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Medicaments Used in the Treatment of Periradicular Diseases: A Review of Literature

Research Article

Rukhsaar Akbar Gulzar[1], Iffat Nasim[2*]

[1] Post Graduate Student, Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.
[2] Head of Department, Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.

Abstract

The success of endodontic therapy is based on the triad of mechanical debridement, through disinfection and a three dimensional obturation. The ethics of reasonable endodontic therapy are focused on prevention, minimization and elimination of infection which are not easy tasks within the condition of a root canal system. The endodontic protocols have evolved with the advent of modern endodontics. Usually the treatment of teeth with vital pulp is done in a single visit, eliminating the need for interappointment dressings. The need for intracanal medicament becomes more relevant in cases of pulp necrosis and periapical pathosis whose treatment is challenging due to the presence of biofilms and complex canal anatomy. The selection of an appropriate medicament plays a vital role. It is often even recommended to use two preparations either in combination or in sequence. The final aim is to achieve a full range of therapeutic effects. The following literature is to review the medicaments that are used in the treatment of periradicular diseases.

Keywords: Apical Periodontitis; Biofilms; Intracanal Medicaments; Multi Visit Endodontics; Octenidine Dihydrochloride.

Introduction

Apical periodontitis occurs as an inflammatory reaction in the periapical tissue due to the presence of bacteria in the root canal system [1]. Microorganisms grow in the canal in the form of planktonic cells as well as in the form of complex biofilms which are challenging to eliminate. Biofilms are composed of microcolonies of bacteria in a matrix of exopolysaccharides, proteins, salts and cell material in an aqueous solution which takes up 85% of the volume. It is these biofilms that cause persistent inflammation. The growth of bacteria in biofilms is favoured by the complex anatomy of the root canal system [2, 3]. Further, anaerobic bacteria may invade the dentinal tubules of the canal with necrotic pulps. This makes management of apical periodontitis highly complex and challenging.

Multi visit endodontics is based on the debridement and irrigation of the canal in the first appointment followed by placement of an antibacterial medicament in the canal for one week or more. Kawashima et al defined intracanal medicament as temporary placement of medicaments with good biocompatibility into root canals for the purpose of inhibiting coronal invasion of bacteria. There is documented scientific evidence that mechanical debridement of the canal reduces the microorganisms by 100 to 1000 folds in number but complete elimination is achieved in only 20-40% of the cases[4]. Irrigation with 0.5% sodium hypochlorite is able to disinfect additional 40-60% cases [5]. Application of calcium hydroxide dressing is said to raise the percentage of bacteria negative teeth to 90 to 100% [6]. The rationale behind intracanal medication is to destroy residual microorganisms and their toxins and any residual bacteria that have not been removed during the root canal preparation.

Our institution is passionate about high quality evidence based research and has excelled in various fields [7-17].

Previously our team has a rich experience in working on various research projects across multiple disciplines [12, 18-31] Now the

***Corresponding Author**:
Dr. Iffat Nasim,
Head of Department, Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.
Tel: 9940063567
E-mail: iffatnasim@saveetha.com

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growing trend in this area motivated us to pursue this project.

Ideal Requirements Of Intracanal Medicaments [32, 33]

(By Louis I grossman, Endodontic Practice, 10th edition)

1. It should be an effective germicide and fungicide
2. It should be non irritating to the periapical tissue
3. It should remain stable in solution
4. It should have prolonged antimicrobial effect
5. It should be active in the presence of protein derivatives of tissues, blood and serum
6. It should have low surface tension
7. It should not interfere with the repair of periapical tissues
8. It should not stain tooth structure
9. It should be capable of inactivation in a culture medium
10. It should not induce cell mediated immune response
11. It should have no deleterious effect on vital tissues
12. It should not alter the physiologic activities of the host tissues
13. It should have good penetrating ability to be effective in the dentinal tubules
14. It should reduce pain
15. It should induce healing and hard tissue formation
16. It should eliminate apical exudates
17. It should control inflammatory root resorption
18. It should have reasonable shelf life
19. It should be readily available
20. It should not be inexpensive

Objectives Of Intracanal Medicaments [34]

1. To dry persistently wet or the so-called weeping canals.
2. To eliminate any remaining microbes in the pulp space.
3. To render root canal contents inert.
4. To neutralize tissue debris
5. To act as a barrier against leakage from an interappointment dressing in symptomatic cases.
6. Reduction of postoperative pain.

