliminating remaining viable bacteria unaffected by the chemomechanical preparation of the root canal, intracanal medicaments have been advocated for other reasons. They should also act as a physicochemical barrier, precluding the proliferation of residual microorganisms and preventing the reinfection of the root canal by bacteria from the oral cavity[21].

IV. Placementof $Ca(OH)_2$as amedicament

Calcium Hydroxide should come in contact for tissues to act. Mixture should be thick to carry $Ca(OH)_2$ particles[9].Formaximum effectiveness therootcanalisfilledhomogeneouslytillrootlengthwithaidof syringes,finger spreader ,rotary Lentulo spiral and PasteCarriers.

Recently,single paste system which is injectable is available and most preferable method.Some of the products are Centrix,Calcijet,Prevestcallc,Pyraxcalci.

V. Combinationswith CalciumHydroxide

5.1Combination of Calcium Hydroxide and SodiumHypochlorite

Metzler demonstrated that long-term (7 days) pretreatment with pulpdent paste (Watertown, USA), a non-setting $Ca(OH)_2$ paste, followed by sodium hypochlorite irrigation cleaned canal isthmuses in mandibular molars better than hand instrumentation alone.The amount of debris was reduced in teeth treated with NaOcl for >30s or $Ca(OH)_2$ for 7 days. However, the combination of $Ca(OH)_2$ and NaOcl was more effective than the separate treatments[22].

5.2 Combination of Calcium Hydroxide andChlorhexidine

Chlorhexidine is a cationic biguanide whose optimal antimicrobial activity is achieved within a pH range of 5.5–7.0 and alkalinizing the pH by adding $Ca(OH)_2$ to CHX will lead to precipitation of CHX molecules, thereby decreasing its effectiveness.Athanassiadiset al demonstrated that the alkalinity of $Ca(OH)_2$when mixed with CHX remained unchanged when used as an intracanal medicament, CHX was more effective than $Ca(OH)_2$ in eliminatingE.Faecalisfrominsidedentinaltubulesbymixing$Ca(OH)_2$withCHXtheantimicrobialactivityof$Ca(OH)_2$ isincreased[23].

VI. Effectsof CalciumHydroxide

6.1Diffusion of hydroxyl ions throughdentin

Nerwich et al. investigated pH change over a 4-week period after application of a $Ca(OH)_2$ dressing Concluded that hydroxyl ions derived from $Ca(OH)_2$ dressings diffused in a matter of hours into the inner root dentin,required 1–7 days to reach the outer root dentine and 2–3 weeks to reach peak levels.Hydroxyl ions diffused faster and reached higher levels cervically more than apically[24]. For calcium hydroxide to act effectively as an intracanal medicament, hydroxyl ions must be able to diffuse through dentin.

Saif et al.indicated that a final canal rinse with 3 ml 17% EDTA and 10 ml 6% NaOcl before $Ca(OH)_2$ placement allowed the greatest hydroxyl ion diffusion to the root surface.Diffusion of hydroxyl ions through dentine depends on the period of medication,diameter of dentinal tubules and smear layer removal (patency of dentinal tubules)[25].

6.2Buffering effect of dentin on CalciumHydroxide

Haapasalo et al. said the root canal is a complex mixture of a variety of organic and inorganic components.Hydroxyapatite is the major representative of the inorganic components.Pulptissue,micoorganisms and inflammatory exudate, rich in proteins such as albumin are the major organic components.

A new dentin powder model for studying the inhibitory effect of dentin on various root canal irrigants and medicaments.Dentin, hydroxyapatite and remnants of necrotic pulp tissue as well as inflammatory exudate decrease the antibacterial potential of $Ca(OH)_2$[26].

6.3Effect of Calcium Hydroxide on dentin fracturestrength

The flexural strength of dentin depend on link between two main components of dentin, the hydroxyapatite crystals and the collagenous network.The organic matrix is composed of acid proteins and proteoglycans containingphosphateandcarboxylategroups.Thesesubstancesmayactasbondingagentsbetweenthecollagen network and the hydroxyl apatitecrystals.

Doyon*et al.* examined the resistance of human root dentin with $Ca(OH)_2$ and found that the fracture resistance of dentin was decreased significantly after 6 months[27].

Rosenberg *et al.* (2017) measured the effect of $Ca(OH)_2$ on the microtensile fracture strength (MTFS) of teeth and found that it was reduced by almost 50% following 7–84 days of application[28].

MaríaPacios (2014) evaluated effect of $Ca(OH)_2$ pastes and their vehicles on microhardness of root canal dentin. The vehicles are: distilled water, chlorhexidine, articaine in the anesthetic solution, propylene glycol, monochlorophenol and monochlorophenol - propylene glycol.Samples exposed to the medicaments for 3, 7, and 14 days and microhardness measured using Vickers microhardness machine. It was concluded that all vehicles and pastes, except distilled water,significantly decreased the microhardness of the root dentin;However, calcium hydroxide + camphorated monochlorophenol - propylene glycol and Camphorated monochlorophenol - propylene glycol showed the highest decrease[29].

VII. Efficient methods to remove the IntracanalMedicament

Use of patency filing,combining with type of vehicle used for dilution,EDTA and NaoCl with hand instrumentation and Ultrasonics.

VIII. Conclusion

Calcium hydroxide as an intracanal medicaments has a great value in endodontics, indicated for several clinical scenarios due its varied properties.However poses limitations of reduced antibacterial spectrum that is not effective against the wide range of endodontic microbiota and in disinfecting the entire root canal system after a short-term use. Although numerous materials have been tried for this purpose calcium hydroxide still holds promise and a sets a comparable standard for other evolving materials even today.

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