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Review

Lesion sterilization and tissue repair in non-vital primary teeth: a critical evidence-based appraisal of clinical outcomes and future directions

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Abstract

Aim: Lesion Sterilization and Tissue Repair (LSTR) is a biologically based, minimally invasive therapy for managing non-vital primary teeth through root canal disinfection with antibiotics. This review aims to evaluate current evidence on the clinical and radiographic outcomes of LSTR compared with conventional pulpectomy and to identify factors influencing its success.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and Google Scholar to identify studies evaluating the outcomes of LSTR therapy in non-vital primary teeth. Studies reporting clinical and/or radiographic success outcomes with a minimum follow-up of one month were included, and the findings were qualitatively synthesized.

Results: Evidence indicates that LSTR achieves high short- to medium-term clinical success rates, comparable to pulpectomy. However, radiographic outcomes are less predictable and tend to decline over time. Variability in success appears related to differences in antibiotic formulations, carrier materials, and study protocols. Recent approaches using bioceramic carriers show potential for enhancing long-term healing and treatment consistency.

Conclusion: LSTR offers a promising, biologically favorable, and less invasive alternative to pulpectomy for non-vital primary teeth. However, heterogeneity among studies and limited long-term data emphasize the need for standardized protocols and extended follow-up. LSTR provides pediatric dentists with an effective and time-efficient option that preserves tooth structure and reduces patient discomfort. Incorporating advanced biomaterials may improve treatment predictability, supporting evidence-based decision-making in pediatric endodontics.

Keywords

esion sterilization and tissue repair, primary teeth, pediatric dentistry, endodontics, antibiotic therapy

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Introduction

Preservation of primary teeth until their natural exfoliation is crucial in pediatric dentistry, as these teeth aid mastication, speech, aesthetics, and proper arch development.[1] However, carious lesions in primary teeth can progress rapidly, affecting the pulp tissue and leading to infections.[2] Traditional endodontic treatment methods or tooth extraction can be particularly challenging in pediatric patients with limited cooperation.[3] In this context, LSTR therapy has emerged as a promising alternative, offering a minimally invasive and biologically oriented approach.[4] This review aims to provide a comprehensive evaluation of the basic principles of LSTR therapy, the antibiotic combinations used, clinical application procedures, reported success rates, and its future potential.

Materials and Methods

A comprehensive literature search was conducted to identify studies evaluating the outcomes of LSTR therapy in non-vital primary teeth. Electronic databases, including PubMed, Scopus, and Web of Science, were searched from inception to the most recent available date. Additionally, Google Scholar was screened to identify relevant grey literature.

The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to LSTR and pediatric endodontics. Search terms included "lesion sterilization and tissue repair," "LSTR technique," "LSTR therapy," "LSTR," "3Mix-MP," "3Mix antibiotic paste," "3MIX paste," "chloramphenicol, tetracycline, and zinc oxide-eugenol (CTZ) paste," "non-instrumentation endodontic treatment," "non-instrumentation root canal treatment," "triple antibiotic therapy," and "triple antibiotic paste", combined with "primary teeth," "primary molars," "deciduous teeth," "necrotic primary teeth," "pulpectomy," and "non-vital pulp therapy."

Studies evaluating clinical or radiographic outcomes of LSTR in primary teeth with a minimum one month follow up were included. English-language original studies, reviews, and grey literature were screened by a single reviewer. Data were qualitatively synthesized to assess the clinical and radiographic effectiveness of LSTR in non-vital primary teeth.