Factors Affecting The Antibacterial Properties Of Medicaments [35, 36]

1. The Drug: Certain drugs have more extensive and rapid antimicrobial effects as compared to others. At therapeutic concentrations, certain drugs are bacteriostatic and not bactericidal thereby only impeding the growth of bacteria. Once the drug is removed, it is possible that the bacteria might replenish their numbers. Further, an endodontic infection is multimicrobial and one drug might not have the same effect on all the microorganisms. At present however, there are no single antibiotics effective against all micro-organisms liable to be present in contaminated root canals. A combination of antibiotics or of one or more antibiotics with a chemical antiseptic is therefore necessary. Possible drawback to use of antibiotics.

a. Resistant strains may develop.
b. Allergic response
c. Person who was previously insensitive to an antibiotic may become sensitized following its use in the root canal.

2. Microorganisms: Antimicrobial action of these dressings must reach different types of microorganisms, inhibits osteoclastic activity in root resorption and favours tissue repair. However, certain microorganisms have the inherent ability to survive the action of antimicrobials and develop a resistance. The more accessible they are, the more readily they can be eliminated. Further, bacteria that are grouped in colonies are more resistant to destruction.

Classification Of Intracanal Medicaments According To Grossman (1990)

1. Essential oils
a. Eugenol

2. Phenolic compounds
a. Phenol
b. Parachlorophenol
c. Camphorated parachlorophenol
d. Cresol
e. Formocresol
f. Creosote
g. Cresatin
h. Cresanol

3. N2
4. Salt of heavy metals
a. Metaphen
b. Merthiolate
c. Mercurophen

5. Halogens
a. Sodium hypochlorite
b. Iodides
c. Chlorhexidine

6. Quaternary ammonium compounds
a. 9-aminoacidine

7. Fatty acids
a. Propionic acid
b. Caproic acid
c. Cuprylic acid

8. Sulphonamides.

Intracanal Medicaments

Eugenol

Eugenol is the chemical essence of oil of clove and is somewhat related to phenol. It is both an antiseptic and an anodyne. Its anodyne effect is due to its ability to block the conduction of nerve impulses. It has a bacteriostatic action at therapeutic concentration [37, 38].

Phenolic Compounds

Phenol: Phenol is one of the oldest antiseptic medicines which was introduced into medicine in 1867 by Lord Lister. It is derived from coal tar and has a white crystalline structure with a characteristic odor. The use of phenol as a root canal disinfect-

ant has however declined over the past years owing to its caustic nature.. The mechanism of action is best described as cytocidal. It penetrates the cell wall of bacteria by disrupting it and then precipitates the protoplasmic protein to cause cell death. At lower concentrations it inactivates the essential enzyme systems of the bacteria [37, 38].

Parachlorophenol: They are needle-like crystals which are colourless and turn dark upon exposure to light. It is formed when chlorine replaces one of the hydrogen atoms of phenol. Crystals are soluble in alcohol, ether, alkalies and slightly soluble in water. By trituration with gum camphor it combines to form an oily liquid [32, 38].

Camphorated parachlorophenol: Walkhoft introduced camphorated parachlorophenol into dentistry in the year 1891. By composition it consists of 2 parts P-chlorophenol and 3 parts gum camphor. It is a light amber coloured transparent oily liquid. Pure parachlorophenol is an irritant which is counteracted by addition of camphor which also serves as a diluent and vehicle. Wantulok and Brown have demonstrated that the vapours of camphorated chlorophenol of cresatin will pass through the apical foramen [32, 38].

Camphorated Monochlorophenol (CMPC): Mining of the crystals of para monochlorophenol with camphor in proportion of 3:7 when liquefaction occurs spontaneously forms camphorated monochlorophenol. Whilst CMPC is a more powerful bactericidal agent than phenol. It is much less irritant and doesn't coagulate albumin [32, 38].

Cresol, Creosote,Cresatin, Cresanol: Cresol which is obtained from coal tar is a combination of Ortho, Meta and Para-isomeric cresol and it may contain a trace of phenol. It has a phenolic odor and is a colourless or pinkish liquid. As a disinfectant compared to phenol it is three times more effective. Cresol is also a substitution product of phenol.

Creosote has a sharp pungent aromatic odour and is yellowish and oily. When compared to phenol, it is a better disinfectant, less toxic and irritating. Only the beechwood variety of creosote is used in dentistry.

