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INTRACANAL MEDICAMENTS –A COMPREHENSIVE REVIEW

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ABSTRACT

The primary objective of successful endodontic treatment is the complete elimination of microorganisms and debris from the affected root canals, ensuring thorough sealing and removal of any microbial presence in the canal space. Consequently, intracanal medicaments have been utilized in root canal therapy (RCT). Numerous intracanal medicaments have been evaluated, with calcium hydroxide being the most effective, though it has its own set of limitations and drawbacks. Additionally, some newer materials such as bioactive glass, Triple antibiotic paste, and PDA have been suggested for use as intracanal medicaments. This article aim's to highlight uses and limitations of calcium hydroxide as well as the recent advances in intracanal medicaments. Success of the root canal treatment lies on 1) Biomechanical preparation of the root canals 2) Depuration 3) Obturation. Intracanal medicaments plays an important role in destroy.

KEYWORD: Intra canal medicaments, Root canal, Calcium hydroxide, Disinfection, microorganism, biomechanical preparation.

INTRODUCTION

Microorganisms are pivotal etiologic factor for pulpal and periradicular diseases to occur. However when the infection continuous it leads to necrosis and apical periodontitis furthermore the whole root canal will be infected by microorganisms. The main goal of an endodontic treatment is complete removal of bacteria, nullifying the residual agents which are remaining in the root canal after depurating all the bacteria, and complete sealing of disinfected root canals.

The endodontic treatment success depends on eradication of microorganisms capable of causing intraradicular or extraradicular infection; they depend on intraoperative factors such as irrigation, access size, and the use of medications or the number of appointments. In order to achieve a more effective eradication of these microorganisms, the use of intracanal medications between appointments began to be used when the pulp diagnosis was necrosis or periapical abscess.

The main objective of intracanal medicament usage is to prevent secondary infection and have bactericidal action against microorganism. Cleaning and shaping alone cannot eliminate the microorganisms that are present within dentinal tubules. Hence intracanal medications usage reduces pulpal inflammation, inerts the canal contents, neutralizes the tissue debris, drys up persistent wet canals and acts as barrier against leakage from the temporary restorations.

Intracanal medicaments are indicated to be filled in middle of appointments because their effects are prolonged than the irrigants. The remaining microorganisms might duplicate in same number as the initial stage of the treatment if the antiseptic intracanal medicaments are not applied properly in between the visits. Henceforth it is a necessity to make use of intracanal medicament effectively. Also there is a need to establish medicament which has prolonged outcome and minimal irritation to the apical peridontium. Intracanal medicaments as a part of controlled asepsis should be used only as a root canal disinfectant in infected root canals, secondary to cleaning and shaping of the root canal.[1]

HISTORY OF INTRACANAL MEDICAMENTS

Going back to history of intracanal medicaments origin in early times. Beechwood creosote was mentioned in the 1840 article Creosote and Cotton in Fang Filling[2] In 1884, Richmond recommended applying a small-sized piece of orangewood with phenol in order to devitalise the pulp.[3] Thus, phenolics, which include eugenol (this may be differentially classified as an essential oil), parachlorophenol, camphorated parachlorophenol, camphorated monoparachlorophenol, cresatin (metacresylacetate), cresol, thymol and creosote, are drugs with a long history in the dental field that begins in the 1800s.

Many combinations of these drugs were prepared and played major roles in root canal treatment from the 19th to the 20th century. Formocresol, which is categorised into the aldehydes, was often used as a root canal medicament and played a major role in root canal treatment since[4] Buckley referred to it as an effective intracanal medicament in 1904. Phenolics, aldehydes and their combinations show strong bactericidal effects. Although halides including sodium hypochlorite and iodine, chlorhexidine gluconate, antibiotics, steroids and non-steroidal anti-inflammatory drugs (NSAIDS) have been reported as intracanal medicaments, none of them holds a premier position at present.

