Development of New Methods and Materials for the Restoration of Tooth Pulp

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Abstract: Nowadays, the latest treatment technologies are actively developing in dental practice, namely for the restoration of tooth pulp.

Aim: to evaluate the advantages of using modern materials in the treatment of tooth pulps.

Materials and Methods: We examined 33 patients with pulp diseases: 18 women (54.5%) and 15 men (45.5%) with an average age of (33.2±2.3) years. 18 patients (group I) had conservative treatment; 15 patients (group II) got pulp restoration using Biodentin.

Results: In 33 (100 %) patients of both groups, inflammation of tooth pulps was found; in 5 of 18 (27.8 %) patients of group I and 6 of 15 (40.0 %) patients of group II, the presence of fibrous pulpitis without signs of periodontitis was determined, in patients of group II, 4 of 15 (26.7 %) - acute diffuse pulpitis. Streptococci with α-haemolytic activity, staphylococci and fungi of the genus *Candida albicans* were detected in the plaque. In 93.3% of patients, both clinical and overall success was achieved with Biodentin, and the frequency of isolation of microorganisms of the genus *Streptococcus spp*. with α-haemolytic activity and *Candida albicans* decreased.

Conclusions: Effective pulp restoration, inflammatory process reduction, and conditionally pathogenic microflora suppression were found in patients treated with Biodentin.

Keywords: Pulpitis, biological method of treatment, conservative treatment, Biodentin, microbiocenosis.

1. INTRODUCTION

Restoring the tooth pulps certainly depends on the state of the pulp's vascular and nervous systems that regulate metabolism. In most cases, tooth pulp damage is accompanied by the removal of the contents of the pulp chamber, which means that nutrients are no longer available to the tooth, so first of all, it is necessary to use all possible methods that allow preserving the pulp, ensuring its viability [1, 2].

A regenerative approach to restoring damaged tooth pulp can ensure complete healing of the native tooth structure and improve the long-term outcome of necrotic teeth. The current standard of treatment for irreversibly damaged tooth pulp is root canal therapy, which involves completely removing and treating the pulp space and filling it with inert biomaterial. Revitalisation procedures show promising results for necrotic teeth with mature roots [3]. Coronal and partial pulpotomies have shown an overall high success rate of 88.5% to 90.6% for treating permanent teeth with pulp exposure and signs of pulpitis. However, the evidence available to date on the effect of different pulp preparations and restorative materials on the success of pulpotomy still needs to be conclusive. Pulpotomy can be considered a promising treatment for mature and immature permanent teeth with carious pulp exposure or signs of pulpitis [4].

In recent decades, with the emergence of regenerative dentistry, new therapeutic approaches have moved towards a biological perspective by using materials with biological activity (i.e. by enhancing osteodeninogenic cellular activity) [5, 6]. Despite the above, there is still a lack of diagnostic tools and effective biomaterials with proven clinical relevance. These constitute new treatments, such as revitalisation

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and complete teeth pulpotomy with the symptoms of irreversible pulpitis [7].

Significant progress has been made in developing biocompatible materials with immunomodulatory properties that are used to restore tooth pulps, and the benefits of the host immune system for achieving a specific regenerative result have been shown. Biomaterials that efficiently and predictably modulate cells in the dental pulp complex have significant clinical prospects for improving treatment standards compared to endodontic root canal therapy [1, 8].

Thus, this article evaluates the advantages of using modern materials in treating pulp tissues.

Following the goal, the following *tasks* were set:

– to carry out analysis of world achievements in methods of restoration and treatment of tooth pulps

– to give an overview of the most modern materials used in the restoration of tooth pulps

– to carry out a comparative analysis of the advantages of modern materials in biological treatment to restoretooth pulps.