Cresatin is also known as metacresylacetate. It is the acetic acid ester of Metacresol and has a phenolic acetic odour. It is a clear stable oily liquid of low volatility. It has antiseptic and analgesic properties. It has low surface tension which enhances its antibacterial property. Due to its low vapour pressure, it has a prolonged effect. It is not caustic, less irritating and doesn't precipitate albumin.

Cresanol is formed by combining cresatin, P-chlorophenol and camphor the ratio of 1:1:2. It is slightly more effective as an antiseptic than cresatin and slightly less irritating than chlorophenol [32, 38].

Formocresol

It was introduced in the year 1905 by Buckley. It is a combination of formalin and cresol in the ratio of 1:2 or 1:1. It has 19% of formaldehyde, 35% cresol and 46% of glycerin and water. Formaldehyde can be merely placed in the pulp chamber or in the cervical third of the root canal space and still be effective in the apical portion. The toxic effect of it can however cause necrosis of surrounding tissue [38].

Chlorhexidine [39]

Chlorhexidine consists of two symmetric 4-chlorophenyl rings and two biguanide groups connected by a central hexamethylene chain. For endodontic purposes, CHX can be used in a liquid or in a gel presentation. CHX gel consists of a gel base (1% natrosol, a hydroxyethylcellulose, pH 6-9) and chlorhexidine gluconate (23,31), in a optimal pH range of 5.5 to 7.0. It is basic in nature and is more stable in its salt form. The antimicrobial activity of chlorhexidine is pH dependent. At physiologic pH it readily dissociates releasing the positively charged CH component. The microbial cell walls that are negatively charged serve as sites where this cationic molecule binds and changes the osmotic equilibrium and produces a bactericidal effect at high concentrations by causing coagulation of the cell cytoplasm resulting in the death of the cell. It is bacteriostatic at low concentrations causing potassium and phosphorus to leach out from the cells. It is effective against gram positive and gram negative bacteria, yeast and fungi. It exhibits the property of substantivity by being slowly released from the retention sites thereby exhibiting a prolonged antibacterial effect. However, CHX's incapacity of tissue dissolution has been pointed out as its major disadvantage.

Antimicrobials

Grossman reported the first use of antibiotic paste in endodontics called PBSC, polyantibiotic paste. It is a combination of penicillin for gram positive organisms, bacitracin for penicillin resistant strains, streptomycin for gram negative organisms and caprylate sodium for yeasts. Nystatin replaces sodium caprylate as the antifungal agent in a similar medicament PBSN [40].

Another combination most commonly used is triple antibiotic paste (TAP) which is a combination of metronidazole, ciprofloxacin and minocycline. Minocycline is a bacteriostatic broad spectrum antibiotic, metronidazole is a nitroimidazole compound which exhibits a broad spectrum of activities against protozoa and anaerobic bacteria and Ciprofloxacin is a second-generation fluoroquinolone antibiotic. One of the major drawbacks of TAP is tooth discolouration caused due to minocycline and hence double antibiotic paste was introduced as a combination of ciprofloxacin and metronidazole. Ledermix was developed in 1960 by Schroeder and Triadon and is a glucocorticoid antibiotic paste. It consists of triamcinolone acetonide (1% – for anti-inflammatory effects) and demethylchlortetracycline (3.021% – for antibacterial action). Besides its antibacterial properties, it helps in relieving pain and inhibition of inflammatory root resorption. Depending on the pathological condition being treated, it is proposed that the medicament be left in the canal for 2 to 12 weeks. However, it does have the drawback of discolouration of the tooth [41].

Calcium Hydroxide

Calcium Hydroxide was introduced into dentistry by Hermann in 1920. It is a strong base and it dissociates into calcium and hydroxyl ions when it comes in contact with aqueous fluids. The high alkaline nature of calcium hydroxide is due to the hydroxyl ions which makes it bactericidal. Hydroxyl ions are highly oxi-

dant free radicals that show extreme reactivity with biomolecules. The phospholipid structure of the bacterial cell membrane is destroyed by lipid peroxidation caused due to the hydroxyl ions. Hydrogen atoms from unsaturated fatty acids are removed by the hydroxyl ions and thus a free lipidic radical is generated which reacts with oxygen to generate a free lipidic peroxide radical. This further removes another hydrogen atom from a second fatty acid to generate another lipidic peroxide. An autocatalytic chain reaction is generated due to the peroxides causing extensive membrane damage. Further, the alkaline nature of calcium hydroxide causes protein denaturation by breaking down the tertiary structure of protein by the breakdown of ionic bonds. The hydroxyl ions also split the bacterial DNA strands and inhibit its replication. Lethal mutations might also be induced by free radicals. As long as the pH is retained, calcium hydroxide exerts its antimicrobial action in the canal [42]. However calcium hydroxides inability to completely eliminate E faecalis has been stated in literature [43].

