# ANTIMICROBIAL EFFICACY OF TRIPLE ANTIBIOTIC PASTE: A SYSTEMATIC REVIEW

**Shahul Hameed[1], S.Delphine Priscilla Antony[2], Dr Rajeshkumar Shanmugam[3]**

[1]PhD Scholar, Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University.
[2]Associate Professor, Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences
Saveetha University, 162 , PH Road , Chennai 600077, TamilNadu , India. Orcid ID - 0000-0001-9509-3665

[3]Professor, Nanobiomedicine Lab, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, 162 , PH Road , Chennai 600077, TamilNadu, India.

**Corresponding author:S.Delphine Priscilla Antony,** Associate Professor, Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, 162 , PH Road , Chennai 600077, TamilNadu , India.

## ABSTRACT

**Aim:** To investigate the antimicrobial efficacy of triple antibiotic paste as an intracanal medicament in endodontic therapy.

**Methods**: We have performed a literature search of randomized control trials from the databases of PubMed Central, Embase, and MEDLINE, published in the English language from 2011- 2021. Data regarding triple antibiotic paste, intracanal medicament, and antimicrobial efficacy in endodontics were collected and subjected to descriptive data analysis

A total of 539 articles were searched, of which 45 articles were relevant to our study. Of which, 10 articles were used for quantitative synthesis.

**Results:** Among the 10 studies, sample size varied among 30-60 cases; and heterogeneity among the study parameter to measure the treatment outcome. 4 studies demonstrated reduced microbial load after a week placement of TAP dressing, other comparators reported differences in the postoperative pain and flare-up incidence compared to other medicaments.

**Conclusion:** All included studies have recommended TAP as a suitable intracanal medicament for disinfecting the root canal system by attributing to its combined spectrum of antimicrobial activity and synergetic or additive actions of antibiotics for endodontic success rate.

## INTRODUCTION

Endodontic therapy is done for the complete elimination of pathogens within the root canal system. The microflora of the root canal system is mixed, consisting of aerobic and anaerobic bacteria, among which obligate anaerobes prevail the most. (1) Eradication of causative microorganisms by a combination of aseptic treatment techniques, chemomechanical

preparation, and antimicrobial irrigation and medicaments helps to achieve successful treatment outcomes. However, even after effective chemo–mechanical procedure, the prevalence of bacteria in the inaccessible areas may cause flare-ups due to the presence of root canal peripherals and ramifications that remains uninstrumented during the preparation of the root canal.

Judicious medicaments can play an important role in rendering the canal contents inert and reducing this phenomenon. To reduce postoperative pain and interappointment flare-ups, the employment of intracanal medicaments for disinfection is necessary. Calcium hydroxide, chlorhexidine, ethylenediaminetetraacetic acid, and other commercial pastes such as Ledermix and Septomixine Forte containing corticosteroids are used. (2) Effective control over the intra-canal microbial load before root canal obturation is a key element that increases the success rate of endodontic treatment. (3)

The gold standard agent for optimally disinfecting root canals is the Calcium hydroxide; however, the ability of calcium hydroxide medication to eradicate bacterial species from the root canal has been questioned. (4) Considering the polymicrobial nature of tooth infection, Hoshino's triple antibiotic paste (TAP) (5), a mixture of 3 antibiotics of metronidazole, ciprofloxacin, and minocycline, is useful to achieve asepsis by killing any remaining bacteria in the root canal system.
The review's objective is to evaluate the antimicrobial efficacy of triple antibiotic paste by comparing it with other intracanal medicaments based on the bacterial count or its ability to reduce postoperative pain, flare up and periapical healing.

## MATERIALS AND METHODS

### Study design

This systematic review was done according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines issued in 2009 (Checklist S1).
This review, therefore, evaluates the antimicrobial efficacy of triple antibiotic paste as a root canal medicament.