2. LITERATURE REVIEW

Scientists have focused on developing new treatment methods using modern materials in dental and endodontic practice to restore tooth pulps effectively. The dental pulp is a highly vascularised and innervated tissue inside the tooth, surrounded by dentin, a complex and non-vascularised mineralised tissue. It performs functions that include initiating, shaping, protecting, nourishing, and reparative activities. However, it has relatively low pliability because it is encased in hard tissue [2]. Tooth decay or trauma leads to inflammation, irreversible damage to the tooth pulp and, consequently, necrosis of the pulp tissue, which leads to loss of tooth viability and, ultimately, apical periodontitis requiring endodontic treatment or extraction [1]. Morotomi *et al*. [2] found that 50% of the world's adult population has at least one tooth with apical periodontitis.

According to several authors, traditional root canal therapy effectively treats pulp and periapical diseases. It consists of pulp extirpation followed by a root canal filledwith inorganic materials (gutta-percha and silica cement). On the other hand, the authors [1] argue that endodontically treated teeth are more susceptible to fractures, loss of sensory function and biological defence mechanisms. They are more prone to recurrent caries and apical periodontitis, and their low resistance to damage, such as caries, leads to frequent removal of tooth pulp during endodontic therapy. The loss of tooth pulp often leads to tooth fragility and, ultimately, to a deterioration in the patient's quality of life.

Tissue engineering is often associated with regenerative medicine and is widely used in dental and maxillofacial tissue reconstruction [7, 9]. Researchers [2, 10] have shown that classical tissue engineering relies on three elements: stem cells (synthesis of a new tissue matrix), bioactive growth factors (stimulation and facilitation of functional capabilities) [11] and biomaterials such as scaffolds, which act as a temporary extracellular matrix to promote cellular differentiation, proliferation and biosynthesis [12].

The authors [6, 11] conclude that with the advent of regenerative dentistry, new therapeutic approaches have moved towards a biological perspective by using materials with biological activity (i.e. by enhancing osteodeninogenic cellular activity). In this regard, many scientists [3, 13, 14] are looking for the use of reparative/regenerative methods to address destructive processes such as root perforation or resorption to maintain tooth viability by restoring/regenerating unmineralised tooth tissue.

With the development of biomaterials such as bioceramics and advances in pulp biology, such as the identification of dental pulp stem cells, scholars have offered new ideas for dental pulp preservation, regenerative dental pulp therapy and new biomaterials for direct pulp coverage [2]. Tooth pulp therapy is divided into three categories: direct pulp shelter, vital pulp amputation, and treatment of nonvital teeth.

The authors [14] note that regenerative endodontic treatment is an alternative to traditional root canal therapy, defined as biological procedures designed to regenerate damaged or diseased tooth pulp using biomaterials such as hydrogels. Their bioactivity is mainly related to the nature of the biomolecules or chemical compounds that make up the endodontic hydrogel. Recent research in dental materials and endodontics has increasingly focused on developing innovative bioactive materials that can improve molecular release and promote tissue repair and regeneration [15, 16]. Most endodontic hydrogels

investigated for regenerative endodontic treatment have incorporated bioactive compounds such as antibiotics, peptides, or nanoparticles into their hydrogel, thus making them bioactive [7, 17]. A wide variety of bioactive hydrogels have been investigated in the literature. The majority of them are bioinspired, such as scaffolds based on gelatin (GelMA), fibrin, or hyaluronic acid [6, 17]. In some studies, the authors [18, 19] used scaffolds that react or dissolve at a specific pH or are made of self-assembling peptides; in others, they have used microspheres or nanofibres to build a bioactive scaffold filled with cells or active molecules [19, 20].

It is known that concentrated growth factor (CGF) is a natural biomaterial that contains platelets, cytokines, and growth factors to facilitate the healing process. The authors [21] showed and confirmed a positive effect on the proliferation, migration and differentiation of human dental pulp stem cells exposed *in vitro*. CGF may be a promising alternative biomaterial in regenerative endodontics [21].