Mechanism of LSTR

LSTR is a biologically based treatment method aimed at eliminating microorganisms in infected dentin and pulp tissues while promoting tissue healing. This concept was developed by the Cariology Research Unit at the Faculty of Dentistry, Niigata University.[5] The LSTR approach is based on sterilizing the carious lesion while promoting the host's innate biological capacity for tissue repair and regeneration. Because a single antibiotic rarely achieves complete bacterial elimination, broad-spectrum coverage is typically attained through combinations of multiple agents.[6]

The antibiotic pastes used penetrate deep into tissues via dentinal tubules, effectively controlling the infection. Consequently, the damaged tissues are enabled to heal and regenerate through natural biological processes.[7] This is particularly advantageous in primary teeth, where factors such as root resorption and complex root canal morphology can make conventional endodontic treatments difficult, whereas LSTR offers a less invasive alternative.[8]

Antibiotic Combinations and Carriers in LSTR Therapy

The success of LSTR therapy largely depends on the selection of effective antibiotic combinations and appropriate carriers. The most commonly used formulation is the Triple Antibiotic Paste (TAP), consisting of ciprofloxacin, metronidazole, and minocycline.[9,10] This combination has demonstrated broad-spectrum antibacterial efficacy against root canal pathogens and is typically prepared in either 1:1:1 or 1:3:3 ratios.[11,12] Common carriers, such as propylene glycol and macrogol (polyethylene glycol), are utilized to facilitate the paste's diffusion and penetration into the intricate network of dentinal tubules.[13]

One significant concern associated with minocycline is the potential for tooth discoloration. To mitigate this drawback, numerous alternative antibiotic combinations have been rigorously investigated. Agents such as clindamycin, amoxicillin, fosfomycin, cefaclor, cefroxadine, and roxithromycin have been explored as potential substitutes. These alternatives have shown promising in vitro antibacterial efficacy while concurrently reducing the likelihood of discoloration.[14,15] Recent clinical trials have further evaluated modified formulations, including clindamycin-containing pastes and variations in antibiotic concentrations.[16]

Beyond TAP-based regimens, alternative antibiotic combinations have shown encouraging outcomes. A paste containing ciprofloxacin, tinidazole, and minocycline has been suggested as a viable option. Tinidazole, a second generation nitroimidazole, provides greater potency and fewer adverse effects than metronidazole and is often preferred for single-dose therapy. This combination has demonstrated effectiveness in primary molars with periradicular pathology.[17] Similarly, the ciprofloxacin–ornidazole–minocycline combination has exhibited superior outcomes when compared to conventional 3Mix formulations. Ornidazole, recognized for its prolonged half-life and slower metabolism, provides extended antimicrobial activity and improved clinical efficacy relative to metronidazole.[18] Beyond TAP-based alternatives, other combinations have also yielded promising results. A paste formulated with ciprofloxacin, tinidazole, and minocycline has been proposed as a viable option. Tinidazole, a second-generation nitroimidazole, offers enhanced potency and fewer side effects compared to metronidazole and is frequently recommended for single-dose therapy. This specific combination has been reported to be effective in primary molars presenting with periradicular lesions.[17]

The use of CTZ paste has also been evaluated in LSTR. While it offers clinical outcomes comparable to conventional pulpectomy, concerns remain regarding its biocompatibility and potential for tooth discoloration due to its tetracycline content.[19] Recent in vitro research has also explored enhancing CTZ paste with silver and zinc oxide nanoparticles. This nano-antibiotic formulation allowed for a reduced antibiotic concentration while maintaining significant efficacy against pathogens like S. mutans, suggesting that nanotechnology could optimize traditional LSTR medicaments by lowering the required antibiotic dose.[20] Another noteworthy material is Pulpotec, a non-resorbable, iodoform-based compound with radio-opacity,

supplied in powder-liquid form. A recent clinical study reported significantly higher clinical and radiographic success rates with Pulpotec in LSTR compared to an alternative clindamycin-based 3Mix paste. Consistent with observations in many LSTR treatments, clinical outcomes were found to be more favorable than radiographic ones.[21]

Bioceramics have emerged as promising alternatives to traditional antibiotic-based LSTR, addressing concerns such as tooth discoloration and antimicrobial resistance. Characterized by exceptional biocompatibility and regenerative potential, these materials have demonstrated clinical and radiographic success comparable to conventional pulpectomy in necrotic primary molars. While current evidence is encouraging, long-term longitudinal studies are required to solidify the role of bioceramics in LSTR protocols.[22]

Several other antibiotic combinations have also been investigated, including ciprofloxacin–amoxicillin–metronidazole, amoxicillin–doxycycline–metronidazole, and minocycline–ofloxacin–metronidazole.[23] These diverse formulations have shown variable success, highlighting the continued need to refine antibiotic selection to improve therapeutic efficacy while reducing adverse effects and enhancing patient safety.