Research question
This study sought to determine the clinical outcome of triple antibiotic paste as an intracanal medicament.
The eligibility criteria were based on the PIRD (P - Population, I – Index test, R – Reference standard, and D – Diagnosis of target condition) strategy as follows:

- **Population (P) -** Randomized and quasi-randomized controlled clinical trials evaluated the clinical outcome based on the antimicrobial efficacy of triple antibiotic paste.
- **Index test (I)** - Antimicrobial efficacy based on the bacterial count, reduce postoperative pain, flare-ups, or periapical healing

- **Reference standard (R)** - No intracanal medicament or any intracanal medicament other than the intervention.
- **Diagnosis of Target condition (D)** - Patients who had non-vital permanent mature teeth with apical periodontitis or undergoing root canal treatment in multiple visits or primary or young permanent tooth or immature tooth

**Literature search**

The electronic search of the literature was conducted on the 'PubMed Central, Embase, and MEDLINE' databases with the following MESH terms: "triple antibiotic mixture OR triple antibiotic paste OR tri antibiotic mixture OR tri antibiotic paste OR TAP", "antimicrobial effect OR antibacterial effect", "intracanal medicament OR intracanal medication OR root canal treatment therapy OR root canal" using Boolean operators (AND, OR).

Ongoing clinical trial registries were searched: ClinicalTrials.gov. Hand searching from the reference lists of the retrieved articles in the above databases was also included. Only articles published in English language were included. Citation index of included studies done in Google Scholar. Restrictions to the English language and studies conducted between 2011-2021.

Non-randomized clinical trials, ex-vivo studies, observational, i*n vitro* or animal studies, Case reports, narrative reviews were excluded from this study. The studies where TAP was used as an irrigant and not as an intracanal medicament were excluded.

**Data extraction**

The authors thoroughly studied all the included studies, independently collected the data, and assessed the risk of bias.

All retrieved titles and abstracts from the three described databases were screened to assess eligibility. Then the abstracts of the selected studies were reviewed if they met the selection criteria. Any articles that did not match the standards were excluded. And after full-text articles were assessed for eligibility, some of them were eliminated because of nonconformity to the criteria

The study characteristics extracted were author, participant character, no of patients, age, groups, irrigant used, period of ICM placement, study time interval, outcome domain, and tool for measurement.

