Meghna Nag et al /J. Pharm. Sci. & Res. Vol. 11(9), 2019, 3210-3216

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Chlorhexidine Loaded Calcium Hydroxide as a Potential Antimicrobial Intracanal Medicament – A Systematic Review

Meghna Nag[1], Dr. N.DivyaLalitha[2] , Dr. Sunayana Manipal[3] , Dr. Bharathwaj.V.V[4] , Dr. Rajmohan[3] ,Dr. Prabu.D[5]

[1]Undergraduate, [2]Postgraduate, [3]Reader, [4]Senior Lecturer [5]Professor & Head,
Department of Public Health Dentistry, SRM Dental College.

Abstract:

Background: A successful Root Canal Therapy (RCT) is only possible when the disease causing organisms can either eradicated or reduced to a count which is no longer able to cause infections within the canals. The complexity in the morphology and design of the root canal also making it slightly difficult as compared to other dental surgeries. Chlorhexidine is one of the commonly used antimicrobials and Calcium Hydroxide being a known pulp capping agent. There this combination could eradicate the excess microorganisms causing secondary infection in pulp capping as well as endodontic procedures. The aim of this study was to compare and study the effects of Chlorhexidine loaded Calcium Hydroxide as a potential antimicrobial intracanal medicament.

Methods: A systematic review of the records containing studies comparing the efficacy of this combination or the individual components in comparison to other intracanal medicaments. A literature review was performed using Pubmed, Elsevier Science Direct, Cochrane library, Wiley online library and additional sources. A total of 128 articles were screened, out of which only 6 articles were related to the topic of interest and were thoroughly studied for an outcome. **Results:** After thoroughly studying the articles, it was found that the combination is indeed a very useful one in the field of conservative dentistry and endodontics. Both the individual combinations are extremely strong, and its combination could improve the prognosis of pulp capping and other endodontic therapies.

Conclusion: Chlorhexidine loaded Calcium Hydroxide can be used as pulp capping material. It can also be used as an intracanal medicament in endodontic procedures.

Keywords: Chlorhexidine, Calcium hydroxide, Intracanal medicament, Antimicrobial

INTRODUCTION:

Microorganisms are considered to be the most important etiology behind pulpal, periapical and endodontic infections along with Root Canal Therapy (RCT) failures. For a successful RCT, an intracanal medicament along with proper instrumentation is a must. A medicament is an effective antimicrobial which is placed within a root canal to disinfect it and prevent it from further secondary infections. It is known that along with the bacteria, the complex anatomy of root canals also helps in harboring bacteria and supports their growth, multiplication and interaction. Calcium hydroxide has been shown to not exert any antimicrobial property. [1]For a successful endodontic treatment, the reduction or elimination of infection is one of the most important criteria.[2]In Apical Periodontitis cases, infection can still persist post an endodontic treatment in the dentinal tubules, lateral canals, secondary canals, apical delta ramifications, apical root cementum surface that extends from the root canal lumen. [2]

Calcium Hydroxide (CaOH2) is a chemically strong base with high pH (12.5-12.8). The main antimicrobial property is the ability to release hydroxyl ions in an aqueous environment. [2]It can cause protein denaturation and damage to bacterial DNA and cytoplasmic membrane. [2] Even though it has excellent properties such as tissue compatibility, antimicrobial activity and ability to neutralize bacterial endotoxins, other components are often added to it to broaden its spectrum. [2] Recent studies have shown that the combination of calcium hydroxide and Chlorhexidine (CHX) has good efficiency as a potential antimicrobial agent.

