



NARRATIVE REVIEW

Lesion Sterilization and Tissue Repair (LSTR): A Review

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ABSTRACT

Residual infection in root canal system has always been an area of penumbra for a treating dentist. Lesion sterilization and tissue repair (LSTR) therapy is an endodontic treatment procedure that involves non-instrumentation or minimal instrumentation followed by placement of antibiotic mixture to disinfect root canal systems. It is evolving as an alternate treatment procedure in comparison to traditional pulpectomies/root canal treatment and extractions for treatment of nonvital or pulpless teeth. This article reviews the rationale of the technique, evolution, indications, uses and clinical procedures required in performing the technique.

Key words: Lesion Sterilization and Tissue Repair, Triple-Antibiotic Paste, 3-Mix Paste, Regenerative Endodontics, Non-Instrumentation Endodontics, Revascularization.

Lesion sterilization and tissue repair (LSTR) therapy is a technique that allows disinfection of dentinal, pulpal, and periradicular lesions using a combination of antibacterial drugs.⁽¹⁾ LSTR concept was developed at the *Cariology research unit, School of Dentistry, Niigata University, Japan, 2004.*⁽²⁾ Residual infection in root canal system has always been an area of penumbra for treating dentist. The major purpose of endodontic treatment is to reduce the microbial load in the root canal system.⁽³⁾ Microbial load diminution is not only important before obturation but also in long run so as to decrease the chances of refractory periapical pathosis. Conventionally, microbial load present in root canals is removed by mechanical means (dentin removal) and by chemical means (irrigation).^(2,3) Nevertheless, microbes present in deeper layers of infected root canal dentine may sometimes persist even after

conventional root canal treatment.⁽⁴⁾ These remnant microbes may occasionally lead to recurrence of periapical complications. In this situation, complete elimination of bacteria should be ensured for a successful outcome of endodontic treatment.

Microbial flora of the infected root canal consists of both aerobic and anaerobes with predominantly the anaerobic bacteria.⁽⁵⁾ Hence cleansing should get rid of both organisms. Advancement to cleansing is use by use of various medicaments, which can decrease the load of bacteria. It is reported that the resulting sterilization with antibiotics or antiseptics result in approximately

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20-40% additional cleansing / augmenting the conventional root canal debridement. In this regard, various medicaments like antibiotics and antiseptics have been discussed.⁽⁶⁾ Though each has their own advantages and disadvantages, the selection of antibacterial drugs should be updated so as to provide the best of sterilization of root canal systems.

Several factors influence the activity of antimicrobial drug to bring about sterilization, these are:

Minimal concentration of drug- The amount of drug should be enough so as to cause adequate sterilization. An inadequate concentration means either less or no elimination of microbes. The drug should possess the ability to diffuse periapically from the canal and produce sterilization in cases where regenerative techniques are especially contemplated.⁽⁷⁾

Type of infection- Certain kind of microbial species are resistant to normally used antimicrobials. Species such as Enterococcus group have shown to be viable when exposed to normally used root canal irrigants. Also, since the root canal infection is a mixture of aerobic and anaerobic flora; no single medicament can cause sterilization of the canal. Hence combinations of medicaments are required for this purpose.⁽³⁾

Biocompatibility- The medicaments used in root canals should possess antimicrobial properties, but in addition it should cause least amount of damage to host cells.⁽⁸⁾

Systemic toxicity- The polyantibiotic paste containing penicillin was traditionally used for many years to sterilize root canals but withdrawn because of the potential for sensitization of patients or development of superinfections.⁽⁹⁾

Resistance- Various medicaments and its effects-

The concern of the antibiotic paste is that it may cause bacterial resistance. A combination of antibiotics would therefore decrease the probability of the development of resistant bacterial strains.

Reactivity of drug with dentinal tubule- The chemical composition of dentinal tubule itself can have an inhibitory effect on the bactericidal activity of intra-canal medicaments.⁽¹⁰⁾

Presence of smear layer affects permeability of drug into apical dentinal tubules- Presence of smear layer acts as a barrier to the diffusion of irrigants. Hence removal of smear layer has shown proper diffusion of medicaments bringing about better disinfection. Some of the methodologies available in literature are use of EDTA, use of ultrasonic cleansing. These methods cause removal of smear layer and causing the dentinal tubules to enlarge and open up.

