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Intracanal Medicaments-Are their Use Advocated in Modern Endodontics: A Narrative Review

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Review Article

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ABSTRACT

The main goal of an endodontic treatment is complete removal of bacteria, their byproducts and pulpal remnants from infected root canals and the complete sealing of disinfected root canals. Intracanal medicaments have been thought an important step in killing the bacteria in root canals; however, in modern endodontics, shaping and cleaning has been emphasized greater importance than intracanal medicaments as a means of disinfecting root canals. Furthermore, biocompatibility and stability are essential properties for intracanal medicaments. The more modern meaning of intracanal dressing is for a blockade against coronal leakage from the gap between filling materials and cavity wall. Calcium hydroxide has been determined as suitable for use as an intracanal medicament as it is stable for long periods, harmless to the body, and bactericidal in a limited area. Single-visit endodontics, where intracanal medicaments are not used, is nowadays indicated and various reports have shown that the clinical outcomes between single-and multiple-visit endodontics are almost similar. There is no reason to counsel against single-visit endodontics: however, if multiple-visit endodontics is chosen, an intracanal medicament is strongly recommended. Therefore, aim of this review is to critically appraise the need for an ideal intracanal medicament and to select cases requiring intracanal medicament instead of using it for each and every case.

INTRODUCTION

Should Intracanal Medicaments be used in Modern Endodontics?

Success in endodontic treatment was originally based on the triad of debridement, thorough disinfection and obturation of root canal system, with all aspects equally important [1]. At present, successful root canal treatment is based on much broader principles despite these the core behind any successful treatment. These include diagnosis and treatment planning; knowledge of anatomy and morphology; the traditional concepts of debridement, thorough disinfection, and obturation; and the coronal restoration [2]. With the advent of modern endodontics, the whole scenario of Endodontic protocol has changed a lot. The enhanced visibility and better chemo-mechanical preparation techniques and imaging modalities have drastically changed the outcomes of routine endodontics. In every aspect of endodontic practice the new techniques and methodology has encroached ranging from the access cavity preparation till a definitive restoration [3]. As we all know, access cavity preparation is considered a fundamental step in orthograde endodontic treatment. Looking back to the earlier practice of “Extension for prevention” have changed into “prevention of extension”

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(minimally invasive dentistry). From the concept of minimally invasive dentistry, contracted endodontic cavities (CECs) have stemmed [4]. It has been presented as an alternative to traditional endodontic access cavities (TECs) and is designed to preserve the mechanical stability of the tooth. The contracted cavity design preserves more of the dentin but may influence the geometric shaping parameters [5]. Likewise with the evolution of rotary root canal preparation techniques, canal preparation has become quite easy and quick [6]. Root canal instrumentation is usually accomplished by the use of Endodontic instruments and irrigating solutions under aseptic conditions. Endodontic instruments have underwent a revolutionary change as up until the last decade of past century were manufactured mainly out of stainless steel. But nowadays NITI instrument have proven a valuable adjunct [7]. NITI instruments have undergone a revolution regarding different designs to produce cutting efficiency and resistance to fracture [8]. In spite of all these advances the chemomechanical preparation and complete disinfection of root canal is the key.

Intracanal medicaments have been thought an essential step in killing the bacteria in root canals [9]; however, in modern endodontics, shaping and cleaning may be assuming greater importance than intracanal medicaments as a means of disinfecting root canals. Intra canal medicament is generally recommended when treatment cannot be completed in one appointment, there are chances that surviving intracanal bacteria often proliferate between appointments [10]. Walton stated that "Intra-canal 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" [11]. However, intra-canal medicaments in modern endodontics have a somewhat different rationale. To curtail bacterial regrowth and possibly even improve bacterial suppression, an intracanal medication can be advantageous and successfully used to eliminate the bacterial flora [12]. Interappointment antimicrobial medication acts to inhibit proliferation and further eliminate surviving bacteria, as well as minimize ingress of pathogens through a leaking restoration [13]. Usually, in the treatment of teeth with a vital pulp, there is no need for intracanal medication. The question of the role of intracanal medicaments becomes more relevant, and complex, in the treatment of cases with pulpal necrosis and apical periodontitis. There is overwhelming evidence in the literature that most of the root canals contain viable microorganisms after the completion of the chemomechanical preparation by the end of the first appointment. By using intracanal medicaments it may be possible that a more thorough instrumentation is achieved because of the longer overall time used for the treatment [14]. On the other hand, several appointments can also increase the risk for aseptic complications, for example, through a leaking temporary filling and poor patient compliance [15]. Hence, the more modern meaning of intracanal dressing is for a blockade against coronal leakage from the gap between filling materials and cavity wall. With the introduction of Single-visit endodontics [16], where intracanal medicaments are not used, there is question mark on the importance of intracanal medicaments. Even there are various reports have shown that the clinical outcomes between single and multiple visit endodontics are quite similar [17]. There is no reason to counsel against single-visit endodontics [18]. However, if multiple-visit endodontics is chosen, an intracanal medicament is strongly recommended. Therefore, intra-canal medicaments, which were the earlier the 'shining stars' of endodontic treatments, seem to have been retired from the front line, but still retain some significance. Despite conflicting claims, no medicament appears to be ideal and significant variability exists in clinical dental practice regarding their use.