Chlorhexidine is a broad spectrum antimicrobial which is quite commonly used as a mouthwash agent and has been shown to have good efficiency against anaerobic organisms. It has properties like biocompatibility, substantivity and a wide spectrum against bacteria, fungi and viruses including those present in root canals. [2]As a root canal irrigant and intracanal medication, CHX has an antimicrobial efficacy comparable with that of Sodium Hypochlorite. [3]The combination has also proven to be useful against CaOH2 resistant microorganisms. [3] CaOH2 with 0.5% CHX has been shown to eliminate Candida albicans. [3]This combination tested against bacterial species and was effective against Enterococcus faecalis.[4]

E. faecalisis a normal inhabitant of the oral cavity. The prevalence of E. faecalis is increased in oral rinse samples from patients receiving initial endodontic treatment, those midway through treatment, and patients receiving endodontic retreatment when compared to those with no endodontic history. E. faecalis is associated with different forms of periradicular disease including primary endodontic infections and persistent infections. [4]

Previous studies have shown that not only is this combination effective against treatment, but also in retreatment procedures like re-root canal therapies. [4] It has been shown that CaOH2 applied at intervals of at least 7 days is able to eliminate or reduce the bacterial count surviving even after biomechanical preparation. [4]It also helps in neutralizing lipopolysachharides and helps in cleansing the root canal. [5]Also, the main microorganisms E. faecalis is a very persistent organism due to its ability to form biofilm, which makes them resistant to phagocytosis, antimicrobial agents and antibodies. [6]Despite both these materials having their individual potentials, several microorganisms including E. faecalis are resistant to their effects, making the combination a very interesting and important finding for good prognosis of root canal therapies.

A very useful and convenient way of inserting this combination is in the form of a paste which can be loaded in gutta-percha points which are used in root canal therapies. [7]Gutta Percha points impregnated with various root canal irrigants have been tested in various studies to determine the efficiency. In all, any dental procedure should be aimed at good prognosis of the affected site of the oral cavity along with maintaining an overall oral hygiene and systemic well being of the patient. This systematic review aims at determining the efficacy of Chlorhexidine loaded Calcium Hydroxide microparticles as antimicrobial intracanal medicament.

MATERIALS AND METHOD:

OBJECTIVE:
To characterize Chlorhexidine loaded Calcium Hydroxide as a potential antimicrobial intracanal medicament.

STUDY DESIGN:
"A SYSTEMATIC REVIEW ON CHLORHEXIDINE LOADED CALCIUM HYDROXIDE AS A POTENTIAL PULP CAPPING MATERIAL.

INCLUSION CRITERIA:-
1. Studies containing Calcium Hydroxide and Chlorhexidine in combination were included.
2. In-vitro studies included.
3. Full text articles were included.

EXCLUSION CRITERIA:-
1. Review articles were excluded.
2. Articles emphasizing on Chlorhexidine were excluded.
3. Articles emphasizing on Calcium Hydroxide were excluded.
4. Randomized Control Trials were excluded.

SEARCH STRATEGY:-
Published articles were studied thoroughly for the characterization of Chlorhexidine loaded Calcium Hydroxide as a potential pulp capping material. Articles from databases like Pubmed, Elsevier Science Direct, Cochrane library, Wiley online library, scopus and additional sources were included in the study. The articles collected for analysis were searched using MeSH terms "the characterization of Chlorhexidine loaded Calcium Hydroxide as a potential pulp capping material. According to the guidelines, the terms were altered in every search engine to obtain results which varied from a few to too many.

INCLUDED DATABASES:
-PUBMED
-ELSEIVER SCIENCE DIRECT
-COCHRANE LIBRARY
-WILEY ONLINE LIBRARY
-SCOPUS
-Other additional sources

RESULTS:
A total of 128 articles based on the topic were identified. Of these 93 were detected as duplicated and extracted. After extraction of the duplicates, the remaining articles were screened thoroughly and 35 full text articles were independently assessed. With the application of inclusion and exclusion criteria, 6 studies were included in the systematic review as qualitative research. Figure 1 shows the flow diagram of the above work down.