Modern *in vitro* studies have shown that 3D graphene/silk fibre scaffolds improve dental pulp stem cells' osteo/odontogenic differentiation. Namely, they promote the differentiation of human dental pulp stem cells at the genetic level, increasing the expression of crucial osteo/odontogenic markers and supporting the mineralisation of the extracellular matrix. However, studies [10] did not provide strong evidence of the potential of these scaffolds, and further *in vivo* studies are needed. The process of biomaterial implantation leads to tissue damage with subsequent inflammatory response and wound healing [22, 23]. The intensity, continuation and duration of pulpal tissue repair can be directly affected by the properties of the biomaterial; therefore, it is an essential factor in determining biocompatibility and immunomodulatory properties [1].

However, when faced with pulp tissue regeneration, new and effective therapeutic agents adapted to pulpal and periapical inflammatory processes are needed to target the disease aetiology and catalyse regeneration. Many root canal and tooth extraction procedures can be avoided by proper direct pulp capping or by developing new pulp regeneration therapies using the latest materials and technologies. Considering the current state of science and its evidence based on biomaterials, pulp restoration is a rational approach and a topical issue. This review will focus on the approaches to treating, preserving and restoring dental pulp tissue using modern materials.

3. MATERIALS AND METHODS

The examination was carried out in 33 patients, 33.2±2.3 years old on average, with pulp diseases of mature permanent teeth: 18 women (54.5%) and 15 men (45.5%) who were treated at the Department of Orthopedic Dentistry, Faculty of Dentistry, Bogomolets National Medical University. The patients were representative in terms of age and gender.

The study was approved by the Medical Ethics Committee and conducted following the ethical principles of the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects and the Universal Declaration on Bioethics and Human Rights. All patients provided consent to participate in the study.

All patients were divided into two groups depending on the methods of pulpitis treatment: Group I consisted of patients (n=18) who underwent conservative treatment of pulpitis; Group II (n=15) consisted of patients who underwent biological treatment of pulpitis with Biodentin.

The research design is shown in Figure **1**.

The inclusion criteria were pulp hyperaemia, accidentally exposed pulp, acute focal pulpitis, chronic fibrous pulpitis without signs of periodontitis, and acute diffuse pulpitis. The criteria for not enrolling patients in the biological treatment study were age over 35 years, general somatic diseases (vascular diseases, diabetes), acute respiratory diseases, high caries intensity, chronic oral mucosa diseases, chronic periodontitis/parodontosis, etc.

The viability of the pulp was assessed using generally accepted tests; to determine the electrical excitability of the tooth, the EOM3 for variable and EOM-1 (IVN-1) devices were used.

Conservative treatment of pulpitis. At the first stage of treatment, patients underwent antiseptic treatment of the oral cavity (0.2% chlorhexidine solution) with anaesthesia; the tooth was anaesthetised and isolated with cofferdam, the soft dentin was removed entirely, and after visualisation of the carious pulp exposure, access to the cavity and medicinal products was prepared. Constant rinsing of the carious cavity with antiseptics was performed, and medicines and their combinations were left: sulfonamides with antibiotics, corticosteroids, proteolytic enzymes, glycosamino-glycans and closed with a dressing for two days. After