Properties of an ideal intra canal medicament

- It should be an effective antimicrobial agent.
- It should be non-irritating to the periradicular tissues.
- It should remain stable in solution.
- It should have a prolonged antimicrobial effect.
- It should be active in the presence of blood, serum, and protein derivatives of tissues.
- It should have low surface tension.
- It should not interfere with the repair of periradicular tissues.
- It should not stain tooth structure.
- It should not induce a cell mediated immune response.

Indications of intracanal medicaments

- To dry persistently wet or the so called weeping canals.
- To eliminate any remaining microbes in the pulp space.
- To render root canal contents inert.
- To neutralize tissue debris.
- To act as a barrier against leakage from an inter appointment dressing in symptomatic cases.

Going back to the history of intracanal medicaments, $Ca(OH)_2$ remains the most important medicament till date. Beechwood creosote was mentioned as early in the 1840 article "Creosote and Cotton in Fang Filling" [19]. In 1884, Richmond recommended applying a small-sized piece of orangewood with phenol in order to devitalize the pulp. Thus,

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phenolics, which include Eugenol (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 [20]. Grossman first mentioned about the utilization of polyantibiotic paste as an intracanal medicament in weeping canals or where there was continuous seepage from the pulp space [21]. He mentioned about PBSC containing penicillin, bacitracin, and streptomycin, with caprylate sodium as vehicle. Later on PBSC was revised as PBSN for neomycin as an antifungal agent [22]. PBSC contained penicillin to target Gram-positive organisms, bacitracin for penicillin resistant strains, streptomycin for Gram negative organisms, and caprylate sodium to target yeasts – these components were suspended in a silicone vehicle [23]. Apart from calcium hydroxide, phenolic preparations, formaldehyde, chlorhexidine, halogens and steroids preparation are being used. Calcium hydroxide was introduced into dentistry by Hermann in 1920 [24]. It came to be widely used for root canal treatment in the 1970s and is now regarded as one of the first choices as a multiple visit root canal medication. But years ago, Bystrom et al. in around 1980s suggested that it is antimicrobial and this property was later used for the disinfection of root canals [25]. $Ca(OH)_2$ cannot be categorized as a conventional antiseptic, but it kills bacteria in the root canal space. The importance of $Ca(OH)_2$ in endodontic treatment of necrotic, infected teeth is now well documented [26]. Sjogren in 1991 stated that $Ca(OH)_2$ applied for 7 days eliminated bacteria in canal systems even up to 5 weeks later Bystrom in 1985 confirmed that even at one month of treatment the efficacy of calcium hydroxide is well [27]. Only 0.17% of calcium hydroxide dissolves to form Ca^{++} and OH, and it requires at least 1 day to exert full effect. $Ca(OH)_2$ is a slow-acting antiseptic [28]. Direct-contact experiments in vitro show that a 24-hour contact period is required for complete killing of enterococci. And this is reason why it cannot be used as a successful irrigant as compared to sodium hypochlorite or chlorhexidine [27]. In addition to killing bacteria, $Ca(OH)_2$ has the extraordinary ability to hydrolyze the lipid moiety of bacterial lipopolysaccharides (LPS), thereby inactivating the biologic activity of the lipopolysaccharide and reducing its effect [29]. This is a very desirable effect because dead cell wall material remains after the bacteria have been killed and can continue to stimulate inflammatory responses in the periradicular tissue [30]. Hasselgren et al. in 1988 advocated that $Ca(OH)_2$ completely dissolves porcine muscle over time [31]. This property may be clinically significant when use $Ca(OH)_2$ as intracanal medicament and then rinse out with NaOCl (usually not seen over 30min period by Morgan and Carnes in 1991). To confirm Morgan et al. showed that inter appointment NaOCl + $Ca(OH)_2$ does not enhance debridement of the root canal system apart from chemomechanical debridement [32]. Fava et al. reviewed $Ca(OH)_2$ paste formulations and indications [33]. Vehicle (aqueous, viscous, and oily) plays important role in dissolution kinetics. $Ca(OH)_2$ may be mixed with sterile water or saline; this formula is also available commercially from a number of manufacturers in sterile, single-dose packages (e.g., Calasept; and DT Temporary Dressing. The mixture should be thick to carry as many $Ca(OH)_2$ particles as possible. This slurry is best applied with a Lentulo spiral. Sigurdsson suggested that Lentulo spiral is most effective technique of carrying $Ca(OH)_2$ to working length [34]. For maximum effectiveness, the root canal must be filled homogeneously to the working length. Saturated $Ca(OH)_2$ solution mixed with a detergent is an effective antimicrobial agent suitable for irrigation [35].