COMPOSITION: Several combination of medicaments are tried over years.⁽¹¹⁾ Some of the well-known combinations are:

- Metronidazole and ciprofloxacin plus minocycline (3-mix paste/ Triple Antibiotic paste).⁽¹⁾
- Metronidazole and ciprofloxacin plus amoxicillin.⁽³⁾
- Metronidazole and ciprofloxacin plus cefaclor
- Metronidazole and ciprofloxacin plus cefroxadine
- Metronidazole and ciprofloxacin plus fosfomycin
- Metronidazole and ciprofloxacin plus rokitamycin
- Penicillin, bacitracin, or chloramphenicol and streptomycin (Grossman's polyantibiotic paste)

- Ledermix paste (triamcinolone-a corticosteroid and demeclocycline-a tetracycline antibiotic).¹²
- Neomycin, polymyxin, and nystatin.⁽¹³⁾
- Calcium hydroxide pastes.⁽¹⁴⁾
- Chlorhexidine paste.⁽¹⁵⁾

Among these, the 3- mix paste of Metronidazole and ciprofloxacin plus minocycline is discussed in detail.

Metronidazole and ciprofloxacin plus minocycline (3-mix paste/ Triple Antibiotic paste).

Sato et al, formulated the use of the present

combination of antimicrobials- Metronidazole and ciprofloxacin plus which produced effective destruction of all kinds of endodontic pathogens (aerobic as well as anaerobic).⁽²⁾ Ever since, this combination has been popularly known as 3-mix paste/ Triple Antibiotic paste.

Dosaging-Ciprofloxacin (200mg), Metronidazole (500mg), Minocycline(100 mg), Propylene glycol/ macrogol, Normal saline as carrier.

Disadvantages of Polyantibiotic pastes:

A disadvantage of this mixture is tooth discoloration to a bluish-grey hue. The discoloration brought about by tetracycline family

Action of ingredients

Components		Mode of Action
Ciprofloxacin ⁽¹⁶⁾	Narrow spectrum antimicrobial agent	<ul style="list-style-type: none"> • It belongs to fluoroquinolone group. • It acts through the inhibition of DNA gyrase. • Antibacterial effect present during both duplication stages and latent stage of bacterial growth phases. • Effective against gram negative organisms.
Metronidazole ⁽¹⁶⁾	Narrow spectrum antimicrobial agent	<ul style="list-style-type: none"> • It is a nitroimidazole compound. • Metronidazole permeates bacterial cell membranes. It then binds to the DNA, disrupting its helical structure, and leads to very rapid cell death. • Effective against anaerobic cocci, bacilli (both gram positive and gram negative) and few protozoa. • Effectiveness is both found systemically as well as topically.
Minocycline ⁽¹⁶⁾	Broad spectrum antimicrobial agent	<ul style="list-style-type: none"> • Acts by inhibiting protein synthesis on the surfaces of ribosomes. • Inhibits collagenases and matrix metalloproteinase and is not cytotoxic. • Effective against both gram-positive and gram-negative microorganisms; spirochetes • Also augment the growth of host cells on dentin, via the exposure of embedded collagen fibers or growth factors allowing for successful revascularization and continued development of root to its normal length.⁽¹⁷⁾
Propylene glycol/ macrogol ⁽¹⁸⁾		<ul style="list-style-type: none"> • Macrogol is the International Non-proprietary Name (INN) for polyethylene glycol. • Acts as solvent enhancing better diffusion of the medicaments deep into the dentinal tubules thus enhancing the antimicrobial action.
Saline	Solvent	<ul style="list-style-type: none"> • Dissolution of the ingredients.

is believed to be due to photo-induced reaction. Minocycline binds to calcium-ions through chelation reaction; forming an insoluble complex⁽¹⁹⁾. Patients and parents/guardians should be advised of potential staining and a subsequent need for bleaching. Other alternative is to substitute cefaclor instead of minocycline.⁽²⁰⁾ A modification of the current clinical protocol (Sato et al. 1996, Banchs & Trope 2004) has been promulgated to avoid crown discolouration. This innovative method covers the dentinal tubules of the root dentin, thus preventing any interaction between tri-antibiotic paste and root dentin walls. The coronal walls of access preparation are etched for 20s with 35% phosphoric acid. Bonding agent is applied and cured for 20s. Then, a Root Canal Projector with a size 20 K-file is placed into the root to maintain patency of canals. Space between the projector and coronal dentine is sealed with flowable composite and light cured for 30s.⁽²¹⁾

Method of dispensing: A 20 gauge needle is placed 1-2 mm short of working length and medication is introduced into the canal using a backfill approach to the level of the cemento-enamel junction or alternately paste filler or lentulospirals can be used.

Method of preparation & storage:

Take clean mortars separately on which each tablets/capsules will be placed and ground.

Now equal ratio of tablet powder is mixed to produce a mixture; to which equal amount of propylene glycol is added to produce a creamy paste.

Resultant opaque paste can be stored in air-tight containers for future use.

Change of translucency of paste from opaqueness indicates contamination which should not be used.