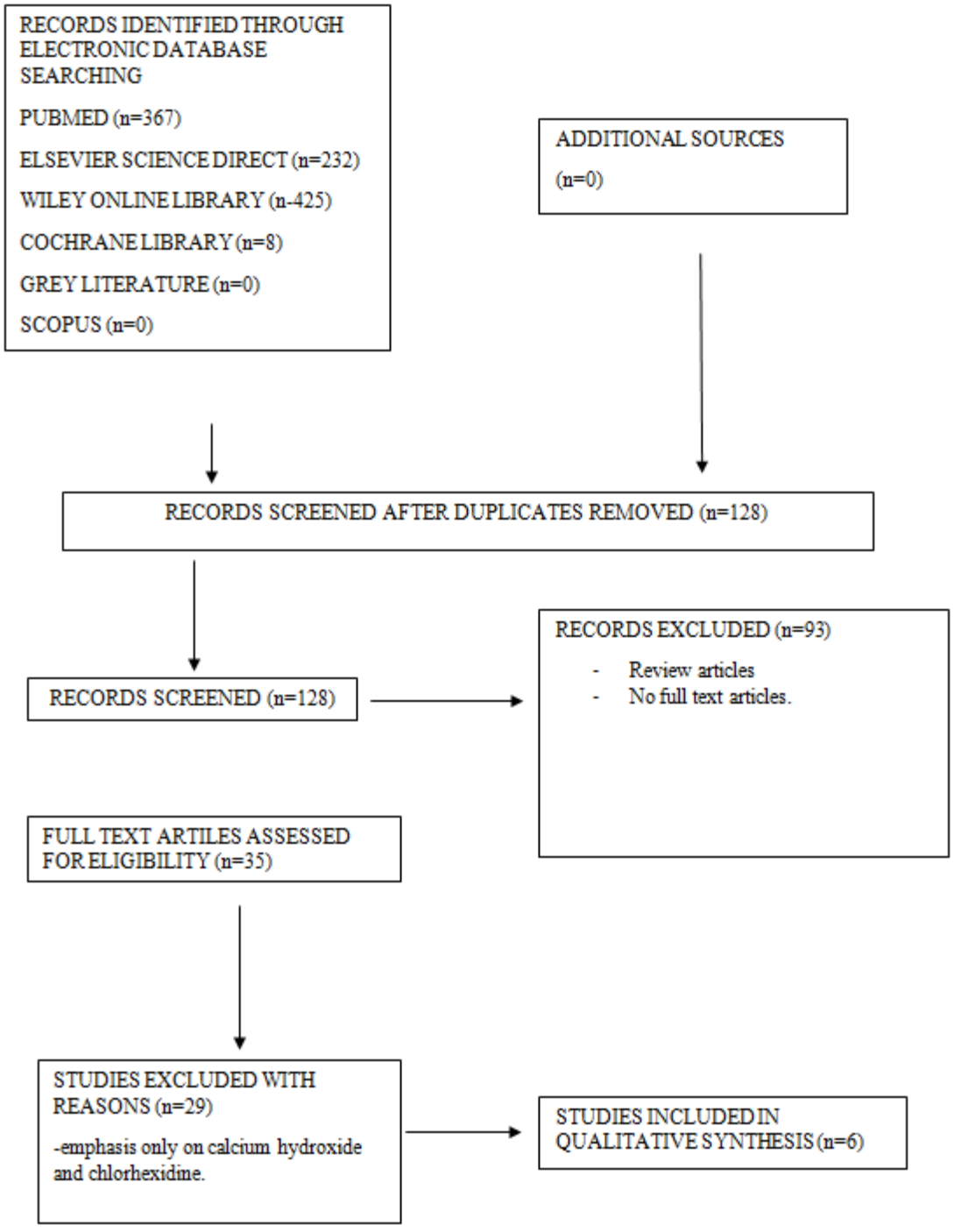

FIGURE 1: FLOW DIAGRAM SHOWING THE NUMBER OF STUDIES IDENTIFIED, SCREENED, ASSESSED FOR ELIGIBILITY, EXCLUDED AND INCLUDED IN THE SYSTEMATIC REVIEW