Limitations of Calcium Hydroxide

In spite of various advantages and indications of calcium hydroxide, it do have some limitations. There are some concerns regarding the use of $Ca(OH)_2$. The handling and proper placement of $Ca(OH)_2$ present a challenge to the average clinician and requires skill. Mixing of calcium hydroxide in a proper consistency to be filled in root canal and proper carry it to the canal is still a challenge [36]. Though various formulations are available but still its placement in posterior tooth is difficult. Also, the removal of $Ca(OH)_2$ is most frequently incomplete, resulting in a residue covering 20% to 45% of the canal wall surfaces, even after copious irrigation with saline, NaOCl, or EDTA [37]. Residual $Ca(OH)_2$ also possess a problem as it can shorten the setting time of zinc oxide Eugenol based endodontic sealers if used for final obturation. Residual calcium hydroxide in the canal is also a concern that it is not totally effective against several endodontic pathogens, including *E. faecalis* and Candida species leading to various incidence of re infection or flare up [38]. There are many published literature questioning the ability of $Ca(OH)_2$ to completely eradicate bacteria from the root canal [39]. For example, in one in vitro studies have shown that dentin can inactivate the antibacterial activity of $Ca(OH)_2$ and one clinical study has shown that the number of bacterial colony in the canals even increased after 1 week medication with calcium hydroxide [40]. Other studies have also indicated that $Ca(OH)_2$ could not predictably eliminate bacteria or that cultures changed from negative to positive after placement of calcium hydroxide intracanal medicament [41]. Therefore, on the basis of the current available evidence, $Ca(OH)_2$ has limited effectiveness in eliminating bacteria from human root canals when assessed by culture techniques. However, clinically there are cases showing a positive response and even resolution of sign and symptoms in between appointment in those cases with intracanal medicament compared to non-medicated root canals [42].

Various other intra canal medicaments and their application in modern endodontics.

Calcium hydroxide has been the prototype of any intracanal medicament used nowadays, but with advancement in the field of Endodontics newer materials have evolved. As we all know that the persistence of microorganisms may be