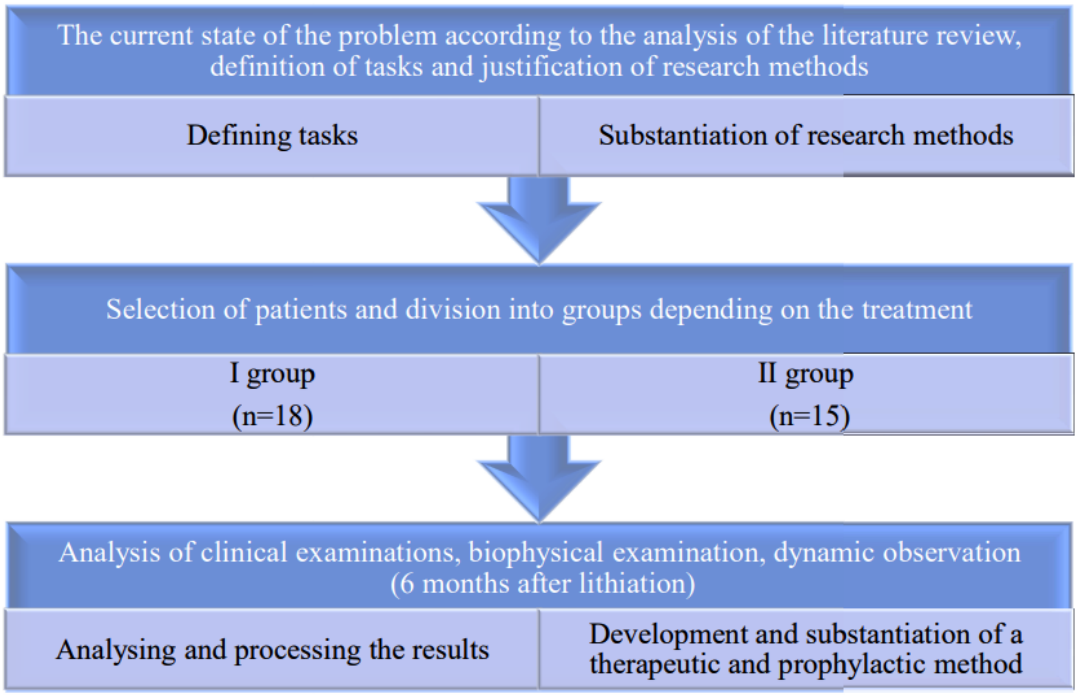

Figure 1: Research Design.

removing the dressing, the cavity was rinsed with a warm antibiotic solution, and a calcium hydroxide paste was applied, again closed with a temporary seal for 4-7 days. After the treatment, a partially temporary filling was left, and a permanent one was applied [24].

Biological method of treatment with the use of Biodentin. The tooth was isolated with a rubber pad, and the infected dentin was removed. The matrix around the tooth was adapted if the tooth wall was missing. In case of pulp bleeding, haemostatic medications were used, and only then was Biodentin applied to the treated pulp [25].

The antimicrobial efficacy after treatment was tested using microbiological methods of studying the species and quantitative composition of plaque. A set of appropriate differential diagnostic breeding grounds was used for this purpose. The level of microbial content was determined by counting colony-forming units in 1 g of material and expressed in decimal logarithms (lg CFU/g).

Statistical processing of the results was performed using the Statistica 6 software package; data analysis was performed using analysis of variance (ANOVA), Fisher's exact test was used to compare small independent samples. The statistical confidence level was estimated at no less than 95.0% ($p<0.05$), with a significance level of 5%.

4. RESULTS

The use of therapeutic manipulations aimed at eliminating the inflammatory process and suppressing conditionally pathogenic microflora while maintaining the maximum integrity of the tooth pulp and its functions was carried out in several patient visits according to current treatment protocols. The conservative treatment methodfor pulpitis was limited to an average of three visits with subsequent dynamic follow-up in 6 months.

Pulpal tissue inflammation was among 1 and 2 molars, in 10 of 18 (55.6%) and 8 of 18 (44.4%) cases in group I and in 8 of 15 (53.3%) and 6 of 15 (40.0%) cases in group II, and was much less common in 3 molars - 1 of 15 (6.7%) cases in group II.

Before applying the conservative method of treatment, the level of damage to the pulp tissues of the teeth was determined: the viability of the dental pulp was clinically assessed by the intensity of pain (rating scale), the presence of a reaction to the percussion test, the results of pulp sensitivity using an electrical pulp test with a score of 0 to 9 and a cold spray.

Inflammation of the pulp before treatment was detected in 33 (100%) patients of both groups, fibrous pulpitis without signs of periodontitis in 5 of 18 (27.8%)

patients of group I and 6 of 15 (40.0%) patients of group II; acute diffuse pulpitis was detected only in 4 of 15 (26.7%) patients of group II.

