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Recent Advances In Drugs Used As Endodontic Irrigants - A Literature Review

Research Article

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Abstract

Bacteria have long been recognized as the primary etiologic factors in the development of pulp and periapical lesions. The primary objective of endodontic treatment relies on the chemical and mechanical debridement of root canals. This article narrates the specifics and requirements of the irrigation solutions.This review is aimed to bring some light over the advances in root canal disinfection reviewing the newly used irrigants.

Keywords: Disinfection, Root Canal Treatment, Advanced Techniques, Endodontic Irrigants.

Introduction

Microorganisms and their toxic metabolic products have long been responsible for the development and persistence of apical periodontitis of endodontic origin.[1]

The effectiveness of endodontic files, rotary instrumentation, irrigating solutions, and chelating agents to clean, shape, and disinfect root canals underpins the success, longevity, and reliability of modern endodontic treatments.[2,3]. However, if microorganisms persist at the time of obturation, or if they penetrate into the canal after obturation, there is a high risk of treatment failure.[4] It is generally believed that mechanical enlargement of canals must be accompanied by copious irrigation in order to facilitate maximum removal of microorganisms so that the prepared canal becomes as bacteria-free as possible.[5,6]

This article reviews recent developments in the identification of new agents to sterilize infected root canal. Previously our team has a rich experience in working on various research projects across multiple disciplines [7-21] Now the growing trend in this area motivated us to pursue this project.

Ideal Requirement Of Root Canal Irrigants

Root canal irrigants must ideally be[22]

(i) have a broad antimicrobial spectrum and high efficacy against anaerobic and facultative microorganisms organized in biofilms,
(ii) dissolve necrotic pulp tissue remnants,
(iii) inactivate endotoxin,
(iv) prevent the formation of a smear layer during instrumentation or dissolve the latter once it has formed,
(v) be systemically nontoxic,
(vi) be non caustic to periodontal tissues,
(vii) be little potential to cause an anaphylactic reaction.

Newer Root Canal Irrigants

Newer root canal irrigants are are as follows:

(1) QMix
(2) Triclosan and Gantrez
(3) Electrochemically activated solutions,
(4) ozonated water
(5) Silver diamine fluoride
(6) HEBP
(7) photon-activated disinfection
(8) Antibiotic intracanal medicaments
(9) herbal irrigants.

QMix

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QMix, a product that is composed of a polyamino carboxylic acid chelating agent, a bisbiguanide antimicrobial agent, a surfactant, and deionized water[23].Qmix is a novel irrigating solution which is been used for the removal of smear layer and also for disinfection with added antibacterial agents as it contains EDTA , Chlorhexidine and water . As it is a clear solution which is ready to use with no chairside mixing required . Previous studies have reported that the efficacy is increased with the use of Qmix in root canal disinfection[80] [81] .Furthermore, QMix™ does not interact with remnant NaOCl to generate a precipitate if used as directed for the final rinse and its ability to penetrate into patent, smear plug-free dentin to kill bacteria present has been demonstrated using a novel model with potentially significant clinical outcomes and implications[24].

Triclosan And Gantrez

Triclosan is a broad spectrum antimicrobial agent, active against gram-positive and gram-negative bacteria as well as some fungi and viruses[25, 26]Nudera et al.[27] evaluated the minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) of triclosan and triclosan with Gantrez® against P intermedia, F nucleatum, A naeslundii, P gingivalis, and E faecalis. The MBC of triclosan ranged from 12-94 µg/ml. The MBC of triclosan with Gantrez® ranged from <0.3-10.4 µg/ml. The addition of Gantrez® enhanced the bactericidal activity of triclosan. Both triclosan and triclosan with Gantrez® demonstrated bactericidal activity against the five specific endodontic pathogens.

Electrochemically Activated Solution

The ECA technology was developed by Russian scientists at the All-Russian Institute for Medical Engineering (Moscow, Russia, CIS). Principle of ECA is transferring liquids into a metastable state via an electrochemical unipolar (anode or cathode) action through the use of an element/reactor ("Flow-through Electrolytic Module" or FEM). Anolyte solution has been termed Superoxidized Water or Oxidative Potential Water. Depending on the type ECA device that incorporated the FEM elements the pH of anolyte varies; it may be acidic (anolyte), neutral (anolyte neutral), or alkaline (anolyte neutral cathodic)[28, 29]. The quality of debridement was better in the coronal and middle parts of canal walls where only scattered debris was noted in contrast to the apical part that contained numerous debris. This observation confirms the previously published results[30].