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considered the primary cause of root canal failure. The ability of *Enterococcus faecalis* (*E. faecalis*) to penetrate into the dentinal tubules and resist bactericidal substances has been claimed to be the reason for this organism to be implicated in persistent root canal infections [43]. Calcium hydroxide is one of the most commonly used intracanal medicaments and owing to the alkaline pH, this material has a wide anti-microbial spectrum [44]. However *E. faecalis* has been shown to be resistant to the actions of calcium hydroxide [45]. This has led to widespread research in endodontics looking for an alternative intracanal medicament. Some of them are even providing more promising results as compared to the calcium hydroxide. Chlorhexidine gluconate (2%) has been recommended as a potential alternative to calcium hydroxide. Many studies have been done regarding the efficacy of calcium hydroxide and CHX mixture and its anti-bacterial property with the concept that their antimicrobial properties interact in a synergistic fashion that enhances their efficacy [46]. Recent studies have evaluated the tissue reactions to the mixture of $Ca(OH)_2$/CHX, showing that the combination exerts good antimicrobial properties and improves healing of the periapical tissues [47]. But chlorhexidine do have some limitations in clinical application. A suggested clinical protocol for treating dentin prior to root canal obturation consists of irrigation with NaOCl to dissolve the organic components, irrigation with EDTA to eliminate the smear layer, and irrigation with CHX to increase the antimicrobial spectrum of activity and impart substantivity [48]. Although such a combination of irrigants may enhance the overall antimicrobial effectiveness, possible chemical interactions between the irrigants may occur having deleterious effect on overall treatment. When NaOCl and CHX are combined, a precipitate known as Para chloroaniline (PCA) is formed leading to color changes [49]. The formation of a precipitate could be explained by the acid-base reaction that occurs when NaOCl and CHX are mixed together. PCA has been shown to be toxic in humans with short term exposure, resulting in cyanosis, which is a manifestation of methemoglobin formation. Furthermore, the combination of CHX and EDTA produces a white precipitate [50]. The precipitate was produced and redissolved in a known amount of dilute trifluoroacetic acid. CHX was found to form a salt with EDTA rather than undergoing a chemical reaction. Another drawback of chlorhexidine is the premature loss of bond strength that affects adhesive restorations and markedly reduces their durability [51]. Allergic reactions and anaphylactic shock, contact dermatitis, and urticaria have been reported following direct contact to mucosal tissue or open wounds has been reported [52]. Phenol or carbolic acid, is one of the oldest antimicrobial agents used in medicine. Despite the severe toxicity of phenolic preparations, derivatives of phenol, such as paramonochlorophenol, thymol and cresol, are widely available. Phenol is a nonspecific protoplasm poison that has an optimal antibacterial effect at 1% to 2%. Derivatives of phenol are stronger antiseptics and toxins than phenol [53]. Phenolic compounds are often available as camphorated solutions. Camphoration results in a less toxic phenolic compound because it slows the release of toxins to the surrounding tissues [54]. Several in vitro studies have shown that phenol and phenol derivatives are highly toxic to mammalian cells, and their antimicrobial effectiveness does not sufficiently balance their toxicity [55]. Formaldehyde, used as formocresol, has been used extensively in endodontic therapy despite its high toxicity and mutagenic and carcinogenic potential. Formaldehyde is volatile and releases antimicrobial vapors when applied to a cotton pellet for pulp chamber disinfection. All formaldehyde preparations are potent toxins with an antimicrobial effectiveness much lower than their toxicity [56].

Other medicaments such as Ledermix paste have been recommended as routine intracanal medicaments. Ledermix paste has been advocated as an initial dressing, particularly if the patient presents with endodontic symptoms [57]. It is a corticosteroid and antibiotic paste. Ledermix paste contains triamcinolone acetonide as an anti-inflammatory agent, at a concentration of 1%. Ledermix paste is a non-setting, water-soluble paste material for use as root canal medicament or as a direct or indirect pulp capping agent [58]. Studies have shown that triamcinolone is released from Ledermix paste in the root canal and can reach the systemic circulation via diffusion through dentinal tubules, lateral canals, and the apical foramen [59]. After the first 24 hours, 30% of the triamcinolone was released. By the end of 14 weeks, the remaining 70% had been released. In a recent study, the groups treated with Ledermix, triamcinolone and demeclocycline had significantly more favorable healing and more remaining root structure than the group filled with gutta-percha and sealer [60]. Apart from these medicaments, triple-antibiotics regimen, composed of metronidazole, ciprofloxacin, and minocycline, was first tested for its effectiveness against Escherichia coli–infected dentin in vitro [61]. The efficacy of TAP for elimination of bacteria was first discussed by Hoshino et al. Its bactericidal efficacy against microbes from carious dentin and infected pulp has also been tested concluding that the mixture of antibiotics is sufficiently potent to eradicate the bacteria. The clinical effectiveness of the triple-antibiotic paste in the disinfection of immature teeth with apical periodontitis has been reported [62]. Metronidazole (2%) has been shown to be superior to calcium hydroxide in inhibiting *E. faecalis*. But in spite of its good antibacterial efficacy to eliminated intra canal bacterial flora one potential concern of using an intracanal antibiotic paste is that it may cause bacterial resistance. Additionally, intracanal use of minocycline can cause tooth discoloration, creating potential cosmetic complications [63]. To overcome this disadvantage Double antibiotic paste eliminating Minocycline has been advocated. The antibacterial activity of these medicaments is well described but little is known about the potential toxicity on surviving cells in the peri apical region. Potential toxicity of these medicaments is a major concern as they are in direct contact with periapical tissue. When in contact with the periapical tissue, a cytotoxic medicament can lead to DNA damage of conjunctive cells, leading to prevention and retardation of healing along with other phenotypic changes [64].