Phenol and formocresol have been shown to exhibit marked cytotoxicity[5-6], and formocresol has also been reported to show teratogenicity and tumorigenicity 7-8 and induce immune reactions.[9-10] Antibiotics may be transported from the apical opening to the entire body and induce the development of resistant strains, microbial substitution and allergy.[11] The effects of steroids and NSAIDs on periapical pathosis are still uncertain, and they are suggested for routine use. However, aqueous solutions of sodium hypochlorite, a typical halogen disinfectant, are still in wide use as root canal irrigant; as well, chlorhexidine gluconate is also reported to be effective for root canal irrigation in certain circumstances.[12] Calcium hydroxide has been used as pulp-dressing material, since Hermann applied it to dentistry in 1920.[13,14,15]

OBJECTIVES FOR INTRA CANAL MEDICAMENTS

- **Eradication of bacteria:** The primary goal of intracanal medicament is elimination or to depurate all microorganisms which are present in root canal.
- **Making canal contents inactive:** using chemicals that will mummify or deactivate the tissue/ debris which are present in the pulp space.

- **To prevent the after treatment trauma:** The crucial goal of endodontic treatment is to reduce the inflaming reaction. The antibacterial action of the intracanal medicaments will reduce post treatment inflammation.
- **Enhancing anesthesia:** In few conditions in which anesthetizing pulp is difficult, but there are some preferable agents that are given to decrease the pain in the inflamed pulp.[16]

INDICATIONS OF INTRACANAL MEDICAMENTS*:*

Eradication microorganisms: To sterilize (destroy all viable microorganisms) or to disinfect (destroy all pathogens) in the canal space.

Making contents of canal inert: This represents the attempt usually by chemical means to "mummify", fix or neutralize tissue or debris left intentionally or unintentionally in the pulp space.

Prevention or control of post treatment pain: The objective is to reduce or alter the inflammatory response.

Enhancing Anesthesia: By reducing the sensitivity of the inflamed, difficult to anesthetize pulp.

Control of persistent periapical abscess: In cases of continually "weeping" canal or significant pain or swelling medicaments have been suggested as a means of controlling this difficult situation.[17]

IDEAL REQUISITES OF AN INTRACANAL MEDICAMENT

- Should be an effective germicide and fungicide.
- Should not irritate the periapical tissues.
- Should remain stable in solution.
- Should have a prolonged antimicrobial effect.
- Should be active in the presence of blood, serum and protein derivatives of tissues.
- Should have low surface tension.
- Should not interfere with repair of periapical tissues.
- Should not stain the tooth structure.
- Should be capable of inactivation in a culture medium.
- Should not induce a cell mediated immune response.
- Should be easy to handle (place and remove)
- Should be Cost effective.[18]

CLASSIFICATION OF INTRACANAL MEDICAMENTS

Grossman (Table-2), Dental clinics of North America (Table-3) and Ingle (Table-4) had proposed globally accepted classifications as listed below along with general classification (Table-1).[19-22]

GROSSMAN‟S CLASSIFICATION	
ESSENTIAL OILS	Eugenol
PHENOLIC COMPOUNDS	Para ChloroPhenol Camphorated Parachloro phenol (CMPP) Formocresol Glutaraldehyde Cresatin
HALOGENS	Sodium hypochlorite Iodide
QUATERNARYAMMONIUMCOMPOUNDS	Aminoacridine

DCNA CLASSIFICATION - 1984	
PHENOLIC COMPOUNDS	Eugenol Camphorated monoparachlorophenol (CMCP) Parachlorophenol (PCP) Camphorated parachlorophenol (CPC) Metacresylacetate (Cresatin) Cresol Creosote (Beechwood) Thymol
ALDEHYDES	Formocresol Glutaraldehyde
HALIDES	Sodium hypochlorite Iodine- Potassium iodide
ANTIBIOTICS	
STEROIDS	
CALCIUM HYDROXIDE	
COMBINTIONS	

ESSENTIAL OILS

The chemical component of clove oil is eugenol, which is related to phenol. It is both an anodyne and an antiseptic, but it is a little more irritating than clove oil. Eugenol has been found by Trowbridge et al. to block intradental nerve impulses. Eugenol is used as a dressing to temporarily relieve pain following crucial pulp exposure and as a root canal filling material when combined with other cements, such as zinc oxide. It is mostly used for its analgesic properties and has a well-established but restricted antibacterial activity.[23] Zinc oxide eugenol cement (ZOE), Calen paste thickened with zinc oxide (Calen/ZO), Sealapex sealer and EndoREZ sealer act against 5 common bacterial strains found in endodontic infections