TABLE 1: CHARACTERISTICS OF THE INTERVENTIONS IN THE INCLUDED STUDY

AUTHOR	YEAR	SAMPLE SIZE	GROUP CHARACTERISTICS	INTERVENTION
S. Haenni et al[8]	2003	80 Extracted Teeth, single rooted, canines and premolars of same diameter.	G1-Ca(OH)2 mixed with unbuffered isotonic saline. G2- unbuffered isotonic saline. G3- 0.5% CHX Digluconate Ca(OH)2 paste. G4- 0.5% CHX G5- 1% NaOCl + Ca(OH)2 paste. G6-1% NaOCl G7-, 5% IPI +Ca(OH)2 paste. G8-5% IPI	All teeth were stored in 0.1% Thymol solution; crowns were amputated till Cemento Enamel Junction (CEJ), following which Root Canal Treatment was done. Teeth were then randomly divided into 8 groups. The material was then applied by lentulo spiral and solutions with 26 gauge needles.
Basrani et al[9]	2002	98 Freshly Extracted Teeth.	G1- 2% CHX gel. G2- 0.2% CHX gel. G3- 2% CHX aqueous solution. G4- Ca(OH)2 powder mixed with vehicle gel. G5- , calcium hydroxide mixed with 0.2% CHX gel. G6- 2% CHX solution with a single 25% CHX-containing CRD. G7- sterile saline. G8- vehicle gel alone.	The teeth were immersed in 0.5% NaOCl for 24 hours and after which uniform 6mm specimens were produced after which the root canals were enlarged post which they were divided into the mentioned groups. The solutions were filled upto the entire length for 7 days post which E.faecalis was inoculated for 21 days. After this dentin samples were obtained for checking bacterial growth.
Freire et al[10]	2009	10 Bovine incisor teeth.	G1- 2% CHX gel. G1d- 2% CHX gel added of dentin powder. G2- 2% CHX + Ca0H2 G2d- - 2% CHX + Ca0H2 added of dentin powder. G3- Ca0H2 + Propylene Glycol. G3d- - Ca0H2 + Propylene Glycol added of dentin powder.	The teeth were autoclaved after which they were cut perpendicularly till below the CEJ to obtain the dentin powder. After determining the pH of the medicaments, dentin powder was added as 1.8% of the total volume after which they were divided into the groups. The pH was then determined at different time intervals of 24h, 7, 14 and 21 days.
Sharifian et al[11]	2008	100 extracted single rooted teeth without caries, micro cracks or root-end curvatures.	G1- 2% CHX for 1 day. G2- 2% CHX for 3 days. G3- 2% CHX for 7 days. G4- Ca0H2 + Distilled water for 1 day G5- Ca0H2 + + Distilled water for 3 days. G6- Ca0H2+ Distilled water for 7 days. G7- 2% CHX + Ca0H2 for 1 day. G8- 2% CHX + Ca0H2 for 3 days. G9-2% CHX + Ca0H2 for 7 days. Positive control group- normal saline (5 teeth) Negative control group- no microbial suspension inoculated post autoclaving.	The teeth were disinfected using 5.25% NaOCl solution after which the canals were prepared using step-back technique. E.faecalis was then inoculated every 2 days except negative control group. After this, samples were checked for bacterial growth post which the groups were made and the intracanal medicament was inoculated. After 1, 3, 7 days, intracanal medicament was rinsed with 5ml of normal saline and another sample was taken. The teeth were then taken out of the resin blocks, and dentin chips were obtained which were inoculated in BHI Agar and growth was checked.
Samiei et al[12]	2018	132 extracted single rooted teeth.	G1- Ca0H2+ 0.12% CHX paste. G2- Zinc Oxide Nanoparticle gel. G3- Zinc Oxide + silver nano particles gel. G4- normal saline as control.	Post sterilization, all teeth were removed at CEJ and root canal treatment was done. 200 µL of the bacterial culture was placed in the lumen of the root canal with micropipette and incubated for 21 days and growth was checked using Scanning Electron Microscope. After this, the teeth were randomly divided into the groups and intracanal medicament was placed within and bacterial count was checked for 3, 7 and 14 days.
Maekawa et al[13]	2010	120 extracted single rooted teeth.	According to auxiliary chemical substance used, 3 groups: G1- 2.5% NaOCl G2-2% CHX gel. G3- pyrogen free solution. G4- pyrogen free saline as control. Further subdivided according to intracanal medicament(ICM) used: GA- CaOH2 paste. GB-Polymyxin B GC- CaOH2 paste with 2% CHX gel.	After extraction, the teeth were sterilized and root canal treatment was done and the apex was sealed with resin. After distributing the teeth randomly, they were contaminated with 10 µL of E. coli suspension for 14 days and contamination confirmation was checked after which they were first divided into groups according to irrigant used and then according to ICM. The canals were loaded with the material and kept for 14 days after which the canal contents were collected and the canal was loaded with saline and after 7 days another sample was taken. After this, the antimicrobial activity of the medicaments was determined.