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Halogens are also used as an intracanal dressing in the form of chloramine-T, an N-chloro tosylamide sodium salt [65]. Iodine, in the form of IKI, is a very effective antiseptic solution with low tissue toxicity. IKI is an effective disinfectant for infected dentin and can kill bacteria in infected dentin in 5 minutes. IKI releases vapors with a strong antimicrobial effect [66]. The solution can be prepared by mixing 2 g of iodine in 4 g of potassium iodide; this mixture then is dissolved in 94 ml of distilled water. Tincture of iodine (5%) has proved to be one of the few reliable agents for disinfection of rubber dam and tooth surfaces during the preparation of an aseptic endodontic work field [67]. Natural remedies are increasingly finding their way into endodontic treatment with agents like Morinda citrofolia, triphala, curcumin and propolis being evaluated as irrigants and intracanal medicaments. Curcumin (diferuloylmethane), the main yellow bioactive component of turmeric has a wide spectrum of biological actions, including antimicrobial, anti-inflammatory and antioxidant activities. Its antibacterial activity against *E. faecalis* has been documented in many studies [68]. Sometimes even combination of the two medicaments has been used to check for a possible additive or synergistic effect. With the versatility of each case and patient different materials have their own implications. To answer the question "should intracanal medicament be used in Modern Endodontics" it is very important to discuss these medicaments available nowadays apart from calcium hydroxide. There are various studies regarding the efficacies of these medicaments and their successful result on the outcome of endodontic therapy.

In spite of the fact mentioned above, placement of intracanal medicament has always been a topic of controversy in the Endodontic literature. Particularly in root canals that contain vital pulp tissue as these are not infected prior to instrumentation or in contaminated canals which have been cleaned and shaped with modern instrumentation technique, do not require medicaments. However, if a root canal is heavily infected prior to instrumentation, it is highly probable that a few bacteria will remain [69]. In these circumstances, placement of an intracanal dressing to the full length of the canal is the treatment of choice. Intracanal dressing is also indicated in teeth with large periapical lesion and in cases where it is necessary to control the passage of periapical exudates into the canal [70]. Intracanal medicament accelerates the natural healing of periapical lesion, regardless of the bacterial status of the root canal at the time of placement of the material [71]. From the above discussion it is quite clear that the main aim of placement of these medicaments is to disinfect root canal system to receive a biologically acceptable obturating material. Several new technologies have been introduced during the last few years to improve the effectiveness of root canal disinfection. Increasing attention has been focused on the use of ozone, photo activated disinfection with low-energy laser, electrochemically activated water, and electric current [72]. One of the latest new developments for canal disinfection are bioactive materials such as bio (active) glass [73]. Recent experiments with Nano metric bioactive glass indicated excellent antimicrobial effect in a human dentin model. With the advent of these new technologies the use of intracanal medicament can be surpassed but it cannot be totally eliminated in each and every cases. Other contrary, there are studies that reported no significant differences in healing between teeth filled after positive or negative cultures from the root canal, or between treatments performed in one or two appointments with intracanal medicaments placed [74]. But these results can be attributed to the fact that ''intracanal sampling techniques suffer from deficiencies that limit their predictive value [75]." Therefore it is important as our part to select a proper case and proper intracanal medicament for each and every patient individually and it is very prudent to understand that irrigation and local antibacterial dressings in the root canal are part of a concerted effort to control endodontic infections. Alone they cannot guarantee success if there are problems in quality of some other parts of the treatment.

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