(Kocuria rhizophila, Enterococcus faecalis, Streptococcus mutans, Escherichia coli and Staphylococcusaureus).[24]

PHENOLS / PHENOL DERIVATIVES

In the past, phenols or their derivatives, such as paramonochlorophenol and cresol, were the most frequently employed intracanal medications in between sessions. These substances were often mixed with camphor to produce camphorated solutions, which release phenol more gradually and make them less caustic. Cresol and formaldehyde are commonly combined to create formocresol. All of these compounds indiscriminately agglomerate cell contents and cause tissue necrosis when touched. These compounds have been shown to be very toxic and tissue-irritating, with minimal antibacterial activity.[25,26]

Phenols, also known as carbolic acid, is the oldest compound used to control microorganisms. It was first introduced by Lord Lister in 1867. It is a white, crystalline substance with a distinctive smell that comes from coal tar. Phenol is a protoplasm poison that causes necrosis of soft tissues by penetrating and disrupting the cell wall of bacteria and then the protoplasm. This substance is very effective at concentrations as low as 1 to 2%. Because of its high toxicity-to-efficacy ratio, phenol is no longer utilised in endodontics.

30% phenol, 60% camphor, and 10% ethyl alcohol make up camphorated phenol. It is the least poisonous of all phenolic compounds and has good antibacterial and analgesic properties. The objective of the camphorating method is to create a medication that is less caustic due to the delayed release of phenol. Camphor is used as a diluent and a vehicle.

Paramonochlorophenol is the most potent of the three isomers of monochlorophenol (MCP), a phenol derivative. Walkhoff developed Camphorated Paramonochlorophenol (CMPCP) in 1891, although MCP is a stronger antiseptic that may be dangerous. CMPCP contains 65% camphor and 35% monochlorophenol. Despite having potent antibacterial qualities, it is very damaging to tissues.[26,27,28]

Metacresylacetate, another name for cresatin. It possesses both obtundant and antibacterial qualities. Cresatin has less of an antibacterial impact than formocresol or CMPCP. Phenol and its derivatives are combined to form creosote. Endodontic therapy has traditionally made use of beachwood creosote.[18]

ALDEHYDES

Water-soluble protein-denaturing chemicals including formaldehyde, paraformaldehyde, and glutaraldehyde are frequently employed in dentistry, specifically endodontics, as possible disinfectants. Despite being employed as a surface disinfectant for medical equipment, aldehydes are highly poisonous, allergic, and occasionally carcinogenic.

Formaldehyde is the principal ingredient in formocresol, which is still a commonly used medication for pulpotomy treatments in primary teeth. The usage of neutral buffered formalin has been discontinued due to its contentious characteristics. The polymeric version of formaldehyde, known as para formaldehyde, is most commonly found in root canal filling materials like endomethasone and N2. It breaks down gradually to produce formaldehyde, its monomer.

FORMOCRESOL

Between 1904 and 1906, Buckley is credited with using formocresol as a pulp treatment. Buckley explained using a mixture of formalin and cresol to cure necrotic or "putrescent" pulps. In the 1930s, Sweet developed a multiappointment pulpotomy procedure that immediately became well-known and was the basis for the current single-appointment pulpotomy. In his papers, he proposed a five-appointment procedure, which he later modified to three appointments. Since then, a lot of research has been done on formocresol.[29]

Buckley's formocresol was popularised in 1906 by combining 19% formaldehyde with 35% cresol, 15% glycerol, and 31% water. Formalin is a potent disinfectant that fixes tissues by combining with albumin to create an insoluble, indestructible material. The alkalinity of formaldehyde and the proteolizing impact of cresol caused the pulp to fix when it was placed against the pulp tissues.