Laser Activation Irrigants

The laser technology had evolved recently and showed relatively better results and safety which was proposed for various dental treatments such as reducing the tooth sensitivity , root canal preparation , removing caries , disinfecting the dental tissues and bleaching . Some of the effects of lasers which include vaporization of soft tissue , melting of dentin surfaces , removal of smear layer or intracanal medicament . The mechanism of the laser activation devices with irrigating solutions originates from the absorption of laser energy , formation of vapor bottles , acoustic streaming which finally leads to cavitation[80] . Lasers which have been widely used in the dental field for disinfection of the root canal are Co2 ,Nd:YAG , ER:YSGG, Nd:YAG , argon and diode lasers which have been used for root canal disinfection . It has been stated in previous studies that the photothermal property of diode lasers in the root canal can increase the temperature of the irrigant at any concentration[83] .

Ozonated Water

Ozone is a very powerful bactericide that can kill microorganisms effectively. It is an unstable gas, capable of oxidizing any biological entity. It was reported that ozone at low concentration 0.1ppm, is sufficient to inactivate bacterial cells including their spores[31]. Shockwave generation can also enhance the breakdown of agents such as hydrogen peroxide and ozone dissolved in water and thereby enhance their disinfecting and debriding actions [32, 33]

Study by Hems et al. however found that NaOCI was superior to ozonated water in killing E. faecalis in broth culture and in biofilm[34]. Ibrahim and Abdullah studied that 1.31% NaOCI might allow passage of oxidation of ozonated water, thus increasing their antibacterial effect compared to 1.31% NaOCI or ozonated water alone [35].

Silver Diamine Fluoride

A 3.8% w/v silver diamine fluoride (Ag[NH 3] 2 F) solution has been developed for intracanal irrigation. This represents a 1:10 dilution of the original 38% Ag(NH 3) 2 F solution used for root canal infection.[36] The study on the antibacterial effect of 3.8% Ag(NH3) 2 F against a E faecalis biofilm model concluded that Ag(NH3) 2 F has potential for use as an antimicrobial root canal irrigant or interappointment medicament to reduce bacterial loads.[37] E faecalis was completely killed by Ag(NH 3) 2 F after exposure to these agents for 60 min. The silver deposits were found to occlude tubular orifices after removal of the smear layer.

HEBP

HEBP (1-hydroxyethylidene- 1, 1-bisphosphonate), also known as etidronic acid or etidronate, has been proposed as a potential alternative to EDTA or citric acid because this agent shows no short-term reactivity with NaOCl.[38] HEBP is nontoxic and has been systematically applied to treat bone diseases.[39] The demineralization kinetics promoted by both 9% HEBP and 18% HEBP were significantly slower than those of 17% EDTA.[40] De-Deus et al. reported that the soft chelating irrigation protocol (18% HEBP) optimized the bonding quality (3.1-6.1 MPa) of Resilon/Epiphany®.[41]

Photon-Activated Disinfection

PDT is based on the concept that nontoxic photosensitizers can be preferentially localized in certain tissues and subsequently activated by light of the appropriate wavelength to generate singlet oxygen and free radicals that are cytotoxic to cells of the target tissue[42].

Methylene blue (MB) is a well-established photosensitizer that has been used in PDT for targeting various gram-positive and gram-negative oral bacteria and was previously used to study the effect of PDT on endodontic disinfection [43-45]. Several studies have shown incomplete destruction of oral biofilms using MB-mediated PDT due to reduced penetration of the photosensitizer [46-

48]. Soukos et al. used the combined effect of MB and red light (665 nm) exhibited up to 97% reduction of bacterial viability [44].

Herbal Irrigants

Turmeric(Curcuma Longa)

Curcumin is a hydrophobic polyphenolic compound that is derived from rhizome of the herb (Curcuma longa) which possesses a wide range of biological applications. It is an yellow bioactive pigment, one of the major constituent of turmeric which has a wide spectrum of biological actions such as anti-inflammatory, antioxidant, antifungal and antibacterial activities.[49]Circumin was incorporation into polymeric fibers which was then tested for its antimicrobial properties and its potential uses in the root canal disinfection . As it is effective an alternative to TAP in controlling the infection , also curcumin requires a minimal concentration of 2.5mg / ml .Components of the turmeric which are named as curcuminoids (curcumin or diferuloyl methane , demethoxy curcumin and bisdemethoxycircumin) as they are polyphenols with a strong antioxidant property .[50][75][76] Recently it had been reported in a study that curcumin in aqueous preparations exhibited a phototoxic effect against gram positive and gram negative bacteria [77]