This narrative review synthesizes the principles of LSTR, antimicrobial formulations and carriers, clinical protocols, and reported outcomes in non-vital primary teeth, highlighting recent evidence and future directions. The detailed data are provided in Supplementary Table 1.

Clinical Application Protocol for LSTR Therapy

A meticulous clinical protocol is critical for the success of LSTR therapy, ensuring effective disinfection and promoting tissue healing. The procedure is generally performed as follows:

Preparation of the Antibiotic Paste

To maintain potency, the antibiotic paste should be freshly prepared. The constituent antibiotics are pulverized into a fine powder.10 This powdered mixture is then combined with a liquid vehicle, typically a blend of macrogol and propylene glycol, to achieve a thick, consistent paste. A commonly employed formulation involves mixing the antibiotic powders and the liquid vehicle at a 7:1 powder-to-liquid ratio by weight.[24]

Tooth Preparation and Disinfection

Following the administration of local anesthesia and rubber dam isolation, an access cavity is prepared. All carious tissue and old restorations are removed to expose the pulp chamber. The coronal pulp and any necrotic tissue are excavated down to the canal orifices. To enhance the retention of the medication, medication cavities (approximately 2 mm deep and 1 mm wide) can be prepared at the entrance of each canal orifice using a sterile round bur. The access cavity was thoroughly irrigated with 2.5% sodium hypochlorite (NaOCl) and then dried. In cases where hemostasis could not be achieved, a sterile cotton pellet soaked in 5-10% NaOCl was placed in the pulp chamber to control bleeding.[25,26]

Medication Application and Final Restoration

The antibiotic paste is compacted into the canal orifices, ensuring direct contact with the pulp floor. Following application, the tooth is immediately restored with a glass ionomer cement base and a definitive restoration, typically a stainless steel crown, to provide a hermetic coronal seal. Longitudinal follow-up is mandatory to monitor clinical symptom resolution and radiographic healing.[27]

Ethical Approval

This manuscript is a narrative review based exclusively on previously published literature and does not involve newly collected human or animal data.

Reporting Guidelines

As this article is a narrative review, no formal reporting guideline checklist was mandated. Nevertheless, the review was prepared in accordance with the general principles of transparent, accurate, and evidence-based scholarly reporting for review articles.

Results

The efficacy of LSTR therapy has been extensively investigated through numerous clinical trials and systematic reviews, comparing its outcomes with conventional endodontic treatments like pulpectomy. While LSTR consistently demonstrates high clinical success, its radiographic outcomes tend to be more variable and may decline over longer follow-up periods, highlighting a critical area for further research and refinement.

Comparative Studies of LSTR and Iodoform-Based Pastes (Vitapex)

A significant body of research has focused on comparing the TAP used in LSTR with iodoform and calcium hydroxide-based pastes, most notably Vitapex. A systematic review which included four RCTs, found that both LSTR and Vitapex treatments in necrotic primary teeth showed high clinical success at the 12-month follow-up. However, the review also noted a decline in radiographic success for both groups beyond this period and highlighted that all included studies had a high risk of bias.[28]

Supporting these findings, Nakornchai et al. demonstrated that while LSTR and Vitapex yield comparable initial clinical success, iodoform-based materials offer superior and more stable radiographic outcomes.[29] In another study, Doneria et al., compared a modified 3Mix-MP paste, Vitapex, and zinc oxide-ozonated oil in 64 primary molars over 18months. Long-term evaluations revealed a progressive decline in LSTR's efficacy compared to the sustained success of Vitapex and ozonated oil formulations.[30]