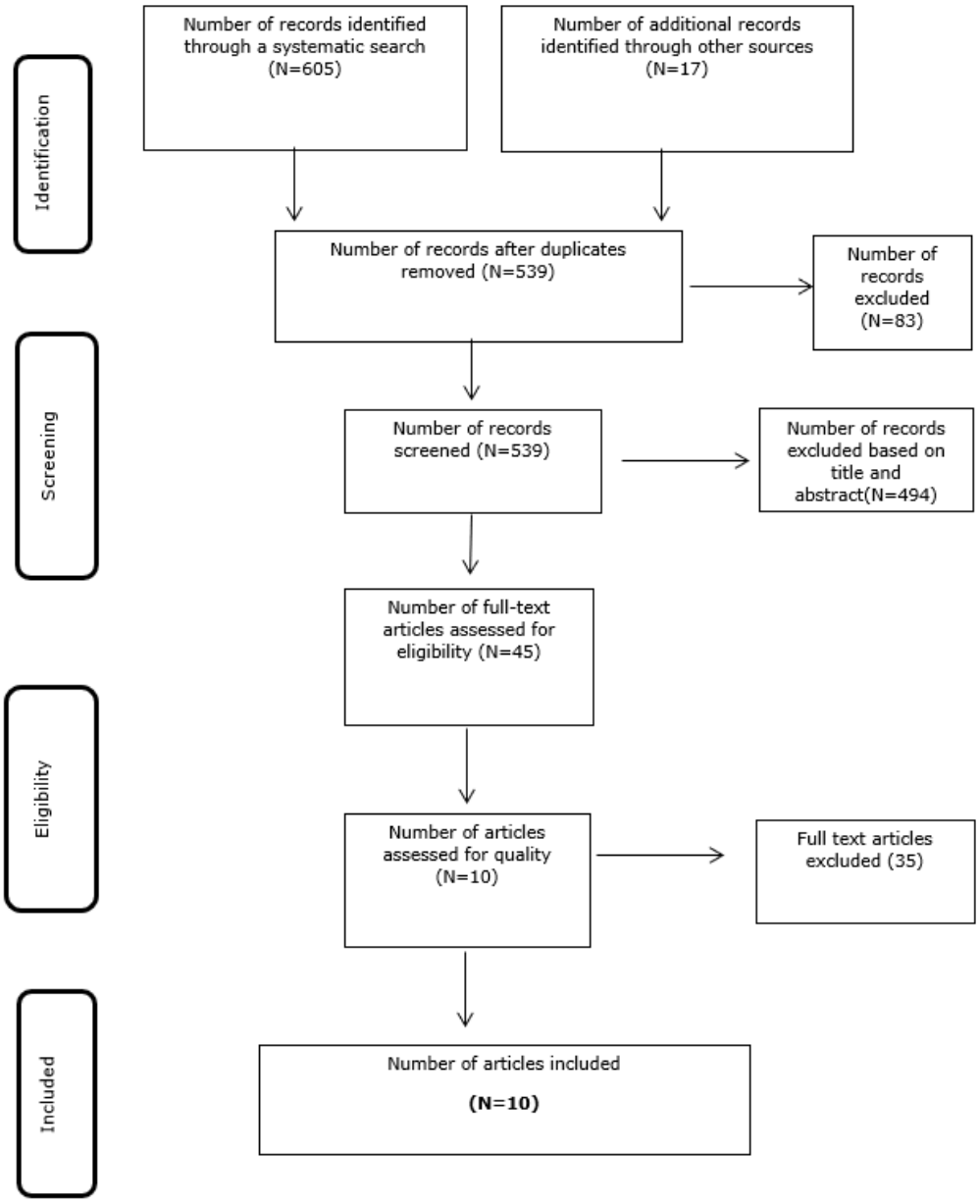



**Fig 1:** PRISMA flow chart showing identification and selection process of articles included.

### Quality assessment of selected studies

A quality assessment of the selected studies was performed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS 2) tool, which measures the diagnostic quality based on four domains:

- Patient selection
- index test
- Reference test
- Flow with timing

Decisions regarding the selection of answers such as "**yes/no/unclear/not applicable**" for each leading question. In each domain, if the answers for all of the leading questions were yes, then it was judged as "low risk of bias" and applicable concerns. If one answer was unclear and others were yes, it was judged to have a "moderate risk of bias". Even if 1 question was no, then it had a "high risk of bias".

If a study was judged as low on all domains relating to bias or applicability, then it was deemed to have an overall judgment of low risk of bias or low concerns regarding applicability. Conversely, if a study was judged as high or unclear in 1 or more domains, it was considered at risk of bias or as having concerns regarding applicability.

### Data collection

Independent articles were extracted depending on the keywords used. The more relevant data included antibacterial efficiency in randomized control trials, whether in reducing bacterial count, postoperative pain or flare-ups, or periapical healing in primary/young permanent /permanent non-vital tooth, was selected. The articles used were quantitative analysis, with meaningful information about the keywords used for the reviewing process.

## RESULTS

### Search results

After searching the electronic sources, 622 records were identified; 539 were selected after duplicate removal using Endnote reference manager. Next, 45 articles were extracted, and their abstracts and full texts were assessed for qualitative analysis. Finally, about 10 articles were included in this study after the abstract and full text were assessed.

### Data items

The following set of data were extracted from each included study: methods – diagnostic criteria, study design, participants – selection criteria, setting and country; tooth type, tooth condition, gender/ age, number randomized/analyzed; , intra-canal medication placement technique and period; interventions – groups, cleaning and shaping technique, irrigation method, outcomes – outcome measurement and duration.