Liquorice

Liquorice is an extract from the Glycyrrhiza glabra plant which contains glycyrrhizic acid. Liquorice extract showed the largest zone of inhibition (3.97 ± 0.24) when compared to mixture of liquorice and calcium hydroxide and CaOH alone in a study by satti et al[51]. Similarly, Chittrarasu et al[52]. determined that liquorice extract has higher activity than calcium hydroxide against enterococci and better activity on biofilms. The antimicrobial effect of liquorice extract against E. faecalis may be related to the glycyrrhizin[53]

Propolis

Propolis is a natural product that has gained increased interest due to its antimicrobial activity against a wide range of pathogenic microorganisms.[54] It is composed of resin and balsams (50-60%), pollen (5-10%), and other constituents like amino acids, minerals, vitamins A and B complex, and highly active biochemical substance known as bioflavonoids (vitamin P), phenols, and aromatic compounds.[55] Three studies assessed propolis extracts in different concentrations and solvents (4% in dimethylsiloxane, 25% aqueous extract of propolis, and 11% ethanolic extract of propolis) and 0.9% saline solution.[56-58] In all of these studies, propolis showed an antimicrobial effect but that was only comparable to that of calcium hydroxide and saline[59].

Triphala

Triphala is an Indian ayurvedic herbal formulation consisting of dried and powdered fruits of 3 medicinal plants (Terminaliabellerica, Terminaliachebula, Emblicaofficinalis). It has a potential of antibacterial activity and anti-inflammatory activity. he major ingredients of T. bellerica are ellagic and gallic-acid; E. officinalis has several gallic acid derivatives including epigallocatechin gallate and in T. chebulagallic acid is the major ingredient. The presence of these active ingredients of phenolic nature may be responsible to scavenge the free radicals generated by the bacteria. [60,61] Triphala and GTPs are very good chelating agents [62,63] and Triphala, in particular, contains fruits that are rich in citric acid that may aid in removal of the smear layer.

Morinda Citrifolia

Morinda citrifolia (MCJ) has a broad range of therapeutic effects, including antibacterial, antiviral, antifungal, antitumor, anthelmintic, analgesic, hypotensive, anti inflammatory, and immune-enhancing effects [110-113].MCJ contains the antibacterial compounds L-asperuloside and alizarin[64,65]. Murray et al. proved that, as an intracanal irrigant to remove the smear layer, the efficacy of 6% MJC was similar to that of 6% NaOCl in conjunction with EDTA [66]. The use of MCJ as an irrigant might be advantageous because it is a biocompatible antioxidant and not likely to cause severe injuries to patients as might occur through NaOCl accidents.[67]

Aloe Barbadensis(Av)

Aloe vera consists of the chemical constituent anthraquinones which is responsible for its antibacterial, antiviral and analgesic effects.[68] The reason for its significant increase in microbial load thereby showing reduced efficacy against both E. faecalis and C.albicans is that though AV possess antibacterial effect, the concentration of substances are affected by growth, harvesting, and processing of the aloe leaves therefore it does not have sufficient efficacy due to its dissolution nature. It loses its antibacterial property once it is exposed to the environment.[69]

Azadirachta Indica(Neem)

Interest on neem is based on its properties like antibacterial, antifungal, antiviral, antioxidant, anti inflammatory, antipyretic and analgesic effects.[68-70] The extracts has undergone extensive pharmacological screening and found to have several pharmacological activities due to the presence of several active constituents like nimbidin, nimbin, nimbolide, gedunin, azadirachtin, mahmoodin, margolone and cyclic trisulphide responsible for its antibacterial action.[70] Its anti-adherence activity by altering bacterial adhesion and the ability of organism to colonize has resulted in AI having the maximum reduction in adherence of E. faecalis to dentin.[71] Use of AI as an endodontic irrigant might be advantageous because it is a biocompatible antioxidant and thus not likely to cause the severe injuries to patients that might occur via NaOCl accidents. In a study by jaju et al, 0.033% AI was highly efficient to 5.25% NaOCl in reducing both E. faecalis and C.albicans within the root canals when compared with other extracts. Bitter taste associated with this plant can be altered by different formulations due to addition of sweeteners and flavors to increase the patient's compliance and acceptability.[72] In recent study it has been proven that the neem extract has moderate activity against E.Faecalis , the antimicrobial activity of neem extracts were similar to that of the 17 % of EDTA against E.Faecalis [73]

Green Tea Polyphenols (GTP)

GTP are derived from fresh leaves of tea (Camellia sinensis), an important component of traditional Japanese and Chinese cultures. They have shown significant antibacterial activity in E. faecalis biofilms grown on dental culture, killing E. faecalis com-

pletely within 6 min [65-74].