*CHX-Chlorhexidine, CaOH2-Calcium Hydroxide, IPI-Iodine Potassium Iodide, NaOCl-sodium hypochlorite.

TABLE 1 shows the characteristics of intervention in the included studies. In all the 7 studies, the combination of calcium hydroxide and chlorhexidine was evaluated in a controlled group which differed in sample size, and number of teeth used.

TABLE 2: OUTCOME DATA AS REPORTED IN INCLUDED STUDIES

AUTHOR	YEAR	OUTCOME	RESULTS
S. Haenni et al [8]	2003	-no significant difference found in the dentine thickness among groups. - No significant difference in OH ion penetration on removing cementum. - change in pH between test and control after 2 weeks ($P < 0.05$), at weeks 3 and 5 ($P < 0.005$) - For CHX/CaOH2 group after 3 weeks and NaOCl/CaOH2 group after 5 weeks ($P < 0.05$). - No significant difference in pH values measured for different values of CaOH2 ($P > 0.05$). - Inhibition zone did not differ as much on addition of CaOH2 ($P > 0.05$), larger areas were obtained with CHX alone.	The mixture of CaOH2 and any irrigant with it does not increase the antimicrobial effect and has the same properties as conventional CaOH2/ Saline.
Basrani et al [9]	2002	The outcome was based on Optical Density values (OD) of the broth. G3, the inner samples had significantly lower OD values than outer samples (($P < 0.04$). G4, the inner samples had significantly higher OD values than outer samples (($P < 0.03$). In other groups it did not differ much significantly. Samples from groups 1,3 and 6 had significantly lower OD values than those from groups 7 and 8(positive control) for both samples.	OD values show the inability of CaOH2 alone or in combination with CHX as a potent intracanal medicament.
Freire et al [10]	2009	Analysis was done in triplicate and pH values were recorded. Results of paired student's t-test showed:- Significant difference in G1d and G2d ($P < 0.05$).	The mixture of CaOH2 and any irrigant with it does not increase the antimicrobial effect and has the same properties CaOH2/deionized water.
Sharifian et al [11]	2008	In negative control group, all samples were negative. In positive control group, 38% decrease in E. faecalis was observed. Statistically, neither the intracanal medicament nor the time was significantly effective in decreasing E. faecalis colony ($P>0.05$). In CaOH2/CHX, bacteria was completely removed in 1 week, there was no significant difference among the 3 medicaments in dentin disinfection in varying time intervals ($P>0.05$).	Mixture of CaOH2/CHX had greater efficacy in removing E. faecalis contamination provided the alkalinity is maintained.
Samiei et al [12]	2018	There were no statistically significant differences among the mean reduction in colony count (RCC) in different time interval in each group ($p=0.09$). The significant difference was observed in the mean RCC of different dressing materials ($P<0.001$). Interaction between time and material was significant ($P=0.015$). Mean RCC was higher in group 1 than other groups ($P<0.001$). Antibacterial effect was not significant between groups 2 and 3 ($P>0.05$). Group 4 had minimum antibacterial effect ($P<0.0001$).	The mixture CaOH2/CHX as an intracanal medicament is more effective than zinc oxide or zinc oxide/silver nanoparticles.
Maekawa et al [13]	2010	In quantification of endotoxins, in the 1st and 2nd collections, NaOCl and CHX were similar to each other ($p>0.05$) and different from pyrogen free saline ($p<0.05$). In the 3rd collection, it was noted that groups G1A, G1B, G1C.G2A, G2C, G3A, G3C were significantly different from their control group G4 ($p<0.05$). The groups G1C, G2A, G2C and G3C were equal to groups G1A, G1B, G3A, G3B ($p>0.05$), with low endotoxin values. In 4th collection, G1B had low endotoxin value equal to G1A, G1C, G2A,G2B, G2C,G3B,G3C ($p>0.05$). Groups G1A, G1B, G1C, G2A, G2C, G3B, G3C had less endotoxins compared to control group G4 ($p<0.05$).	A mixture of CaOH2/CHX is effective in inactivating the endotoxins and can be used as an intracanal medicament.

