

Review article

## Antimicrobial Effectiveness Of Various Drug Combinations Used As Intracanal Medicaments- A Systematic Review

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### Abstract:

Endodontic infections are a result of polymicrobial nature of root canal flora and their complete eradication may not be possible with routine chemico-mechanical method. Hence there is a need for studying combination of antimicrobial agents as intracanal medicaments. This systematic review compiles scientific evidence regarding the effectiveness of various antimicrobial agents used in combination in patients undergoing root canal treatment. A systematic search of databases including PubMed, EBSCOhost, SCOPUS and Google Scholar was done. The limits used were all full text articles in English dated from 1<sup>st</sup> January 2009 to 31<sup>st</sup> October 2019 was made. Following the application of inclusion criteria, 5 articles based on In-vivo studies were selected for detailed analysis. In conclusion it could be stated that intracanal medicament combinations like Calcium hydroxide and Chlorhexidine, TAP, etc. show better efficacy against *E. faecalis*, Obligate anaerobes, Facultative anaerobes and *Candida. albicans*.

**Key words:** Drug combinations ,Antimicrobials, Intracanal medicaments, Endodontic therapy

### Rationalae:

Pulpal and periapical inflammation is an immunological self defence reaction against sustained bacterial stimuli; therefore, strategies for endodontic treatment are directed towards the removal of these bacteria and their by-products from the root canal system .<sup>[1]</sup> For effective removal of bacteria, intracanal medicaments serve as disinfection materials as an adjunct to mechanical removal and chemical

cleansing. Walton<sup>[2]</sup> wrote that “Intracanal medicaments have traditionally gone hand-in-glove with endodontics. They are generally considered to be an integral part of treatment and important to the success of root canal therapy”. Calcium hydroxide has been widely utilised in endodontic therapy as an intracanal dressing<sup>[3]</sup>. Along with other agents having antibacterial properties used inside the root canals, the use of antibiotics in local form also gained importance over time. Due to the

polymicrobial nature of infected root canal, single empirical antibiotic is insufficient in disinfection of the root canal. Non specific antibiotic suppress most of the microbial flora and allow residual virulent micro-organisms to repopulate the root canal. Therefore it is essential to use combination of antibiotics to act against all endodontic pathogens and to prevent resistance.<sup>[4]</sup> In teeth with periapical lesions that were infected with *Enterococcus faecalis* (*E. faecalis*) and required re-treatment, two-week application of Calcium Hydroxide  $\text{Ca}(\text{OH})_2$  and Chlorhexidine (CHX) as an intracanal medicament significantly decreased the count of this resistant microorganism.<sup>[5]</sup> Triantibiotic paste containing ciprofloxacin, metronidazole and minocycline has been introduced for lesion sterilization and repair which has been widely used as reported in published case reports.<sup>[6]</sup> However to the best of our knowledge there was no systematic review on antimicrobial effectiveness of various drug combinations used as intracanal medicaments In-vivo. Hence the need to conduct this systematic review.

**Focused question:** How effective are various drug combinations as antimicrobial agents when used as intracanal medicaments in endodontic therapy?

**Objectives:** To determine the antimicrobial effectiveness of various drug combinations used as intracanal medicaments.

**Eligibility criteria:**

**Inclusion criteria:** Articles in English language or those having summary in English, Full text articles, In-vivo studies done on human participants, studies on use of drug combinations as intracanal medicaments in Apical Periodontitis.

**Exclusion criteria:** Review, letter to editorials, short communications, Studies only with abstract or with no available abstract, articles on In-vitro studies and case reports, studies performed on animals, articles having any single drug as intracanal medicament.