RCTs by Agarwal et al. confirmed LSTR as a viable clinical alternative to conventional ZOE pulpectomy, while the inclusion of bioactive agents like simvastatin in LSTR protocols has shown clinical equivalence to instrumentation-based methods.[31] Sefa et al. evaluated LSTR (3Mix-MP) and pulpectomy (Metapex) in 142 primary molars with poor prognosis. They found 100% clinical success for both treatments at 12 months, but radiographic healing was limited in both groups.[26] Collectively, these studies suggest that while LSTR is a clinically effective

option, iodoform-based materials like Vitapex may offer more predictable radiographic healing over the medium to long term.

Studies on Alternative Antibiotic Combinations and Materials

A clinical practice guideline by Coll et al. strongly discouraged the use of tetracycline-containing pastes (including minocycline and doxycycline) due to the risk of discoloration and associated lower success rates.[32]

To address the discoloration concerns associated with minocycline, various antibiotic substitutions have been evaluated. Comparative studies by Pinky et al. and Nanda et al. demonstrated that replacing minocycline or metronidazole with ornidazole yields high clinical and radiographic success, validating ornidazole-based combinations as effective alternatives.[33,34]

Culfa and Demir, investigated a clindamycin-based 3Mix-MP formulation in 45 primary molars over 12 months. They found no statistically significant difference in clinical success between the standard 3Mix-MP and the clindamycin-alternative group.[25] Aşık et al. demonstrated that the efficacy of clindamycin-based LSTR therapy remains consistently high across different pediatric age groups and behavioral categories, supporting its reliability in clinical practice.[35] Another study evaluated a paste composed of amoxicillin, doxycycline, and metronidazole in 45 primary molars. They reported a high clinical success rate of 95.6% after a 12-month follow-up.[15] Shankar et al. investigated antibiotic concentration in 32 primary molars over 3 months. They found no significant difference in success between a paste mixed at 1 mg/mL versus 1 g/mL, indicating that lower concentrations could be equally effective and potentially safer.[16] El Kharadly et al. evaluated the efficacy of a TAP-simvastatin combination, finding that while clinical and overall radiographic outcomes were comparable to traditional mixtures, simvastatin significantly enhanced bone density in the furcation area. This highlights simvastatins potential as a biocompatible adjunct with potent anti-inflammatory and osteogenic properties, making it a promising component for managing non-vital primary molars, particularly in cases involving inflammatory root resorption.[36]

Arangannal et al. investigated a combination of ciprofloxacin, metronidazole, and doxycycline in 40 non-vital primary molars. They reported 100% clinical success at 12 months, with 80% of cases showing radiographic improvement.[37] Beniwal et al. compared LSTR using a classic 3Mix-MP paste with traditional pulpectomy using a $Ca(OH)Ca(OH)_2$ and ZnO mixture in 50 primary molars. At 6 months, while clinical success was comparable, the pulpectomy group showed significantly better radiographic success compared to the LSTR group.[38] In an in vivo study conducted by Jaya et al., two different antibiotic combinations used in LSTR therapy were compared: 3Mix-MP versus Ciprofloxacin, Minocycline, and Tinidazole. After a 24-month follow-up period, no statistically significant difference was observed between the two groups. These findings suggest that tinidazole may serve as a suitable alternative and can be effective in preserving primary teeth with periradicular lesions.[17] CTZ paste has been evaluated as another alternative. Lokade et al. conducted an RCT on 63 primary molars over 12 months, comparing a modified 3Mix paste (ornidazole, ciprofloxacin, cefaclor) and a CTZ paste. Clinical outcomes were similarly favorable across groups, while radiographic results were superior when the modified 3Mix was applied after removing accessible radicular pulp.[39] Moura et al. conducted an RCT comparing LSTR with CTZ paste to conventional ZOE pulpectomy in 88 primary molars with pulp necrosis over a 12-month period. They found no significant difference in clinical success or radiographic success. However, the LSTR procedure with CTZ was significantly shorter in duration.[27] A follow-up study by the same research group at 36 months confirmed these findings, with similar clinical and radiographic success rates, although radiographic success declined for both groups over the longer term. The study also highlighted that the presence of a furcation lesion at baseline was a significant risk factor for failure.[40]