### General characteristics of the study

All original research studies published in the year 2011-2021 were included, among which 10 articles met the inclusion criteria, which were randomized control trials.
All of the studies that were included were randomized parallel multi-arm clinical trials conducted in a single centre. The settings of those included studies were done in dental college hospitals or university. All types of teeth either single or multiple rooted teeth, were included. The intervention of interest was a combination of three antibiotics (metronidazole,

ciprofloxacin, and minocycline) mixed with inert vehicles to form a paste. In the included studies, comparators were reported – either calcium hydroxide paste or 2% chlorhexidine gel. The general characteristics of all 10 studies intervening in the antimicrobial efficacy of triple antibiotic mixture are illustrated in **Table 1**.

**Table 1 – Summary of studies**

| Study | Participants | Age | No. of patients | Groups | Irrigant used | Period of ICM placement | Outcome domain | Tool for measurement | Study time intervals |
|---|---|---|---|---|---|---|---|---|---|
| Datta B et al (6) | Non vital primary maxillary and mandibular molars with interradicular/periapical radiolucencies No antibiotics taken for the last 3 months | 4-6yrs | 48 | calcium hydroxide paste, 2% chlorhexidine gel, and triple antibiotic paste | 2.5% NaOCl and normal saline | 1 week | Treatment success and failure | Reduced E,faecalis colony count in agar media | 1 week |
| Safeya et al. (7) | Necrotic teeth with apical periodontitis | 16-55 yrs | 44 | Multiple visits with TAP medicament, single visit without medicament | sodium hypochlorite 2.6% and 5 ml 17% EDTA solution | 1 week | Postoperative pain | Numerical rating scale | 24,48, 72 hrs and 1 week |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Sarah et al (8) | necrotic premolars with apical periodontitis | 20 - 50 yrs | 36 | Calcium hydroxide, TAP | 2.5% sodium hypochlorite | 1 week | Postoperative pain | Numerical rating scale | 6,12,24,48hrs |
| Tirukkolluru et al (9) | Single rooted teeth with chronic apical periodontitis | 35 - 50 yrs | 45 (Type II DM) | calcium hydroxide, propolis with moxifloxacin and triple antibiotic paste | 1% sodium hypochlorite followed by 2 ml of 10% sodium thiosulfate | 1 week | Treatment success and failure | Colony count - E. faecalis and Streptococcus spp in agar media | 1 week |
| Yasmin et al (10) | Non vital primary maxillary and mandibular molars with interradicular/periapical radiolucencies | 4-6yrs | 39 | Calcium hydroxide, TAP | Normal saline | 1 week | Treatment success and failure | Reduced microbial count via Real-time PCR | 1 week |
| Pai et al (11) | Single rooted anterior and premolar | 18 - 60 yrs | 50 (Type II DM) | Calcium hydroxide, TAP | 2.5% sodium hypochlorite, normal saline, and 0.2% chlorhexidine | 2 week | Interappointment flare-up | Verbal rating scale | 1,2,3,7,14 days |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Sinhal et al (12) | The tooth with a primary endodontic infection | Above 20 yrs | 36 (Type II DM) | 2% chlorhexidine gel, triple antibiotic paste, calcium hydroxide | 2.5% sodium hypochlorite, 17% ethylene diaminetetraacetic acid, and normal saline | 2 week | Interappointment flare-up | Verbal rating scale | 1,2,3, 7,14 days |
| Sanu et al (13) | Mandibular first molars with symptomatic apical periodontitis | 18-45 yrs | 207 | Calcium hydroxide, TAP | Normal saline | 1 week | Postoperative pain | Visual analogue scale | 8,24,48hrs |
| Prasad et al (14) | acute and chronic apical periodontitis and acute and chronic irreversible pulpitis, necrotic tooth | - | 30 | Calcium hydroxide, TAP | 2.5% sodium hypochlorite, 17% ethylene diaminetetraacetic acid, and normal saline and 0.2% chlorhexidine | 1 week | Pre-operative, interappointment and postoperative pain | Visual analogue scale | 1,48hrs and 7 days |
| Reddy et al (15) | Primary molars and incisors | 4-10 yrs | 60 | TAP, formocresol dampened cotton | 1% sodium hypochlorite solution and | 2 week | Treatment success and outcome | Clinical and radiographic finding | 2 week, 3rd,6th, 12th month |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | distilled water | | | | |