Formocresol is a non- specific bacterial medicament most effective against both aerobic and anaerobic organisms in root canals. It is also used as an medicament in emergency endodontic treatment and in situations where pulpal inflammation is confined to the pulp chamber to relieve pain. It is also mutagenic and carcinogenic at high concentration. hence has to be used in low concentration. Currently we use 1/5th concentration of buckley‟s formacresol formula of 120 ml dilutent and 150 ml formocresol. Dilutent is made up of 3parts of glycerin (90 ml) and 1 part distilled water (30 ml). In Endodontics the vapors of

formocresol are made use of. It is soaked with cotton pellet and placed in pulp chamber of a tooth where vapors will penetrate the entire canal preparation.[25,26]

2% GLUTARALDEHYDE

It has a slightly acidic response, is colourless, and is slightly soluble in water. It was initially recommended by Gravenmade to be used as an intracanal medication at a dose of 2% glutaraldehyde. It is a potent disinfectant and fixative agent. Unlike formaldehyde, glutaraldehyde did not cause any immunological reactions. Glutaraldehyde has a bacteriostatic antibacterial effect. The degree of toxicity is lower than that of formaldehyde. Because of its higher molecular weight than formaldehyde, it is unable to enter the periapical tissues.[29]

HALOGENS

Halogens used in endodontic formulations include sodium hypochlorite, iodine, and chlorine. They possess potent oxidising properties and rapid effects of microorganisms. Chlorine is released by both sodium hypochlorite and chlorine. The latter releases active chlorine slowly and has been used as a temporary root canal dressing include compounds containing chlorine and iodine. In 1847, Semmelweis used hypochlorite for the first time as a hand disinfectant. Carrel and Dakin disinfected wounds with sodium hypochlorite rather than potassium hypochlorite.[30]

Hypochlorite reacts with tissue proteins to create formaldehyde, acetaldehyde, and nitrogen. The disruption of the peptide links causes the proteins to disintegrate. During the process, hydrogen in the amino groups (-HN-) is replaced by chlorine (-NCl-), producing chloramine, which is essential to the effectiveness of antibiotics. Pus and necrotic tissue break down as a result, facilitating the antimicrobial agent's access to the cleaning of the afflicted areas.[31] Bystrom and Sundqvist have demonstrated that using a 0.5% or 5% concentration of NaOCl did not significantly affect the rate of root canal disinfection. Higher NaOCl concentrations (2.5% and 5%) target living tissue without appreciably enhancing treatment (i.e., antibiotic action). NaOCl acts quickly but effectively.[32,33]

Iodine is utilised in potassium iodide, iodine, and iodophors—organic molecules containing iodine that gradually release iodine.Iodine compounds are currently used as an irrigating solution, 2% iodine solution in 4% aqueous potassium iodide, and, more recently, as a component in gutta-percha points for filling.[33]

QUATERNARY AMMONIUM COMPOUNDS

Aminoacridine is a moderate antiseptic. It is more effective than Cresat but less effective than CMCP. It works by inhibiting bacteria from synthesising proteins. It has been used more as an irrigant than an intracanal drug due to its low surface tension.

Heavy metal salts of copper, silver, and mercury constitute ICM. They coagulate proteins and act as inhibitors of enzymes. Mercury salts are toxic and less effective when tissue fluid proteins are present in the root canal. Their use is therefore restricted.

N2 includes paraformaldehyde, phenylmercuric borate, eugenol, and other substances like antibiotics, lead, and corticosteroids. It is said to be a sealer as well as an ICM. The mechanism of action indicates that the "Quats" are positively charged and the bacteria are negatively charged. Consequently, the chemical sticks to the microbe and causes the charge to be reversed, resulting in a surface active activity. Salvizol is another detergent that is suggested for irrigation during root canal therapy because of its chelating activity; nevertheless, it only marginally irritates tissue.[34]

CALCIUM HYDROXIDE

Calcium hydroxide has proven to be a very powerful antibacterial agent for intracanal dressings. In 1920, Hermann made the initial proposal for intracanal antiseptic. Hermann also recommended applying calcium hydroxide as a wound dressing after pulpotomy and pulp capping.