Calcium hydroxide powder has been mixed with different vehicles for placement in the canal such as water, CMCP, normal saline, cresatin, glycerin and propylene glycol. The dissociation of calcium hydroxide into its ions depends on the vehicle. Thus the vehicle would in turn have an effect on its antimicrobial property. Some authors have stated that camphorated monochlorophenol increases the antimicrobial effect of calcium hydroxide [44] while high concentrations of glycerol and propylene glycol decreases it [45].

Octenidine Dihydrochloride As An Antimicrobial Compound

Octenidine hydrochloride (OCT), developed by Sterlig Winthrop Research Institute, is a bis pyridine derivative, N,N'-[1,10-decanediyldi-1(4H)-pyridinyl-4-ylidene] bis(1-octanamine) dihydrochloride. It has two non interacting cationic centres in the molecule separated by a long aliphatic hydrocarbon chain. Microbial cell envelopes are negatively charged and hence octenidine being cationic in nature readily binds to it. It has a particularly strong adherence to lipid bacterial cell membrane components such as cardiolipin which explains its high antimicrobial efficacy without affecting epithelial tissue. Further it interacts with the enzyme system and polysaccharides in the cell wall of microorganisms and induces leakage in the cytoplasmic membrane. Since it binds readily to the negatively charged surfaces, it has a sustained antimicrobial action.

More than 20 years ago, octenidine dihydrochloride was introduced as an antiseptic for skin, mucous membranes and wounds. Octenidine and phenoxyethanol show synergistic effects and are hence used in combination. Octenidine has a broad antimicrobial spectrum against gram positive and gram negative bacteria. Its efficacy is 3 to 10 times higher than that of chlorhexidine with minimum inhibitory concentrations and like chlorhexidine, it does not form chloranaeline when it comes in contact with sodium hypochlorite. It is chemically stable and has low toxicity. In Vitro studies of octenidine being used as a disinfectant in root canals has obtained positive results. Octenidine is currently used in the treatment of gingival and periodontal diseases for the oral cavity as mouth washes [46].

Conclusion

The use of intracanal medicament is highly recommended in treated cases of pulp necrosis and periradicular diseases and the selection of an appropriate medicament plays a vital role. It is often even recommended to use two preparations either in combination or in sequence. The final aim is to achieve a full range of therapeutic effects.

References

[1]. Nair PN. On the causes of persistent apical periodontitis: a review. Int Endod J. 2006 Apr;39(4):249-81. Pubmed PMID: 16584489.

[2]. Mohammadi Z, Palazzi F, Giardino L, Shalavi S. Microbial biofilms in endodontic infections: an update review. Biomed J. 2013 Mar-Apr;36(2):59-70. Pubmed PMID: 23644234.

[3]. Siqueira JF, Rôças IN, Ricucci D. Biofilms in endodontic infection. Endodontic Topics. 2010 Mar;22(1):33-49.

[4]. Byström A, Sundqvist G. Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. Scand J Dent Res. 1981 Aug;89(4):321-8. Pubmed PMID: 6947391.

[5]. Byström A, Sundqvist G. Bacteriologic evaluation of the effect of 0.5 percent sodium hypochlorite in endodontic therapy. Oral Surg Oral Med Oral Pathol. 1983 Mar;55(3):307-12. Pubmed PMID: 6572884.

[6]. Bystrom A, Claesson R, Sundqvist G. The antibacterial effect of camphorated paramonochlorophenol, camphorated phenol and calcium hydroxide in the treatment of infected root canals. Endod Dent Traumatol. 1985 Oct;1(5):170-5. Pubmed PMID: 3865763.

[7]. Vijayashree Priyadharsini J. In silico validation of the non-antibiotic drugs acetaminophen and ibuprofen as antibacterial agents against red complex pathogens. J Periodontol. 2019 Dec;90(12):1441-1448. Pubmed PMID: 31257588.

[8]. J PC, Marimuthu T, C K, Devadoss P, Kumar SM. Prevalence and measurement of anterior loop of the mandibular canal using CBCT: A cross sectional study. Clin Implant Dent Relat Res. 2018 Aug;20(4):531-534. Pubmed PMID: 29624863.

