Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies *NLM ID: 101716117*

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr Indian Citation Index (ICI) Index Copernicus value = 100

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Review Article

Lesion sterlization tissue repair

[1]Manpreet Kaur Khurana, [2]Animesh, [3]Nikhil Srivastava, [4]Navpreet Kaur

[1]Intern, Swami Vivekanand Subharti University, India;
[2]Intern, Subharti Dental College and Hospital Swami Vivekanand Subharti University, Meerut, India;
[3]Professor and Head, [4]Assistant Professor, Department of Pedodontics and Preventive Dentistry, Subharti Dental College and Hospital Swami Vivekanand Subharti University, Meerut, India

ABSTRACT:
Lesion Sterilization and Tissue Repair (LSTR) is an innovative, minimally invasive endodontic treatment designed to disinfect the root canal system using antibiotic mixtures rather than traditional mechanical instrumentation. The primary goal of LSTR is to eradicate microbial infections from both primary and permanent teeth, thus facilitating natural tissue repair. Conventional root canal treatments rely on mechanical debridement and chemical irrigation, but they often fail to eliminate deep-seated anaerobic bacteria, leading to treatment failure. The LSTR technique, introduced by researchers at Niigata University, Japan, in 2004, involves applying a triple antibiotic paste (TAP) containing metronidazole, ciprofloxacin, and minocycline to sterilize infected tissues.
This review explores the historical development, indications, contraindications, classification, and clinical application of LSTR. It highlights various drug combinations, including polyantibiotic paste (PBSC, PBSN) and TAP, and their efficacy in treating periradicular pathosis, root resorption, and traumatic dental injuries. Additionally, the paper discusses the use of calcium hydroxide and mineral trioxide aggregate (MTA) in tissue repair, their antimicrobial mechanisms, and their role in mineralization.
Despite its advantages, LSTR has challenges, such as tooth discoloration, potential antibiotic resistance, and cytotoxic effects on fibroblasts. However, the technique remains a promising alternative to conventional endodontic therapy, particularly for young permanent teeth and severely infected primary teeth. LSTR is a time-saving, painless, and patient-friendly approach that can preserve natural dentition, preventing premature extractions and the complications associated with tooth loss.
Keywords: Lesion Sterilization and Tissue Repair (LSTR), endodontic therapy, root canal disinfection, triple antibiotic paste, calcium hydroxide, mineral trioxide aggregate, periradicular pathosis, microbial infection, regenerative endodontics, tissue mineralization.

Received: 23 January, 2025 Accepted: 20 February, 2025

Corresponding author: Manpreet Kaur Khurana, Intern, Swami Vivekanand Subharti University, India

This article may be cited as: Khurana MK, Animesh, Srivastava N, Kaur N. Lesion sterlization tissue repair. J Adv Med Dent Scie Res 2025; 13(3):6-11.

INTRODUCTION

In dentistry, the most common issue is the attack on hard tissue by microbes, which leads to cavities. If cavities are not treated, they can affect the pulp and eventually result in losing the tooth. Studies on animals and humans have clearly shown how germs contribute to pulp and periapical diseases. The microbes found in an infected root canal include both aerobic and anaerobic pathogens, with anaerobic pathogens being the most common. The main goal of endodontic treatment is to lower the number of these bacteria in the root canal system. During standard root canal treatment, dentists usually remove these microbes by using files or chemical irrigation agents. However, some pathogens might remain in the deeper layers of infected tooth tissue, even after intervention, which can lead to more challenges and failure of the root canal process. Therefore, entirely getting rid of these pathogens is vital for a successful outcome. To eliminate these microbes, it's important to thoroughly clean the infected pulp and then use medications inside the canal. Intracanal medicaments are chemical agents placed inside the root canal system, used between visits to help relieve pain and fight germs. Calcium hydroxide is the most popular choice for these treatments because it helps kill bacteria and

supports tissue healing[1]. However, it can wash out of the root canal if left in for too long, which can allow for reinfection. Therefore, we need extra methods to ensure the root canal is well disinfected and that we can kill as many bacteria as possible. Studies show that using antibiotics or antiseptics can provide an additional 20-40% cleaning, improving the standard root canal cleaning process[2]. In 2004, the cariology research unit at the School of Dentistry in Niigata University, Japan, introduced the idea of Lesion Sterilization and Tissue Repair (LSTR). This therapy is an endodontic procedure that uses little to no instruments, followed by applying an antibiotic mixture to disinfect the root canal system.