TABLE 2 shows the outcome data of the accuracy and reliability of chlorhexidine loaded calcium hydroxide as an effective antimicrobial agent. All the 6 studies discussed had the same criteria assessed. The calculations and statistics done to evaluate the benefit of the combination of CHX and CaOH2 for this criteria varied from one study to another and are mentioned under the results column.

DISCUSSION:

This systematic review mainly focuses on the importance of various intacanal medicaments and their affects on prognosis of root canal systems and pulp capping. The main focus of interest was calcium hydroxide in combination with chlorhexidine as an antimicrobial agent. According to Mohammadi et al [14], this combination potentially kills microorganisms by generating excessive oxygen species. Also, according to Byström A et al [15], root canals when treated with calcium hydroxide had lesser bacterial count as compared to when treated with camphorated monochlorophenol or camphorated phenol. However, this contradicts to the study conducted by Grossman et al[16], who had done the same study on root canals of an adult cat, found that all forms of Calcium Hydroxide, whether in the form of Pulpdent, supernatant liquid or as a slurry, is much less effective an antimicrobial as compared to camphorated chlorophenol.

Haenni et al[8] mainly took equivalent mixtures of Calcium Hydroxide and irrigating solutions and compared them to the mixture of Calcium Hydroxide in saline and conducted the efficacy on extracted single rooted human teeth. However, on comparison they found that as such there was no difference in the antimicrobial properties of calcium hydroxide compared to conventional saline mixture. Although, it is definitely a very strong alkali and does not have any change in properties when mixed with weak acids or alkalis in aqueous suspensions. Another study conducted by Basrani et al[9], aimed mainly at comparing various intacanal medicaments and their properties on 98 root canals of extracted teeth. The results were similar to that of Hanni et al[8], concluding that as such the Optical Density values did not indicated the combination as a very potent antimicrobial agent. [8-9]However, they did also say that Endodontic infections are mixed infections which cannot be restricted to one particular bacterial pathogen, as root canals are quite complex with harboring vast organisms, and that further studies are necessary to conclude with that statement.[9]The third study, which was conducted by Freire et al[10], also gave similar results as above, however it was studied on bovine incisor teeth, and also concluded with the result that in combination or alone, the properties of calcium hydroxide remain the same.