Carrier selection significantly influences LSTR effectiveness. Dengre et al. evaluated various vehicles, including macrogol–propylene glycol, aloe vera gel, and distilled water, finding that while aloe vera achieved high success rates, no statistically significant differences existed among the carriers. This suggests that carrier optimization remains a potential avenue for enhancing LSTR outcomes.[41]

Prabhakar et al. evaluated the clinical and radiographic outcomes of LSTR therapy using 3Mix-MP. Two treatment approaches were compared: removal of only necrotic coronal pulp (Group A) versus removal of both necrotic coronal and accessible radicular pulp (Group B). After 12 months, Group A demonstrated 93.3% clinical and 76.7% radiographic success, whereas Group B achieved 100% success for both parameters. These findings highlight the potential influence of the extent of pulp tissue removal on the overall success of LSTR therapy.[42]

LSTR in Teeth with and without Root Resorption

The initial condition of the tooth, particularly the presence of root resorption, appears to be a critical factor in determining the most appropriate treatment. The clinical practice guideline by Coll et al. provided a key recommendation based on a meta-analysis. It concluded that pulpectomy showed superior outcomes in non-vital primary teeth without preoperative root resorption. Conversely, LSTR was found to be significantly more effective ($p<0.001$) in cases where physiological or pathological root resorption was already present.[32] This is supported by Grewal et al., who compared LSTR with conventional pulpectomy in 50 primary molars over a 36-month period. They found that the rate of root resorption was significantly slower in the LSTR group, suggesting LSTR may be more successful in preserving the tooth's functional lifespan.[43]

Long-Term Radiographic Outcomes: Challenges and Discrepancies with Clinical Success

While clinical symptoms often resolve quickly with LSTR, long-term radiographic success remains a critical concern, frequently demonstrating a significant disparity when compared to clinical outcomes. A systematic review by Ghorpade et al., which analyzed eight clinical trials, consistently reported a progressive decline in radiographic success over time. Specifically, while clinical success might appear high, radiographic success appeared low at 24-27 months.[44] This alarming trend is further corroborated

by a clinical study, which evaluated 58 primary molars over a 27-month period, revealing a clinical success rate of 82.7% but a starkly lower radiographic success rate of only 36.7%.[45]

The clinical-radiographic discrepancy stems from differing success criteria: clinical success is defined by symptomatic relief (absence of pain, swelling, and fistula), whereas radiographic success requires objective evidence of bone regeneration and lesion resolution. The latter remains more challenging to achieve consistently, driving current research toward novel formulations and bioactive components to enhance long-term radiographic outcomes. Thakur et al. investigated 3Mixtatin, a novel formulation incorporating statins into the antibiotic mixture. The inclusion of statins was specifically highlighted for their potential to promote bone regeneration, directly targeting the improvement of long-term radiographic prognosis.[46] Furthermore, studies by Duarte et al. and Alrayes et al. have also examined LSTR effectiveness, with Alrayes et al. explicitly pointing out the inconsistent radiographic and clinical success rates across various studies and underscoring the urgent need for further clinical trials on 3Mix with diverse compositions.[47,48] A recent study, similarly reported that clinical success was higher than radiographic success in LSTR therapy over a 12-month follow-up, and critically observed a significant decline in the overall success of the 3Mix-MP group over time, reinforcing the imperative for enhanced formulations to achieve more reliable and sustained radiographic healing.[25]