It is becoming a modern treatment option compared to traditional pulpectomies, root canal treatments, and tooth extractions for dealing with teeth that have no vitality or pulp. The main idea is that if we completely disinfect the lesions, we can expect the tissue to heal. Initially, metronidazole was used as the only antibiotic in intracanal treatment because it effectively kills a wide range of bacteria, especially anaerobes found in the mouth. However, even at high doses, metronidazole couldn't remove all the bacteria in the lesions[3]. As a result, two other antibacterial drugs, ciprofloxacin and minocycline, were introduced (Sato et al., 2005). Many different medications, including antibiotics and antiseptics, have been examined for this purpose. Each option has its own pros and cons, so it's important to keep updating the choice of antibacterial drugs to ensure the best sterilization of root canal systems. Therefore, this comprehensive review aims to gather and review all the current methods and medications available, explaining the technique's reasoning, its development, when to use it, its applications, and the clinical steps needed for a better understanding and application of lesion sterilization and tissue repair.

DISCUSSION

Both primary and permanent teeth are very important for our overall health. Dental caries, or tooth decay, is a common problem that needs attention. If we ignore it in the early stages, it can affect the tooth's pulp and lead to more serious issues, including the need to remove the tooth. Losing primary teeth too early can create several problems, such as incorrect tooth eruption, changes in the order teeth come in, shifting of already erupted teeth, loss of space for the permanent teeth that come afterward, development of bad habits like tongue thrusting, changes in speech, and difficulty with chewing[4]. Losing a permanent tooth early is also challenging because it leads to complicated procedures for replacing it. If we don't replace the lost tooth, other teeth may shift or grow too much into the empty space. Therefore, it is crucial to keep our teeth healthy and in place as long as they can function properly and are free from disease.

DEFINITION

Nugroho R and his team described LSTR, also known as non-instrument endodontic treatment (NIET), in 2015 as an innovative treatment for cases with or without pulp and periapical infections, utilizing a mixture of three antibiotics for disinfection[5].

INDICATIONS

1) Periradicular Pathosis of Young Permanent Teeth with Immature Apices
2) Periradicular Pathosis of Both Primary and Permanent Teeth with Mature Apices
3) Infected Teeth with an Abscess/Sinus Tract
4) Root Resorption
5) Radiolucency in the Bifurcation Area and/or Loss of Alveolar Bone
6) Traumatic Luxation or Avulsion of Teeth with Immature Pulp

CONTRAINDICATIONS

1) Teeth with a Perforated Pulpal Floor
2) Radiographic signs of severe internal resorption
3) Significant bone loss in the furcation area affecting the developing tooth
4) In teeth that cannot be saved

CLASSIFICATION

Intra-canal medications can be divided into two main categories: lesion sterilization (drugs) and tissue repair (materials). Different mixtures of drugs have been tested over the years. The first drug mixture was the polyantibiotic paste (PBSC), introduced by Grossman in 1950. This paste contained penicillin, bacitracin, streptomycin, and caprylate sodium. In 1975, nystatin replaced caprylate sodium, and the new mixture was called PBSN. However, the Food and Drug Administration banned this combination because it caused allergic reactions and raised concerns about resistance. In 1996, Sato and colleagues introduced the triple antibiotic paste, which included metronidazole, ciprofloxacin, minocycline, and propylene glycol[7].

The materials commonly used as intra-canal medications are calcium hydroxide and mineral trioxide aggregate. Calcium hydroxide was first introduced by Herman in 1930[8] and has been in use ever since. Mineral trioxide aggregate became available in 1990 and continues to be widely used today.