Although, a certain group of studied did show positive results of the combination. Studies conducted by Sharifian et al[11] did show results stating that combination is quite effective with the limitation that alkalinity is maintained. As calcium hydroxide has a pH of 12.5, it makes the compound highly alkaline which abides by its mechanism of action as well. Another study conducted by Waltimo et al [17] also gave positive results for this combination against Candida Albicans, another potent fungus in the root canals and oral cavity. It compared sodium hypochlorite, iodine potassium iodide, chlorhexidine, calcium hydroxide and a combination of chlorhexidine and calcium hydroxide and found out that on combining Calcium Hydroxide with Chlorhexidine or Sodium Hypochlorite did give a wide antimicrobial spectrum, increasing positive prognosis of endodontic therapy. Samiei et al[12] also concluded that this combination holds better prognosis as compared to the test, which was zinc oxide or zinc oxide/silver nanoparticles. Zinc Oxide is commonly also used in the form of Zinc Oxide Eugenol which is used as an intracanal medicament in day to day endodontic practice and due to its obtunding effect, holds good prognosis. Aguiar AS et al[18] also evaluated the pH of Calcium Hydroxide and zinc (micro or nano particles) with 0.4% Chlorhexidine solution, and found that the combination of both with CHX was more effective, which was proved using Agar Diffusion method. Maekawa et al [13] also conducted a study evaluating auxiliary chemical substances and intracanal medications on Escherichia coli and found that only CHX/CaOH2 was able to neutralize the endotoxins within the canal. According to Boddeda et al[19], Calcium Hydroxide is considered to be the 'gold standard' for pulp capping and showed 100% success rates. Its combination with CHX increases chances of pulp capping by killing the organisms which might harbor in the pulp on exposure. Another study conducted by Arruda et al [20] in which triple solution involving CaOH2/ 2% CHX gluconate/ and an antibiotic solution (metronidazole/ciprofloxacin/minocycline) showed significantly lesser bacterial count.

LIMITATIONS:

After thorough evaluation and strict emphasis on the inclusion and exclusion criteria, only 6 studies were found pertained to the topic of interest, making it insufficient for a proper conclusion. Also, without the inclusion of Randomized Control Trials, only In Vitro studies lack the appropriate environment like that of the oral cavity and an individual's systemic health status, which does indeed have a huge impact on clinical practice, therefore limiting this study to only the quantitative analysis of this combination.

CONCLUSION:

The combination is controversial and has to be still researched in order to come to a conclusion as unsuccessful endodontic therapies and pulp capping procedures are multifactorial and a simulated environment, which fits all criteria is still one of the most important goals which has not been achieved yet, making it quite difficult to point the exact cause of such failures.

Chlorhexidine loaded Calcium Hydroxide is indeed a successful pulp capping material and can also be used in endodontic procedures as an intracanal medicament. However, the combination has also shown to not have very high success rate in various studies unsuccessful endodontic therapies and pulp capping procedures are multifactorial, and therefore the combination should continue to be a topic of research for successful dental treatments.

REFERENCES:

1) Barthel CR, Zimmer S, Zilliges S, Schiller R, Göbel UB, Roulet JF. In situ antimicrobial effectiveness of chlorhexidine and calcium hydroxide: gel and paste versus gutta-percha points. Journal of endodontics. 2002 Jun 1;28(6):427-30.

2) Silva LA, Romualdo PC, Silva RA, Souza-Gugelmin M, Pazelli LC, De Freitas AC, Faria G, Nelson-Filho P. Antibacterial Effect of Calcium Hydroxide With or Without Chlorhexidine as Intracanal Dressing in Primary Teeth With Apical Periodontitis. Pediatric dentistry. 2017 Jan 15;39(1):28-33.