**PICO:**

**POPULATION-** Patients with Apical Periodontitis undergoing root canal therapy

**INTERVENTION-** Antimicrobial drug combinations used as intracanal medicaments

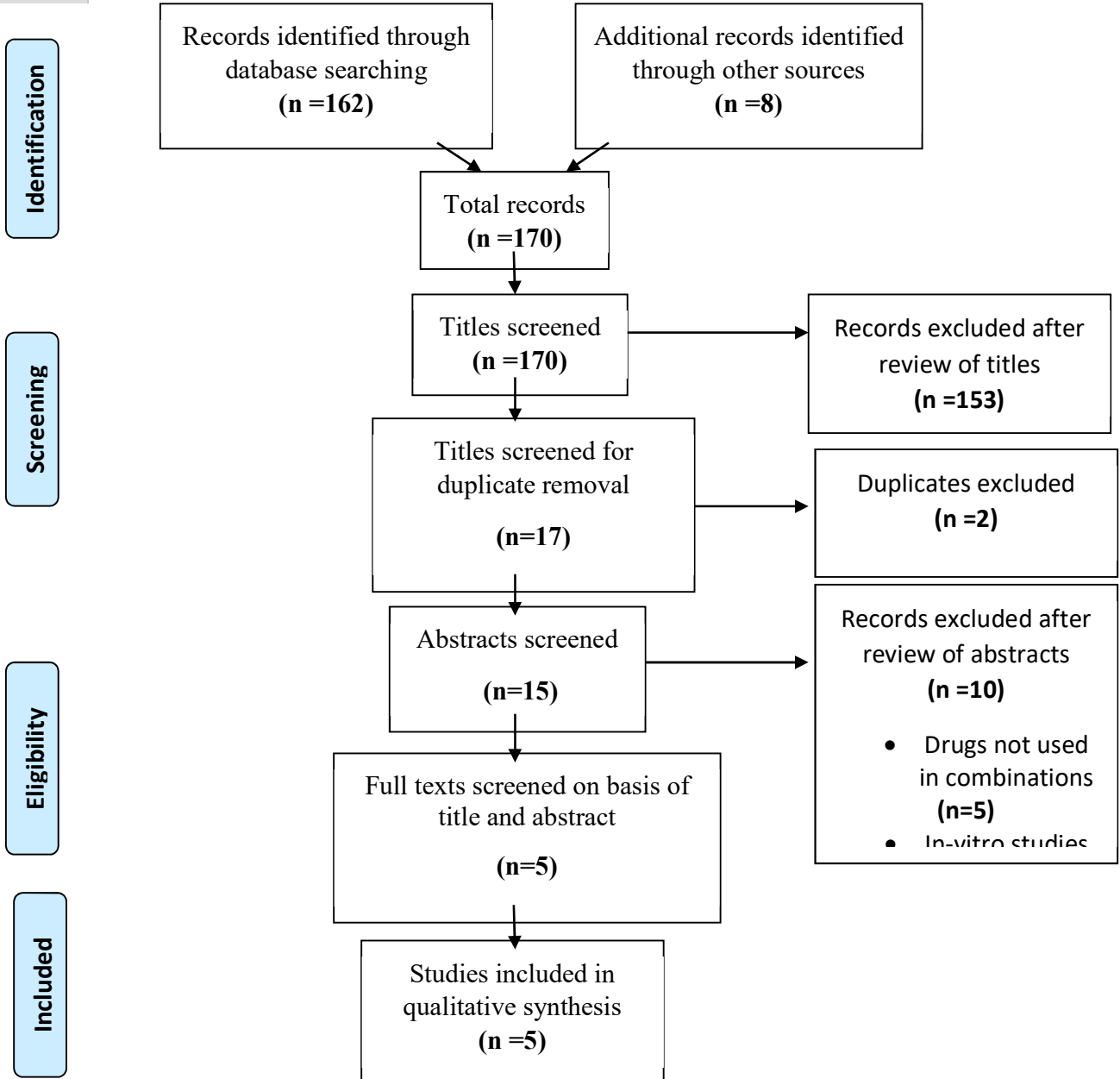
**COMPARISON-** Amongst various drug combinations

**OUTCOME-** Antimicrobial Effectiveness

**Information sources:**

Two Internet sources of evidence were used in the search of appropriate papers satisfying the purpose: the National Library of Medicine (MEDLINE PubMed) and the Cochrane Central Register of Controlled Trials (CENTRAL), Google Scholar, Google, Clinical trials registry and manual search using DPU college library resources. All cross reference lists of the selected studies were screened for additional papers that could meet the eligibility criteria of the study. The databases were searched up to and including 31<sup>st</sup> October 2019 using the search strategy.

**Search:** The following databases were searched on PubMed (the limits used were all full text articles in English dated from 1<sup>st</sup> January 2009 to 31<sup>st</sup> October 2019), EBSCOhost, SCOPUS and Google Scholar. For the elective search strategy, the following terms were used as keywords in several combinations. (fig.1)



(fig. 1)