Myristica Frangrans(Mf)

M. fragrans (both nutmeg and mace) is known to exhibit strong antimicrobial activity against animal and plant pathogens. The constituent responsible for MF for its antibacterial activity is myristic acid.[49]

Terminalia Chebula(Tc)

Its paste with water is found to be anti-inflammatory, analgesic and having healing capacity for wounds. Its powder is a good astringent dentifrice in loose gums, bleeding and ulceration in gums. The chief constituent; tannin is responsible for the antibacterial action of TC.[73-75]

Our institution is passionate about high quality evidence based research and has excelled in various fields [11][50][76-85]

Antibiotic Intracanal Medicaments

Septomixine Forte

Septomixine Forte paste contains dexamethasone, halethazole tartrate, neomycin sulfate, polymyxin B sulfate, and tyrothricin. Septomixine Forte paste, however, is no longer recommended because the antibiotics (neomycin and polymyxin B sulfate) are unsuitable for use against endodontic bacteria due to their inappropriate spectra of activity.[86]

MTAD

Bio Pure MTAD (Dentsply, Tulsa, OK) is a mixture of a tetracycline isomer, an acetic acid, and Tween 80 detergent (MTAD)—was designed to be used as a final root canal rinse before obturation.[87]

Tetracycline has many unique properties of low pH and thus can act as a calcium chelator and cause enamel and root surface demineralization.[88] MTAD mixture is effective against E. faecalis, and it is also less cytotoxic than a range of endodontic medicaments, including eugenol, hydrogen peroxide (3%), EDTA, and calcium hydroxide paste [65,89,90]. Ruff et al. showed that 6% NaOCl and 2% chlorohexidine were equally effective and statistically significantly superior to BioPure MTAD and 17% EDTA in antifungal activity [91][51]. Clegg et al. questioned the ability of MTAD to remove or disrupt bacterial biofilms in root canals [89-92].

Tetraclean

Tetraclean (OgnaLaboratoriFarmaceutici, Muggiò (Mi), Italy), like MTAD, is a mixture of an antibiotic, an acid, and a detergent. However, the concentration of the antibiotic, doxycycline (50 mg/mL), and the type of detergent (polypropylene glycol) differ from those of MTAD[93]

Giardino et al. compared the surface tension of 17% EDTA, Cetrexidin, Smear Clear, 5.25% NaOCl, MTAD and Tetraclean[93]. The NaOCl and EDTA had the highest surface tension, whereas Cetrexedin and Tetraclean had the lowest values[50].Only the NaOCl could disaggregate and remove the biofilm at every time interval tested although treatment with Tetraclean caused a high degree of biofilm disaggregation at each time interval when compared with MTAD[94].

Triple Antibiotic Paste

Combination of antibiotics are required for the reduction of likelihood of the development of resistant bacterial strains like a combination of Metronidazole, Ciprofloxacin and Minocycline[95]. The use of TAP contains metronidazole of 500mg, ciprofloxacin of 200mg and minocycline of 100mg in the ratio of 1:1:1 as recommended by Hoshino et al.[96]. TAP is radiolucent[96], propylene glycol as a vehicle of TAP may be difficult to remove from the dentin surface, an additional appointment is required to remove TAP and re-opening the tooth to remove TAP introduces a risk of recontamination. Antibiotic containing scaffolds can solve the problems.

Bottino MC et al.[97] have suggested that the polymer-based antibiotic-containing electrospun scaffolds may act as a biologically safe antimicrobial drug delivery system for regenerative endodontics. This can improve drug delivery due to high surface area fibers arranged in an interconnecting structure that allows controlled drug release[98]

Conclusion

During instrumentation canals should be irrigated using copious amounts of irrigants.The use of antibiotics containing dental agents should be carefully justified, in order to avoid bacterial resistance. Future studies of irrigants should focus on the production of a single solution that is biocompatible, has tissue-solubilizing properties, removes the smear layer, and has antibacterial effects.

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