**Results of individual studies based on the outcome**

1. Treatment success and failure

Treatment outcomes were determined based on the reduced colony count obtained after 7 days of placement of intracanal medicaments. In addition, Datta et al (6) reported that a new combination (TAP + CHX) exhibited better effectiveness in reducing *E. faecalis* count than CH alone ($p < 0.001$). The rationale behind his study of using intracanal medicament in primary teeth is based on the concept that ribbon-shaped pulp spaces cannot be completely disinfected following chemomechanical preparation, and a combination of antimicrobial agents would have an additive/synergistic effect to address these diverse microflorae.

Regarding the total microbial load, Tirukkolluru et al (9) reported application of intracanal medicament with TAP for a time of 7 days, relatively shows higher antimicrobial efficacy in comparison to the results obtained in various studies where the number of positive samples ranged from 11% to 60% in a statistically significant way.

Yasmin et al. (10) asserted the necessity of the application of intracanal medicament in primary teeth. However, the study showed that *E. faecalis* bacterial counts decreased significantly in groups treated with TAP compared with that of the control group ($P \leq 0.001$). This confirms the findings of Faria et al. (16), wherein they reported that the primary teeth treated with TAP were clinically more successful than the conventional pulpectomy.

Based on the clinical and radiographic findings, Reddy et al. (15) reported that the clinical signs and symptoms reduced, accounting for 97% success at each time interval. Furthermore, based on the strict radiographic criteria of success, 17 out of 30 participants were healed in the triple antibiotic paste group, and 13 out of 30 participants were static in the conventional pulpectomy group. However, the present data showed that topical application of intracanal medicaments in infected primary teeth is necessary to achieve efficient pulpectomy of bizarre and tortuous root canals, which is still a challenge in primary teeth.

2. Interappointment flare-ups

On evaluating the incidence of flare-ups, Pai et al. (11) reported that 15% of diabetic patients in the calcium hydroxide group experienced interappointment flare-up, with no flare-up seen in the triple antibiotic paste group. Sinhal et al. (12) reported no flare-up incidence in either chlorhexidine or triple antibiotic paste groups, but 40% incidence in the calcium hydroxide group.