[9]. Ramesh A, Varghese S, Jayakumar ND, Malaiappan S. Comparative estimation of sulfiredoxin levels between chronic periodontitis and healthy patients - A case-control study. J Periodontol. 2018 Oct;89(10):1241-1248. Pubmed PMID: 30044495.

[10]. Ramadurai N, Gurunathan D, Samuel AV, Subramanian E, Rodrigues SJL. Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial. Clin Oral Investig. 2019 Sep;23(9):3543-3550. Pubmed PMID: 30552590.

[11]. Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Oral Pathol Med. 2019 Apr;48(4):299-306. Pubmed PMID: 30714209.

[12]. Ezhilarasan D, Apoorva VS, Ashok Vardhan N. Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells. J Oral Pathol Med. 2019 Feb;48(2):115-121. Pubmed PMID: 30451321.

[13]. Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of Streptococcus mutans, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial. Clin Oral Investig. 2020 Sep;24(9):3275-3280. Pubmed PMID: 31955271.

[14]. Samuel SR. Can 5-year-olds sensibly self-report the impact of developmental enamel defects on their quality of life? Int J Paediatr Dent. 2021 Mar;31(2):285-286. Pubmed PMID: 32416620.

[15]. R H, Ramani P, Ramanathan A, R JM, S G, Ramasubramanian A, et al. CYP2 C9 polymorphism among patients with oral squamous cell carcinoma and its role in altering the metabolism of benzo[a]pyrene. Oral Surg Oral Med Oral Pathol Oral Radiol. 2020 Sep;130(3):306-312. Pubmed PMID: 32773350.

[16]. Chandrasekar R, Chandrasekhar S, Sundari KKS, Ravi P. Development and validation of a formula for objective assessment of cervical vertebral bone age. Prog Orthod. 2020 Oct 12;21(1):38. Pubmed PMID: 33043408.

[17]. Vijayashree Priyadharsini J, Smiline Girija AS, Paramasivam A. In silico analysis of virulence genes in an emerging dental pathogen A. baumannii and related species. Arch Oral Biol. 2018 Oct;94:93-98. Pubmed PMID: 30015217.

[18]. Govindaraju L, Gurunathan D. Effectiveness of Chewable Tooth Brush in Children-A Prospective Clinical Study. J Clin Diagn Res. 2017