### Summary of evidence:

The historical origins of intracanal medicaments date back to very early times. Hermann applied Calcium Hydroxide [  $\text{Ca}(\text{OH})_2$  ] to dentistry in 1920 and it came to be widely used for root canal treatment in the 1970s. It is now regarded as one of the first choices as a multiple-visit root canal medication and is mixed with various vehicles and is available in many commercial products.<sup>[7]</sup> The use of antibiotic in endodontics was first reported in 1951 by Grossman which was known as polyantibiotic paste (PBSC), a mixture of penicillin, bacitracin, streptomycin and caprylate sodium. Penicillin was used for targeting against Gram-positive organisms, bacitracin for penicillin-resistant strains, streptomycin for Gram-negative organisms and caprylate sodium to target yeasts.<sup>[8]</sup> Maekawa *et al.* 2013 conducted a study to evaluate the effectiveness of glycolic propolis (PRO) and ginger (GIN) extracts,  $\text{Ca}(\text{OH})_2$ , chlorhexidine (CLX) gel and their combinations as ICMs (ICMs) against *Candida albicans*, *Enterococcus faecalis*, *Escherichia coli* and endotoxins in root canals. The antimicrobial activity and quantification of endotoxins by chromogenic test of *Limulus* amoebocyte lysate were evaluated after contamination and instrumentation at fourteen days on ICM application and seven days after ICM removal. On fourteenth day, it was concluded that all ICMs were effective; however,  $\text{Ca}(\text{OH})_2$  was more effective in neutralizing endotoxins and less effective against *C. albicans* and *E. faecalis*, requiring the use of medication combinations to obtain higher success.<sup>[9]</sup> Sinha N *et al.* 2013, compared the antimicrobial efficacy of  $\text{Ca}(\text{OH})_2$ , 2% gel (CHX) gel and a combination of both, on obligate anaerobes, facultative anaerobes and *Candida* spp. The study concluded that CHX with or without  $\text{Ca}(\text{OH})_2$  was more effective than CH alone against all the tested micro-organisms.<sup>[10]</sup> Hamed S *et al.* 2014, conducted a study to

evaluate the effect of adding CHX or sodium hypochlorite [NaOCl] on the antibacterial activity of  $\text{Ca}(\text{OH})_2$  against *Streptococcus* spp. and *Klebsiella* spp. As a result,  $\text{Ca}(\text{OH})_2$  and 2.5% NaOCl had antibacterial effects on both tested bacteria while 2% CHX appeared to be less effective. Pastes of  $\text{Ca}(\text{OH})_2$  and 2% CHX were effective on *Klebsiella* spp., while mixing of  $\text{Ca}(\text{OH})_2$  with 2.5% NaOCl had significant effect on both types of bacteria and it was more effective against *Streptococcus* spp.<sup>[11]</sup> Donyavi Z *et al.* 2016, conducted a study and compared the root canal microbial count of necrotic teeth after irrigation with 6% NaOCl (single session treatment) and two session root canal treatment with two-week application of  $\text{Ca}(\text{OH})_2$  mixed with 0.2% CHX. The study concluded that  $\text{Ca}(\text{OH})_2$ +CHX caused significant reduction in the aerobic, anaerobic and *E. faecalis* colony counts. Thus, two sessions treatment with ICMs achieved predictable results.<sup>[5]</sup> Arruda M *et al.* 2018, conducted a RCT and carried root canals of single rooted teeth with apical periodontitis using a reciprocating single-instrument technique with 2.5% NaOCl irrigation and then medicated for 1 week with either a triple antibiotic solution (minocycline, metronidazole, and ciprofloxacin) at 1 mg/ml (n = 24) or a  $\text{Ca}(\text{OH})_2$  paste in 2% CHX gluconate (n = 23). Samples were taken from the canal at the baseline (S1), after chemomechanical preparation (S2), and after intracanal medication (S3). DNA extracts from clinical samples were evaluated for total bacterial reduction using a 16S ribosomal RNA gene-based quantitative polymerase chain reaction assay. All S1 samples counts were substantially reduced after treatment procedures and S2 to S3 reduction was 97% in the antibiotic group and 39% in the  $\text{Ca}(\text{OH})_2$ /CHX group.

### Limitations:

There are limited number of articles on drug combinations used as intracanal medicaments. Also, published In-vivo research is less.

### Future implications:

More drug combinations should be tried and further In-vivo comparative studies are required, considering the diverse microbiota in Apical Periodontitis.

### Conclusion:

Minimum two weeks use of Calcium hydroxide in combination with Chlorhexidine was more effective against *E. faecalis*, Obligate anaerobes, Facultative anaerobes and *Candida albicans*. Intracanal medication with Triple Antibiotic Paste at the concentration of 1mg/ml had good antimicrobial efficacy. Antimicrobial effects of Triple Antibiotic Paste were found to be similar to Calcium hydroxide and Chlorhexidine combination. Calcium hydroxide and 2.5% Sodium hypochlorite showed significant antimicrobial effectiveness against *Streptococcus* spp. and *Klebsiella* spp.

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