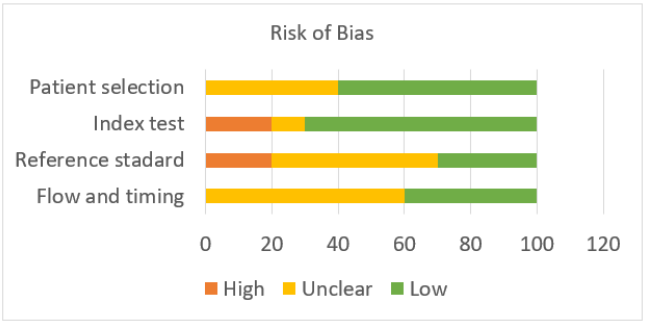
3. Postoperative pain

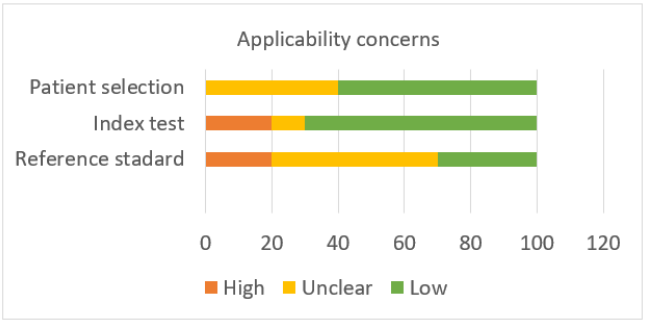
Regarding postoperative pain, Safiya et al. (7) reported an incidence of moderate and severe pain ranging from 18.2% to 0% even after multiple visits. Prasad *et al.* (14) found that the mean of postoperative pain after one week was 0.86, while Sarah et al. (8) found that postoperative pain after 24 and 48 hours was 0.08. In Safiya et al. (7) study, nearly 95% of the participants were asymptomatic after 72 hours postoperatively. All these studies attributed the reduced pain after performing the endodontic treatment in single/multiple visits with triple antibiotic paste compared to calcium hydroxide to the synergetic or additive action of antibiotics found in TAP and combined spectrum of antimicrobial activity.

**Figure 2: Risk of bias**

| RISK OF BIAS | | | | | APPLICABILITY CONCERNS | | |
|---|---|---|---|---|---|---|---|
| **Study** | Patient selection | Index test | Reference standard | Flow and timing | Patient selection | Index test | Reference standard |
| Datta B et al | + | - | + | + | + | - | + |
| Safeya et al | + | + | - | + | + | + | - |
| Sarah et al | + | + | + | ? | + | + | + |
| Tirukkolluru et al | + | + | - | ? | + | + | - |
| Yasmin et al | ? | + | ? | ? | ? | + | ? |
| Pai et al | + | ? | ? | ? | + | ? | ? |
| Sinhal et al | ? | + | ? | + | ? | + | ? |
| Sanu et al | + | - | ? | ? | + | - | ? |
| Prasad et al | ? | + | + | + | ? | + | + |
| Reddy et al | ? | + | ? | ? | ? | + | ? |

+ LOW ? UNCLEAR - HIGH




**Quality assessment of included studies – Risk of bias**

Six articles had a low risk of bias, and low applicability concerns and 4 had moderate bias risk and applicability concerns in the patient selection domain. In the index test domain, 7 articles had a low risk of bias and low applicability concerns, whereas 1 article had moderate risk and 2 had a high risk of bias and concern. 5 articles had a moderate risk of bias and concerns in the reference standard domain, whereas 2 had high risk and 3 had low risk. In the flow and timing domain. 4 articles had a low risk of bias, and low applicability concerns and 6 had moderate risk and concern. (**Figure 2**)

## DISCUSSION

Root canal treatment mainly focuses to prevent or manage apical periodontitis by decreasing the intra-canal microbial load. The presence of residual microflora decreases the endodontic

success rate, regarding postoperative pain and radiographic healing, by about 10%–15%. Maximum removal of the bacteria and irritants in the root canal system is essential to a better prognosis (17). Placement of inter-appointment dressing has been previously recommended to disinfect the root canal system completely. For the broad-spectrum action against oral microorganisms and ability to disinfect dentin, Triple Antibiotic Paste (TAP), a combination of metronidazole, ciprofloxacin, and minocycline, has been widely used. (18) TAP has been found to remain active for 30 days (19) and shows better antibacterial efficacy than calcium hydroxide in previous *in-vitro* studies. (20) TAP has been used clinically in case reports and series to treat cases with large periapical lesions when using calcium hydroxide cannot eliminate the symptoms.

The main aim of this systematic review was to assess the effectiveness of triple antibiotic paste as an intracanal medication for endodontic treatment of non-vital teeth with apical periodontitis in terms of reduced microbial load, postoperative pain flare-up incidence, clinical and radiographic healing. Therefore, the search strategy in this systematic review was comprehensive to identify all published and unpublished articles.

For any intracanal medicament to exhibit its biological effect either alone or in combination, several factors like drug concentration, drug interaction, better compaction into the canals, and of course, the intracanal microorganisms' virulence should be relied upon on. With the use of intracanal medicaments before obturation of root canals, the predictability and prognosis of endodontic success could be enhanced by many folds. (21)
The development of interappointment flare-up accompanied by pain and swelling of the facial soft tissues and oral mucosa has been considered a true emergency that usually requires an unscheduled visit for treatment. According to Torabinejad *et al.* (22), mandibular teeth were more prone to postoperative pain and flare-up than maxillary teeth.