LIST OF DRUG COMBINATIONS FOR INTRACANAL TREATMENT

1) POLYANTIBIOTIC PASTE (PBSC)
2) POLYANTIBIOTIC PASTE (PBSN)
3) TRIPLE ANTIBIOTIC PASTE

After the interdict on polyantibiotic paste, Sato and his team resumed the use of antibiotics in endodontic treatment in 1996. They formulated a formula that included metronidazole to target anaerobic microorganisms, ciprofloxacin for aerobic and gram-

negative microorganisms, and minocycline for both gram-positive and gram-negative microbes.

Protocol for Preparing 3 Mix: Macrogol Propylene

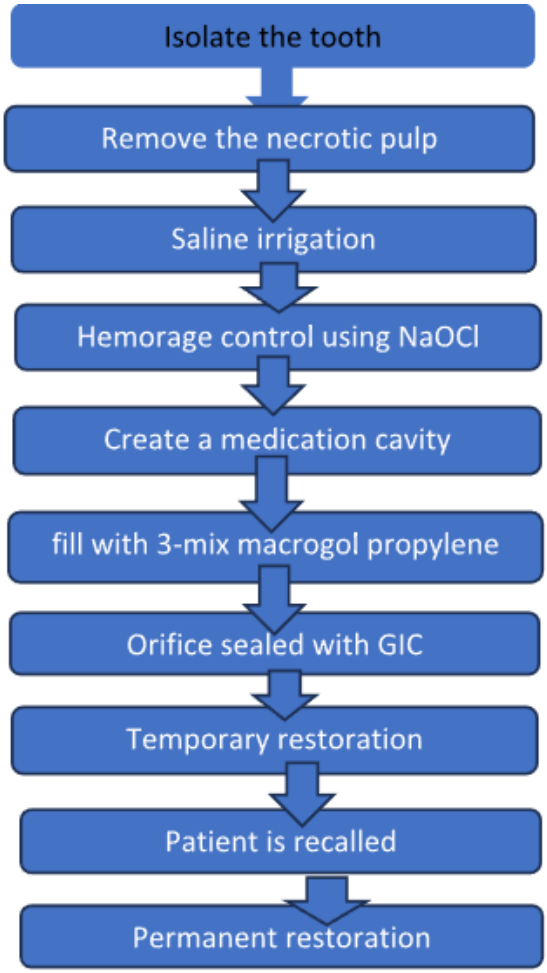
3Mix-Macrogol Propylene should be mixed on the day of treatment. However, each medication can be powdered and stored in a dry, tightly sealed container ahead of time. The powdered drugs should be used within a month, and any powder that becomes wet should be thrown away.

Preparation of 3Mix-Macrogol Propylene

a) According to Takushige and his team, the 3Mix is made by combining 1 part of ciprofloxacin (200mg), 3 parts of minocycline (100mg), and 3 parts of metronidazole (500mg). Takushige provided two different mixing ratios for 3Mix and macrogol propylene. The first method is the standard mix, which involves combining 1 part of Macrogol Propylene with 7 parts of 3Mix to create a blend that spreads easily. The second method combines 1 part of macrogol propylene with 5 parts of 3Mix[6].

b) According to Hoshino and his team, they used the same medications as Takushige but with a slight change in the mixing ratio. Instead of the 1:3:3 ratio, they used 1 part of ciprofloxacin (200mg), 1 part of minocycline (100mg), and 1 part of metronidazole (500mg).

METHOD FOR PLACING TRIPLE ANTIBIOTIC PASTE



Flowchart 1:-Protocol for preparing 3-Mix: Macrogol Propylene

LESION STERILIZATION

A) DRUGS

1) POLYANTIBIOTIC PASTE

2) TRIPLE ANTIBIOTIC PASTE

i) METRONIDAZOLE

Metronidazole is the first nitroimidazole drug that was introduced in 1959 to treat trichomoniasis. Later, it was discovered to be very effective against amoebas.