Few studies regarding Triple Antibiotic pastes:

Sato et al investigated this drug combination in vitro and established it to be very effective in the decontamination of deep caries, necrosed pulp, and infected root canals of primary teeth.⁽²¹⁾

Hoshino et al determined that a combination of ciprofloxacin, metronidazole, and minocycline with a dilution of 25 µg each per millilitre of paste has ability to decontaminate infected root canal dentin in vitro.⁽²²⁾

Banchs F et al suggested that the MIC method may not be suitable for determining whether combinations of drugs can kill all the bacteria in a flora.⁽²³⁾

Ozan U1&Er K reported on endodontic treatment of a large cyst-like periradicular lesion using a combination of antibiotic drugs.⁽²⁴⁾

Ozlem reported on use of triple antibiotic paste for a traumatized immature tooth with a periapical lesion.⁽²⁵⁾

Primary teeth with periradicular lesions with or without physiologic root resorption were treated successfully by the LSTR endodontic therapy.⁽²⁶⁾

Uses of LSTR or Triple antibiotic paste:

Periradicular pathosis of permanent tooth with mature apices-As discussed earlier, it is reported that the resulting sterilization with antibiotics or antiseptics result in approximately 20-40% additional cleansing / augmenting the conventional root canal debridement.⁽⁶⁾

Periradicular pathosis of permanent tooth with immature apices-Conventional apexification procedures have been replaced with newer methodologies. Initially intra-canal medicaments like calcium hydroxide were used for apexification; and are now contraindicated as they inhibit further root growth. Recently, Mineral Trioxide Aggregate (MTA) has been used in one-step apexification procedures to create an artificial

apical barrier on which the obturation material can be compacted. MTA apexification though regarded successful does not help to strengthen the root, and in the absence of continued development of the root, the roots stay thin and fragile.⁽²⁷⁾ So, a total change in the management of immature, necrotic/pulpless teeth has occurred based on biological principles. This utilizes the regenerative capacity of cells. Regenerative abilities of cells compensate for loss of structures. Cells in the periapical area like the osteoblasts, cementoblasts, fibroblasts and specially few undifferentiated mesenchymal cells retain the ability to multiply and renew structures. Stimulation of these structures can be fruitful in continued root development in case of an immature root. Regenerative endodontics using triple antibiotic paste can allow continuation of root growth thus reducing the risk of root fracture in a young permanent tooth which would otherwise normally occur with traditional 'apexification' procedures where the roots remain thin and weak. Banchs and Trope demonstrated disinfection and regeneration in an immature tooth with apical periodontitis.⁽²³⁾

Endodontic Regenerative Procedure (ERP):

ERP, as discussed includes conventional instrumentation either minimal or no instrumentation followed by placement of intracanal medication and later bleeding is induced from periapical region. The bleeding from periapex would lead a matrix for movement & growth of new vital tissue in root canal spaces.⁽²²⁾

No need for surgical intervention for periradicular pathosis of permanent tooth with mature apices:

Traditionally few endodontic failure cases were treated using surgical techniques (surgical endodontics). Surgical endodontics has following

drawbacks like- 1) Post-Operative pain, 2) Damage to surrounding anatomic structures, especially the neurovascular tissue, 3) Need for surgery.⁽²⁸⁾ But with the invent of triple antibiotic pastes, the need for surgical endodontics is reduced.

Periradicular pathosis of primary tooth:

Root canal complexity of primary teeth is well known. Compounding to root canal complexity, the traditional use of thorough mechanical debridement cannot be performed in primary teeth as compared to permanent teeth due to thin dentinal walls & flaring primary roots. Also the cautious use of irrigants is exercised during pulpectomy to prevent undue effects of irrigants on periapical tissue due to its easy passage into periapical tissues (presence of resorbing apices). Especially caustic chemicals like sodium hypochlorite, hydrogen peroxide and dentin softening agents like EDTA is somewhat contraindicated in such teeth. A combination of these problems always creates a doubt in the mind whether the disinfection of root canal is likely. In this regard several reports are being published to improve the effect of root canal disinfection using LSTR.^(29,30) Few studies are-Jaya AR reported on primary teeth with the periradicular lesions showing healing after a 24 Month follow up.⁽³¹⁾ Takushige Tet al showed normal physiologic root resorption of primary teeth with periradicular lesions and; proper eruption of successor teeth erupted without any disorders utilizing LSTR therapy.⁽²⁶⁾ In this regard LSTR can be a useful adjuvant to routine pulp therapies or alternate to pulpectomies in special cases (e.g. Un cooperative children, non-negotiable canals).

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How to cite this article:

Anila B, Murali H, Cheranjeevi J , Kapil RS. Lesion Sterilization and Tissue Repair (LSTR). A Review. *Journal of Scientific Dentistry* 2014;4(2):49-55

Source of Support: Nil, **Conflict of Interest:** None declared