In order to disinfect pulp that was contaminated with necrosis, calcium hydroxide was rediscovered in the 1960s. In modern endodontic practice, it is currently the preferred intracanal dressing. The extremely high pH (12.5) that results from the dissociation of OH- ions is thought to be the cause of calcium hydroxide's antibacterial properties in a water carrier. Glycerine has also been used as a vessel for the calcium hydroxide suspension in powder form. A glycerine paste has a better flow because Ca(OH)2 dissolves more easily in glycerine than in water. This is false, though, because glycerine does not split the hydroxide ion. Water is necessary for calcium hydroxide to have an antimicrobial effect.[35]

Hydroxyl ions are extremely reactive, highly oxidant free radicals that react with a variety of biomolecules.[36,37] Their deadly effects on bacterial cells are most likely caused by

denaturation of proteins, damage to DNA, and damage to the bacterial cytoplasmic membrane.

To make placement easier, the calcium hydroxide is typically combined with a liquid, such as water, glycerin, anaesthetic solution, methyl cellulose, or other intracanal medications.[17]

ANTIBIOTIC PREPARATIONS

Antibiotics and other topical drugs may be used in endodontic therapy. However, the risk of drug hypersensitivity, the potential for bacterial resistance, and the tendency to conceal some causal factors restrict their usefulness. Two antibiotic-containing formulations were evaluated in early research: Grossman's polyantibiotic paste, which contains penicillin, bacitracin or chloramphenicol, and streptomycin, and a mixture of neomycin, polymyxin, and nystatin. As intracanal medications, both of these were reasonably successful.

In vitro studies using antibiotic combinations such ciprofloxacin, metronidazole, and minocycline as topical root canal treatments have shown more positive outcomes. Windley et al[37] investigated the effects of a triple antibiotic paste including metronidazole, ciprofloxacin, and minocycline in an animal investigation and discovered that it was successful in disinfecting the teeth of young dogs with apical periodontitis. Ledermix is a paste that dissolves in water and contains 1% triamcinolone and 3% demeclocycline. Triamcinolone can be used at low dosages that are unlikely to cause systemic side effects because it is four times more powerful than cortisone.[37,38]

In order to disinfect oral infectious lesions, such as dentinal, pulpal, and periradicular lesions, Cariology research unit of Niigata University School of Dentistry developed the concept of "Lesion Sterilisation and Tissue Repair (LSTR) therapy," which uses a triple antibiotic paste of ciprofloxacin, metronidazole, and minocycline. The medication combination has also been used in a 1:1:1 ratio. Minocycline-induced tooth discolouration is a drawback of the triple antibiotic paste. Cefaclor and fosfomycin are proposed as possible alternatives for minocycline, in terms of their antibiotic effectiveness.[39,40]

FREQUENCY OF MEDICATION

Disinfectant dressings should ideally be changed every week, but no more than every two weeks, according to general guidelines for treating root canals since periapical exudate dilutes them and they degrade when they come into touch with germs. Traditionally, the

access cavity was closed, a small blunt absorbent tip soaked with the medication was introduced into the canal, and a cotton pellet containing excess medication was placed in the pulp chamber. It can be injected with a 30 gauge needle, placed in the pulp chamber using cotton pellets, or inserted into the canal using a lentulospiral and then compressed with a finger plugger. A cotton pellet that has been moistened with medication is pressed up against a dry absorbent tip that has been put into a narrow canal.

The cavity is sealed once the extra medication is absorbed using a dry cotton pellet.[48]

RECENT ADVANCES

Herbal Medicaments

Propolis (Beeswax): demonstrated Propolis contains bioactive compounds like flavonoids, phenolics, and aromatic acids. It has antimicrobial, anti-inflammatory, antioxidant, and cytotoxic activities. Due to its effectiveness against Enterococcus faecalis, it is used both as an intracanal medicament and irrigant, often in combination with calcium hydroxide to enhance disinfection.[41]

Aloe Vera (Aloe barbadensis miller): Aloe vera gel contains active compounds like aloin and aloe-emodin. It exhibits significant antibacterial, antifungal, and anti inflammatory effects. These properties make it suitable for use in endodontics as both an intracanal medicament and an irrigating solution.[42]

Ginger (Zingiber officinale): Ginger is known for its anti inflammatory, analgesic, antipyretic, and antimicrobial actions. It has shown high antibacterial activity against E. faecalis, even outperforming chlorhexidine and garlic extract in some studies, making it a promising alternative in root canal disinfection.[43]