CIPROFLOXACIN

Ciprofloxacin is a very strong first-generation fluoroquinolone that works against many types of bacteria.

MINOCYCLINE

It is a broad-spectrum, semisynthetic tetracycline antibiotic.

TISSUE REPAIR

Tissue repair is the process of restoring the structure and function of tissue after an injury. It includes two main processes: regeneration and replacement. Regeneration is when new growth fully restores damaged tissue to its original condition. On the other hand, replacement occurs when severely damaged tissues that cannot regenerate are fixed by forming connective tissue, which is often called scarring. The way a wound heals—whether by regeneration, replacement, or a mix of both—depends on the type of tissue involved. Under the right conditions, dental tissue can repair itself through regeneration[9]. These conditions involve removing the harmful microbes (sterilization) that cause the injury. After sterilizing the area, dental tissues are healed by dental pulp stem cells, which supply the necessary cells to repair the damaged tissues.

B) MATERIALS FOR TISSUE REPAIR

i) CALCIUM HYDROXIDE

Calcium hydroxide was first introduced to endodontics by Herman in 1920 as a pulp-capping agent, but it is now widely used in various endodontic treatments[10]. It is the most common dressing used for treating vital pulp and is also important as an inter-visit dressing to disinfect the root canal system.

MODE OF ACTION FOR TISSUE REPAIR

i) Antimicrobial

The antimicrobial effect of calcium hydroxide comes from the release of hydroxyl ions in water. Hydroxyl ions are powerful oxidizing agents that can react strongly with many biological molecules (Freeman & Crapo 1982)[11] . Because of their high reactivity, these free radicals usually do not move away from where they are produced. Their harmful effects on bacterial cells likely happen through these proposed methods:

a) As noted by Halliwell (1987) and Cotran et al. (1999)

– Damage to the bacterial cytoplasmic membrane

The bacterial cytoplasmic membrane is crucial for the cell's survival. It protects the cell from its environment and serves as a site for cell recognition and receptors.

Hydroxyl ions from calcium hydroxide cause lipid peroxidation, which damages the phospholipids that make up the cell membrane. These hydroxyl ions take hydrogen atoms from unsaturated fatty acids, creating a free lipid radical. This free radical then interacts with oxygen, forming a lipid peroxide radical, which removes another hydrogen atom from a different fatty acid, creating yet another lipid peroxide. This process triggers a chain reaction that leads to significant damage to the bacterial cell's cytoplasmic membrane, resulting in cell death .

b) As stated by Voet & Voet (1995):

– Protein Denaturation

Cellular metabolism relies heavily on the activities of enzymes. These enzymes work best and stay stable within a narrow pH range, usually leaning toward acidic conditions. When calcium hydroxide raises the pH, it causes the ionic bonds that hold the enzymes' tertiary structure together to break down. This leads to the polypeptide chain becoming tangled and losing its specific shape. Such changes often cause the enzyme to lose its biological function, which disrupts cellular metabolism and can lead to cell lysis.

c) According to Imlay and Linn (1988):

- Damage to DNA

Mineralization Activity

Mineralization can only take place after the area of the lesion has been sterilized. Once the root canals are sterilized using medicaments, mineralization is expected to occur. Calcium hydroxide helps create a calcific barrier (Eda 1961)[12] . Due to the high pH of pure calcium hydroxide, a thin layer of dead tissue forms in the pulp, reaching up to 2 mm deep (Estrela & Holland 2009)[13]. Beyond this layer, only a mild inflammatory reaction appears, and if the area stays free from bacteria when the material is applied, hard tissue can develop (Estrela et al. 1995).

The hydroxyl group in calcium hydroxide is very important because it creates an alkaline environment that promotes healing and calcification. This higher pH not only neutralizes lactic acid from osteoclasts, which helps prevent the breakdown of the mineral parts of dentine, but it can also activate alkaline phosphatases, which are crucial for forming hard tissue (Estrela et al. 1995)[14] . Alkaline phosphatase is an enzyme that works by releasing inorganic phosphate from phosphate esters. It can break down phosphoric esters, releasing phosphate ions that then combine with calcium ions in the bloodstream to create calcium phosphate in the organic matrix. This calcium phosphate is the basic unit of hydroxyapatite (Seltzer & Bender 1975), which is thought to be closely linked to the mineralization process.