Impact of Irrigants and Prognosis

Dimri et al. investigated the role of different irrigants in LSTR. In a study of 40 primary molars, they found that using an endodontic irrigant before placing an alternative 3-Mix (metronidazole, ciprofloxacin, amoxicillin) improved success. Chlorhexidine (2%) showed the best clinical results, while NaOCl (2%) showed the best radiographic results in terms of furcation healing.[49]

Discussion

LSTR represents a paradigmatic shift in pediatric endodontics, prioritizing biological disinfection over mechanical instrumentation. As a time-efficient alternative for uncooperative patients, LSTR's clinical success is well-documented. Baghlaf and Alamoudi recently confirmed that 3MIX-based LSTR is particularly effective when conventional pulpectomy is unfeasible.[50] Notably, Coll et al. demonstrated that LSTR significantly outperforms pulpectomy in teeth with existing root resorption, though pulpectomy remains superior for intact roots.[14]

Despite these clinical gains, a radiographic paradox persists. Duarte et al. highlighted that while clinical resolution is rapid, radiographic success is less consistent compared to pulpectomy, with evidence quality ranging from moderate to very low. This discrepancy necessitates rigorous long-term monitoring.

The trajectory of LSTR is now shifting toward pharmacological refinement. Substituting minocycline with ornidazole or clindamycin addresses staining concerns, while integrating bioceramics and simvastatin signals a transition from simple sterilization to enhanced regenerative potential. Ultimately, LSTR is evolving from a pragmatic "rescue" treatment into a sophisticated, biologically-driven endodontic strategy.[47]

Limitations

Substantial heterogeneity in antibiotic composition, concentration, and carrier vehicles limits direct comparisons between studies. Furthermore, many RCTs exhibit a high risk of bias, and there is a critical shortage of long-term data. The progressive decline in radiographic success complicates the interpretation of long-term outcomes. Additionally, while lower antibiotic concentrations appear effective, the potential risk of antimicrobial resistance warrants ongoing evaluation.

Conclusion

LSTR therapy emerges as a highly valuable, minimally invasive, and biologically driven alternative for managing infected primary teeth. This approach is particularly advantageous in pediatric dentistry, where complex root canal morphologies and limited patient cooperation often preclude conventional endodontic treatments. While clinical studies consistently report high success rates in terms of symptomatic resolution and functional preservation, the primary challenge remains the delayed and variable nature of long-term radiographic outcomes. Despite these radiographic inconsistencies, the inherent benefits of LSTR—specifically its conservative nature and procedural efficiency-underscore its significant clinical utility. To solidify LSTR's role as a predictable and standardized treatment option, future research must prioritize the development of novel antibiotic formulations, such as clindamycin-modified pastes to prevent tooth discoloration, and the refinement of existing protocols. Furthermore, comprehensive investigations into its efficacy across diverse clinical scenarios and patient populations are essential to enhance radiographic predictability and ensure its widespread acceptance in pediatric dental practice.

Ethics Declarations
The authors declare that all procedures performed in this study were conducted in accordance with institutional, national, and international ethical standards.

Animal and Human Rights Statement
This article does not report any original studies involving human participants or animals performed by the author.

Informed Consent
Informed consent was not required because this study did not involve human participants, patient data, or newly collected clinical material.

Data Availability
The datasets used and/or analyzed during the current study are not publicly available due to patient privacy reasons but are available from the corresponding author on reasonable request

Conflict of Interest
The authors declare that there is no conflict of interest.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, and some of the main line, or all of the preparation and scientific review of the contents, and approval of the final version of the article.

Abbreviations

CTZ: Chloramphenicol, tetracycline, and zinc oxide-eugenol
LSTR: Lesion sterilization and tissue repair
MeSH: Medical Subject Headings
MP: Macrogol and propylene glycol
NaOCl: Sodium hypochlorite
RCT: Randomized controlled trial
TAP: Triple antibiotic paste
ZOE: Zinc oxide-eugenol

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