Neem (Azadirachta indica): Neem is a widely used medicinal herb in naturopathy. Its extracts possess strong antimicrobial and antioxidant properties. As an irrigant, neem offers biocompatibility and minimal toxicity compared to sodium hypochlorite, making it a safer option for root canal irrigation.[44]

German Chamomile (Matricaria recutita): Extracted from the dried flowers of German chamomile, this herbal agent contains various acids such as capric, coumaric, and caprylic acids. It has antimicrobial, anti-inflammatory, and antioxidant effects and is effective in smear layer removal due to its mild acidity (pH ~7.6).[45]

Nanoparticles in Intracanal Medicaments

Nanotechnology enhances drug delivery and disinfection by exploiting particles.

Common Types

Silver nanoparticles (AgNPs): Strong antimicrobial action; may be cytotoxic at high concentrations.

Zinc oxide nanoparticles: Biocompatible and antimicrobial; can be incorporated into sealers.

Iron oxide nanoparticles (Fe_3O_4): Generate ROS; have shown synergy when combined with calcium hydroxide.

Advantages

▪ Effective against biofilm-forming organisms like E. faecalis

▪ Can penetrate dentinal tubules

▪ May be engineered for controlled release.

The incorporation of nanoparticles into conventional medicaments (e.g., IONPs + CH) significantly boosts efficacy while reducing required concentrations.[46]

Antimicrobial Photodynamic Therapy (aPDT)

aPDT involves applying a non-toxic photosensitizer to the root canal, which, upon activation with a specific light wavelength, generates singlet oxygen that destroys microbial cells.

Mechanism

1. Application of photosensitizer (e.g., methylene blue).
2. Light activation (typically laser or LED).
3. ROS production leading to bacterial lysis.

Benefits

▪ Targets bacteria in biofilms and inaccessible canal areas

▪ Non-antibiotic; no resistance development

▪ Enhances outcomes in conjunction with traditional irrigation Limitations

▪ Equipment cost and learning curve

▪ Limited penetration in large or complex canal systems.[47]

LIMITATIONS OF INTRACANAL MEDICAMENTS

Discoloration of Tooth: Iodoform-containing calcium hydroxide (CH) pastes can discolor the crown, especially with prolonged use. Similarly, Triple Antibiotic Paste (TAP) causes

staining due to minocycline binding with calcium in dentine. Alternatives like Double Antibiotic Paste (DAP), or substituting minocycline with clindamycin, cefaclor, or augmentin can prevent this. Sealing dentinal tubules or internal bleaching can also manage discoloration.

Dentine Weakening: TAP reduces dentine microhardness and flexural strength due to its low pH and minocycline's chelating effect. High concentrations (1g/ml) show significant damage. Using methylcellulose-based low concentration TAP (1mg/ml) is recommended. CH also reduces dentine strength over time.[48]

Cytotoxicity to Stem Cells: High concentrations of TAP (1g/ml) negatively affect apical papilla stem cells. Safer concentrations between 0.1–2 mg/ml are preferred to reduce cytotoxic effects.

Difficulty in Removal: TAP binds tightly to dentine, making removal difficult. Techniques like the Endovac, Endoactivator, XP-Endo Finisher, and use of 1.5% NaOCl with EDTA help but don't ensure complete removal. CH also presents similar removal challenges, affecting canal sealing.[49] Further in vivo research and clinical trials are needed to validate these promising approaches for daily practice.

CONCLUSION

For a root canal treatment to be successful, microbial contamination must be eliminated from the root canal system. Research indicates that the use of interappointment medicine, irrigation, and mechanical instruments are all crucial in this regard. The significance of thorough canal debridement, proper canal preparation, and irrigation is highlighted. .However, intracanal medicaments should be used only for root canal disinfection as a part of controlled asepsis in infected root canals & their role is secondary to cleaning & shaping of the root canal.

Advances in cleaning and shaping methods have led to the development of single-visit endodontics. As a result, intracanal drugs are only beneficial throughout multiple visits.

The most often used intracanal medications are Formocresol, chlorhexidine, and calcium hydroxide in modified simple delivery methods. All of the antimicrobial materials currently available for root canal irrigation and treatment have limitations, therefore the search for the ideal irrigant and intra-appointment medication is still ongoing.

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