Similarly, individuals with systemic diseases like diabetes have documented alterations in immune functions, such as depressed leukocyte adherence, chemotaxis, and phagocytosis, or more virulent microorganisms in root canals with necrotic pulp, which makes them susceptible to periradicular disease and increased incidence of inter appointment flare-up.(23)
The current evidence states that systemic antibiotics are less effective in endodontic infections and should be prescribed only in cases with systemic spread of disease. However, localized drug delivery of antibiotics alone or in combination would give a better therapeutic outcome for endodontic infections.(24,25) Ideally, in daily clinical practice, with the advancements in disinfection systems, dependency on antibiotics can be preferred
as an adjunctive mode of treatment only when other medicaments and regimens fail to achieve the therapeutic benefit.

## CONCLUSION

Thus, the comprehensive review of clinical studies has demonstrated that a combined spectrum of antimicrobial activity and synergistic action of antibiotics in triple antibiotic paste is helpful to address diverse micro flora and decrease the incidence of pain and flare-up.

## REFERENCES

1. Sundqvist G. Ecology of the root canal flora. J Endod. 1992;18(9):427–30.
2. Chu FC, Leung WK, Tsang PC, Chow TW, Samaranayake LP. Identification of cultivable microorganisms from root canals with apical periodontitis following two-visit endodontic treatment with antibiotics/ steroid or calcium hydroxide dressings. J Endod 2006;32:17-23.
3. American Association of Endodontists, "Guide to Clinical Endodontics," American Association of Endodontists, Chicago, IL, USA, 6 edition, 2013
4. Sathorn C, Parashos P, Messer H. Antibacterial efficacy of calcium hydroxide intracanal dressing: a systematic review and meta-analysis. International endodontic journal. 2007 Jan;40(1):2-10.
5. Hoshino E, Kurihara-Ando N, Sato I, Uematsu H, Sato M, Kota K, Iwaku M. In vitro antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. Int Endod J 1996;29:125-130.
6. Dutta B, Dhull KS, Das D, Samir PV, Verma RK, Singh N. Evaluation of antimicrobial efficacy of various intracanal medicaments in primary teeth: an in vivo study. International journal of clinical pediatric dentistry. 2017 Jul;10(3):267.
7. AbdurRahman S, Aziz SM, Gawdat SI, AbdalSamad AM. Postoperative pain of patients with necrotic teeth with apical periodontitis following single visit endodontic treatment versus multiple visit endodontic treatment using triple antibiotic paste: a randomized clinical trial. F1000Research. 2019;8.
8. Abouelenien SS, Ibrahim SM, Shaker OG, Ahmed GM. Evaluation of postoperative pain in infected root canals after using double antibiotic paste versus calcium hydroxide as intra-canal medication: A randomized controlled trial. F1000Research. 2018;7.
9. Tirukkolluru C, Thakur S. Comparative evaluation of triple antibiotic paste, propolis with moxifloxacin, and calcium hydroxide as intracanal medicaments against Streptococcus spp. and Enterococcus faecalis in type II diabetes mellitus patients: A randomized clinical trial. Contemporary clinical dentistry. 2019 Apr;10(2):191.
10. Ghahramani Y, Mohammadi N, Gholami A, Ghaffaripour D. Antimicrobial Efficacy of Intracanal Medicaments against E. Faecalis Bacteria in Infected Primary Molars by Using Real-Time PCR: A Randomized Clinical Trial. International Journal of Dentistry. 2020 Dec 21;2020.
11. Pai S, Pai AV, Thomas MS, Bhat V. Effect of calcium hydroxide and triple antibiotic paste as intracanal medicaments on the incidence of inter-appointment flare-up in diabetic patients: An in vivo study. Journal of conservative dentistry: JCD. 2014 May;17(3):208.
12. Sinhal TM, Shah RR, Shah NC, Jais PS, Hadwani KD. Comparative evaluation of 2% chlorhexidine gel and triple antibiotic paste with calcium hydroxide paste on incidence

of interappointment flare-up in diabetic patients: a randomized double-blinded clinical study. Endodontology. 2017 Jul 1;29(2):136