Mineral Trioxide Aggregate

Mineral Trioxide Aggregate, or MTA, was first developed by Mohmoud Taorabinejad at Loma Linda University in California in 1993. The U.S. Food and Drug Administration approved it for use in dental treatments in 1998[15]. Later that same year, Denstply Tulsa Dental launched the commercial version known as Proroot MTA.

Mode of Action for Tissue Repair

i) According to E. Koh, 1998:

One key factor that encourages hard tissue formation is the ability of MTA to trigger cytokine release from bone cells. These cytokines play a role in managing bone formation. This process happens in two stages. The first stage focuses on bringing in and developing osteoblast precursors. The second stage involves mature osteoblasts producing and mineralizing the bone matrix[16].

ii) Holland and his team stated in 1999 that tricalcium oxide in Mineral trioxide aggregate interacts with

tissue fluids to create calcium hydroxide. This process leads to the formation of hard tissue, similar to how calcium hydroxide works. Additionally, calcium hydroxide boosts the activity of pyrophosphatase, which helps produce orthophosphatase. Moreover, calcium, the main ion released from Mineral trioxide aggregate, reacts with phosphates to form hydroxyapatite. These chemical reactions contribute to the sealing ability, biocompatibility, and effectiveness of Mineral trioxide aggregate. Hydroxyapatite crystals form and grow between the material and the dentin wall, creating a seal at the Mineral trioxide aggregate-dentin interface.

iii) Torabinejad noted in 1999 that Mineral trioxide aggregate consists of two main phases: calcium oxide and calcium phosphate. This means that while Mineral trioxide aggregate does not contain calcium hydroxide, it does have calcium oxide, which can react with tissue fluids to later produce calcium hydroxide. This final product can then form calcite crystals. Mineral trioxide aggregate leads to a thicker dentinal bridge, reduces inflammation, and minimizes pulpal necrosis[17].

COMPLICATIONS

1. Tooth Discoloration

One significant issue is the discoloration of the visible part of the tooth, as shown in several studies (Kim JH et al 2010, Thomas SM et al 2014). This discoloration is believed to be caused by minocycline, an ingredient in the antibiotic mixture. It is thought that minocycline attaches to the calcium in the dentin and forms insoluble complexes, which leads to the tooth changing color.

2. Antibiotic Resistance

There is concern that antibiotic paste might lead to bacterial resistance (Slots J, 2002; Parasuram VR, 2012). However, there is still no agreement on this issue. One major factor that contributes to antibiotic resistance is the improper use of antibiotics, which can create resistant bacteria and increase the transfer of resistance genes from antibiotic-resistant germs to those that are not resistant (ADA, 1997).

3. Cytotoxic Effects on Fibroblasts

Triple antibiotic paste has been suggested to be harmful to fibroblast cells (Yadlapati et al., 2013). It is possible that the release of antimicrobials into the apical papilla could impact the stem cells found there. Additionally, leftover antimicrobials in the canal might affect these cells during the bleeding that happens as part of the regenerative treatment process (Ruparel et al., 2012).

CONCLUSION

Endodontic therapy is essential for getting rid of bacteria, their waste, and what they feed on by disrupting and eliminating the harmful microbes using both chemical and mechanical methods. Various medications have been suggested to enhance these techniques, with different levels of success. The Lesion sterilization and tissue repair therapy is easy, painless, and saves time, causing less stress for patients both physically and mentally. This makes it more likely that patients will follow through with the treatment. This method can help disinfect severely infected primary teeth and allow them to serve as space maintainers until the permanent teeth come in. This approach is especially worth considering when the outlook is not good for traditional root canal treatments in teeth affected by furcation issues and significant bone loss.

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