Mar;11(3):ZC31-ZC34. Pubmed PMID: 28511505.
[19]. Christabel A, Anantanarayanan P, Subash P, Soh CL, Ramanathan M, Muthusekhar MR, et al. Comparison of pterygomaxillary dysjunction with tuberosity separation in isolated Le Fort I osteotomies: a prospective, multi-centre, triple-blind, randomized controlled trial. Int J Oral Maxillofac Surg. 2016 Feb;45(2):180-5. Pubmed PMID: 26338075.
[20]. Soh CL, Narayanan V. Quality of life assessment in patients with dentofacial deformity undergoing orthognathic surgery--a systematic review. Int J Oral Maxillofac Surg. 2013 Aug;42(8):974-80. Pubmed PMID: 23702370.
[21]. Mehta M, Deeksha, Tewari D, Gupta G, Awasthi R, Singh H, et al. Oligonucleotide therapy: An emerging focus area for drug delivery in chronic inflammatory respiratory diseases. Chem Biol Interact. 2019 Aug 1;308:206-215. Pubmed PMID 31136735.
[22]. Campeau PM, Kasperaviciute D, Lu JT, Burrage LC, Kim C, Hori M, et al. The genetic basis of DOORS syndrome: an exome-sequencing study. Lancet Neurol. 2014 Jan;13(1):44-58. Pubmed PMID: 24291220.
[23]. Kumar S, Sneha S. Knowledge and awareness regarding antibiotic prophylaxis for infective endocarditis among undergraduate dental students. Asian Journal of Pharmaceutical and Clinical Research. 2016;154.
[24]. Christabel SL, Gurunathan D. Prevalence of type of frenal attachment and morphology of frenum in children, Chennai, Tamil Nadu. World J Dent. 2015 Oct;6(4):203-7.
[25]. Kumar S, Rahman RE. Knowledge, awareness, and practices regarding biomedical waste management among undergraduate dental students. Asian Journal of Pharmaceutical and Clinical Research. 2017;10(8):341.
[26]. Sridharan G, Ramani P, Patankar S. Serum metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Cancer Res Ther. 2017 Jul-Sep;13(3):556-561. Pubmed PMID: 28862226.
[27]. Ramesh A, Varghese SS, Doraiswamy JN, Malaiappan S. Herbs as an antioxidant arsenal for periodontal diseases. J Intercult Ethnopharmacol. 2016 Jan 27;5(1):92-6. Pubmed PMID: 27069730.
[28]. Thamaraiselvan M, Elavarasu S, Thangakumaran S, Gadagi JS, Arthie T. Comparative clinical evaluation of coronally advanced flap with or without platelet rich fibrin membrane in the treatment of isolated gingival recession. J Indian Soc Periodontol. 2015 Jan-Feb;19(1):66-71. Pubmed PMID: 25810596.
[29]. Thangaraj SV, Shyamsundar V, Krishnamurthy A, Ramani P, Ganesan K, Muthuswami M, et al. Molecular Portrait of Oral Tongue Squamous Cell Carcinoma Shown by Integrative Meta-Analysis of Expression Profiles with Validations. PLoS One. 2016 Jun 9;11(6):e0156582. Pubmed PMID: 27280700.
[30]. Ponnulakshmi R, Shyamaladevi B, Vijayalakshmi P, Selvaraj J. In silico and in vivo analysis to identify the antidiabetic activity of beta sitosterol in adipose tissue of high fat diet and sucrose induced type-2 diabetic experimental rats. Toxicol Mech Methods. 2019 May;29(4):276-290. Pubmed PMID: 30461321.
[31]. Ramakrishnan M, Bhurki M. Fluoride, Fluoridated Toothpaste Efficacy And Its Safety In Children-Review. International Journal of Pharmaceutical Research. 2018 Oct 1;10(04):109-14.
[32]. Chandra S. Grossman's endodontic practice. Wolters kluwer india Pvt Ltd; 2014.
[33]. Grossman LI. Sterilization of infected root canals. J Am Dent Assoc. 1972 Oct;85(4):900-5. Pubmed PMID: 4561046.
[34]. Kumar A, Tamanna S, Iftekhar H. Intracanal medicaments–Their use in modern endodontics: A narrative review. Journal of Oral Research and Review. 2019 Jul 1;11(2):94.
[35]. Ørstavik D. Intracanal medication. Harty's Endodontics in Clinical Practice. Elsevier. Edinburgh; New York: Churchill Livingstone. 2010.
[36]. E. Nicholls. ENDODONTICS (3RD EDITION) Australian Endodontic Newsletter 2010;10:13–13
[37]. Grossman LI. Endodontic practice. Journal of Endodontics 1982;8:S34–S35
[38]. Abbott PV. Medicaments: aids to success in endodontics. Part 1. A review of the literature. Aust Dent J. 1990 Oct;35(5):438-48. Pubmed PMID: 2073192.
[39]. Gomes BP, Vianna ME, Zaia AA, Almeida JF, Souza-Filho FJ, Ferraz CC. Chlorhexidine in endodontics. Braz Dent J. 2013;24(2):89-102. Pubmed PMID: 23780357.
[40]. GROSSMAN LI. Polyantibiotic treatment of pulpless teeth. J Am Dent Assoc. 1951 Sep;43(3):265-78. Pubmed PMID: 14873439.
[41]. Kim ST, Abbott PV, McGinley P. The effects of Ledermix paste on discolouration of mature teeth. Int Endod J. 2000 May;33(3):227-32. Pubmed PMID: 11307439.
[42]. Siqueira JF Jr, Lopes HP. Mechanisms of antimicrobial activity of calcium hydroxide: a critical review. Int Endod J. 1999 Sep;32(5):361-9. Pubmed PMID: 10551109.
[43]. Evans M, Davies JK, Sundqvist G, Figdor D. Mechanisms involved in the resistance of Enterococcus faecalis to calcium hydroxide. Int Endod J. 2002 Mar;35(3):221-8. Pubmed PMID: 11985673.
[44]. Siqueira JF Jr, de Uzeda M. Influence of different vehicles on the antibacterial effects of calcium hydroxide. J Endod. 1998 Oct;24(10):663-5. Pubmed PMID: 10023249.
[45]. Safavi K, Nakayama TA. Influence of mixing vehicle on dissociation of calcium hydroxide in solution. J Endod. 2000 Nov;26(11):649-51. Pubmed PMID: 11469293.
[46]. Hübner NO, Siebert J, Kramer A. Octenidine dihydrochloride, a modern antiseptic for skin, mucous membranes and wounds. Skin Pharmacol Physiol. 2010;23(5):244-58. Pubmed PMID: 20484966.