13. Narayanan S, Teja KV, Ramesh S. Comparative Evaluation of Inter Appointment Pain and Analgesic Intake with Calcium Hydroxide and Triple Antibiotic Paste As Intracanal Medicaments In Patients With Apical Periodontitis–A Randomized Controlled Single-Blinded Clinical Trial: Interappointment and analgesic intake on using two different medicaments. Brazilian Dental Science. 2021 Oct 1;24(4).
14. Prasad LK, Tanwar BS, Kumar KN. Comparison of calcium hydroxide and triple antibiotic paste as intracanal medicament in emergency pain reduction: in vivo study. Int J Oral Care Res. 2016;4(4):244-6.
15. Reddy GA, Sridevi E, Sankar AS, Pranitha K, Gowd MP, Vinay C. Endodontic treatment of chronically infected primary teeth using triple antibiotic paste: An in vivo study. Journal of conservative dentistry: JCD. 2017 Nov;20(6):405.
16. G. Faria, P. Nelson-Filho, A. C. Freitas, S. Assed, and I. Y. Ito, "Antibacterial effect of root canal preparation and calcium hydroxide paste (calen) intracanal dressing in primary teeth with apical periodontitis," *Journal of Applied Oral Science*, vol. 13, no. 4, pp. 351–355, 2005.
17. Waltimo T, Trope M, Haapasalo M, *et al.*: Clinical efficacy of treatment procedures in endodontic infection control and one year follow-up of periapical healing. *J Endod.* 2005; 31(12): 863–6.
18. Parhizkar A, Nojehdehian H, Asgary S. Triple antibiotic paste: momentous roles and applications in endodontics: a review. Restorative dentistry & endodontics. 2018 Apr 26;43(3).
19. Ordinola-Zapata R, Bramante CM, Minotti PG, *et al.*: Antimicrobial activity of triantibiotic paste, 2% chlorhexidine gel, and calcium hydroxide on an intraoral-infected dentin biofilm model. *J Endod.* 2013; 39(1): 115–8.
20. Adl A, Hamedi S, Sedigh Shams M, *et al.*: The ability of triple antibiotic paste and calcium hydroxide in disinfection of dentinal tubules. *Iran Endod J.* 2014; 9(2): 123–6.
21. Hamid EA, Aziz SA, Sadek HS, Ibrahim AM. Effectiveness of triple antibiotic paste as an intra-canal medication for the root canal treatment of non-vital teeth with apical periodontitis: A systematic review. F1000Research. 2018 Oct 11;7(1627):1627
22. Torabinejad M, Kettering JD, McGraw JC, Cummings RR, Dwyer TG, Tobias TS. Factors associated with endodontic interappointment emergencies of teeth with necrotic pulps. J Endod 1988;14:261-6.
23. Nasim I, Jabin Z, Kumar SR, Vishnupriya V. Green synthesis of calcium hydroxide-coated silver nanoparticles using Andrographis paniculata and Ocimum sanctum Linn. leaf extracts: An antimicrobial and cytotoxic activity. Journal of Conservative Dentistry and Endodontics. 2022 Jul 1;25(4):369-74.
24. Nasim I, Jaju KK, Shamly M, Vishnupriya V, Jabin Z. Effect of nanoparticle based intra-canal medicaments on root dentin micro-hardness. Bioinformation. 2022;18(3):226.
25. Karobari MI, Adil AH, Assiry AA, Basheer SN, Noorani TY, Pawar AM, Marya A, Messina P, Scardina GA. Herbal medications in endodontics and its application—a review of literature. Materials. 2022 Apr 25;15(9):3111.