3) Basrani B, Ghanem A, Tjäderhane L. Physical and chemical properties of chlorhexidine and calcium hydroxide-containing medications. Journal of endodontics. 2004 Jun 1;30(6):413-7.
4) Al-Nazhan S, Al-Obaida M. Effectiveness of a 2% chlorhexidine solution mixed with calcium hydroxide against Candida albicans. Australian Endodontic Journal. 2008 Dec;34(3):133-5
5) Gomes BP, Sato E, Ferraz CC, Teixeira FB, Zaia AA, Souza-Filho FJ. Evaluation of time required for recontamination of coronally sealed canals medicated with calcium hydroxide and chlorhexidine. International Endodontic Journal. 2003 Sep;36(9):604-9.
6) Vasudeva A, Sinha DJ, Tyagi SP, Singh NN, Garg P, Upadhyay D. Disinfection of dentinal tubules with 2% Chlorhexidine gel, Calcium hydroxide and herbal intracanal medicaments against Enterococcus faecalis: An in-vitro study. Singapore dental journal. 2017 Dec 1;38:39-44.
7) Podbielski A, Boeckh C, Haller B. Growth inhibitory activity of gutta-percha points containing root canal medications on common endodontic bacterial pathogens as determined by an optimized quantitative in vitro assay. Journal of endodontics. 2000 Jul 1;26(7):398-403.
8) Haenni S, Schmidlin PR, Mueller B, Sener B, Zehnder M. Chemical and antimicrobial properties of calcium hydroxide mixed with irrigating solutions. International Endodontic Journal. 2003 Feb 1;36(2):100-5.
9) Basrani B, Santos JM, Tjäderhane L, Grad H, Gorduysus O, Huang J, Lawrence HP, Friedman S. Substantive antimicrobial activity in chlorhexidine-treated human root dentin. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2002 Aug 1;94(2):240-5.
10) Freire LG, Carvalho CN, Ferrari PH, Siqueira EL, Gavini G. Influence of dentin on pH of 2% chlorhexidine gel and calcium hydroxide alone or in combination. Dental Traumatology. 2010 Jun;26(3):276-80.
11) Sharifian MR, Shokouhinejad N, Aligholi M, Emaneini M, Katebi A, Assadian H. In vitro comparison of the effectiveness of Chlorhexidine and two calcium hydroxide formulations on Enterococcus faecalis. Iranian endodontic journal. 2008;3(3):50.
12) Samiei M, Torab A, Hosseini O, Abbasi T, Abdollahi AA, Divband B. Antibacterial Effect of Two Nano Zinc Oxide Gel Preparations Compared to Calcium Hydroxide and Chlorhexidine Mixture. Iranian endodontic journal. 2018;13(3):305.
13) Maekawa LE, Valera MC, Oliveira LD, Carvalho CA, Koga-Ito CY, Jorge AO. In vitro evaluation of the action of irrigating solutions associated with intracanal medications on Escherichia coli and its endotoxin in root canals. Journal of Applied Oral Science. 2011 Apr;19(2):106-12.
14) Mohammadi Z, Shalavi S. Is chlorhexidine an ideal vehicle for calcium hydroxide? A microbiologic review. Iranian endodontic journal. 2012;7(3):115.
15) Byström A, Claesson R, Sundqvist G. The antibacterial effect of camphorated paramonochlorophenol, camphorated phenol and calcium hydroxide in the treatment of infected root canals. Dental Traumatology. 1985 Oct;1(5):170-5.
16) Stevens RH, Grossman LI. Evaluation of the antimicrobial potential of calcium hydroxide as an intracanal medicament. Journal of Endodontics. 1983 Sep 1;9(9):372-4.
17) Waltimo TM, Ørstavik D, Siren EK, Haapasalo MP. In vitro susceptibility of Candida albicans to four disinfectants and their combinations. International endodontic journal. 1999 Nov;32(6):421-9.
18) Aguiar AS, Guerreiro-Tanomaru JM, Faria G, Leonardo RT, Tanomaru-Filho M. Antimicrobial activity and ph of calcium hydroxide and zinc oxide nanoparticles intracanal medication and association with chlorhexidine. J Contemp Dent Pract. 2015 Aug 1;16(8):624-9.
19) Boddeda KR, Rani CR, Vanga NR, Chandrabhatla SK. Comparative evaluation of biodentine, 2% chlorhexidine with RMGIC and calcium hydroxide as indirect pulp capping materials in primary molars: An in vivo study. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2019 Jan 1;37(1):60.
20) Arruda ME, Neves MA, Diogenes A, Mdala I, Guilherme BP, Siqueira Jr JF, Rôças IN. Infection Control in Teeth with Apical Periodontitis Using a Triple Antibiotic Solution or Calcium Hydroxide with Chlorhexidine: A Randomized Clinical Trial. Journal of endodontics. 2018 Oct 1;44(10):1474-9.