Before treatment, the plaque in patients of both groups was dominated by representatives of gram-positive facultative anaerobic cocci (streptococci with α-haemolytic activity, in smaller quantities - staphylococci) and fungi of the genus *Candida albicans*. Gram-negative bacteria were found to a lesser extent: *Enterobacter aerogenes*, *Pseudomonas aeruginosa*, *Neisseria spp*. The frequency of microorganism isolation did not differ statistically between the groups (Table **1**).

The results of pulp sensitivity tests after six months showed that only 1 case had a response to the cold test; the number of cases that responded to the electrical pulp test was different between the groups (Table **2**). There were no significant differences between the study groups regarding pain intensity, pain-free status, and mild, moderate, and severe pain, and the percentage of patients was distributed equally.

During the bacteriological examination of dental plaque after pulp treatment, it was found that microorganisms of the genus *Streptococcus spp*. with α-haemolytic activity and *Candida albicans* dominated in the examined patients of both groups (Table **3**). It should be noted that the frequency of their isolation was almost twice as low in patients of group II.

Staphylococcus aureus and *Staphylococcus epidermidis* were isolated from dental plaque in both groups with equal frequency.

Among the conditionally pathogenic microorganisms that are not representatives of the autochthonous microflora of the oral cavity, Enterobacter aerogenes was isolated in 16.7% of patients in group I and 6.7% of patients in group II; Klebsiella pneumoniae in 5.6% of group I and 6.7% of group II; Pseudomonas aeruginosa in 11.1% of group I and 6.7% of group II.

5. DISCUSSION

Modern research emphasises the need for minimally invasive biological methods of treating pulp tissues, as traditional methods, such as conservative therapy, are considered destructive and often not consistently successful in general dental practice. For example, vital pulpotomy is usually considered more technically accessible[26]. In addition to limiting intervention and reducing hard tissue removal,

Table 1: Frequency of Changes in the Composition of Plaque Microflora of the Examined Patients before Treatment

Microorganisms	Frequency of detected violations n(%)	
	Group I (n=18)	Group II (n=15)
Streptococcus spp. with α-haemolytic activity	10 (55.6)	8 (53.3)
Candida albicans	11 (61.1)	9 (60.0)
Candida tropicalis	2 (11.1)	0 (0)
Enterobacter aerogenes	5 (27.8)	3 (20.0)
Neisseria spp.	4 (22.2)	4 (26.7)
Pseudomonas aeruginosa	3 (16.7)	2 (13.3)
Klebsiella pneumoniae	1 (5.6)	1 (6.7)
Enterococcus faecalis	4 (22.2)	2 (13.3)
Staphylococcus aureus	3 (16.7)	3 (20.0)
Staphylococcus epidermidis	3 (16.7)	3 (20.0)

Table 2: Dynamics of Indicators after Treatment

Factors	Group I(n=18)	Group II(n=15)	Test	The value of p<0.05
Cold sample, positive response, n (%)	Not applicable	Not applicable	-	-
Electropulp test, positive response, n (%)	Not applicable	Not applicable	-	-
Percussion test, positive response n (%)	1 (5.6%)	0(0.0%)	Fisher	p>0.05
Clinical success, n (%)	14 (77.8%)	14 (93.3%)	Fisher	p>0.05
Overall performance, n (%)	15 (83.3%)	14 (93.3%)	Fisher	p>0.05

Table 3: Frequency of Changes in the Composition of Plaque Microflora of the Examined Patients (Dynamics of Changes after six Months)

Microorganisms	Frequency of detected violations n(%)	
	Group I (n=18)	Group II (n=15)
Streptococcus spp. with α-haemolytic activity	8 (44.4)	4 (26.7)
Candida albicans	9 (50.0)	5 (33.3)
Candida tropicalis	2 (11.1)	0 (0)
Enterobacter aerogenes	3 (16.7)	1 (6.7)
Neisseria spp.	4 (22.2)	3 (20.0)
Pseudomonas aeruginosa	2 (11.1)	1 (6.7)
Klebsiella pneumoniae	1 (5.6)	1 (6.7)
Enterococcus faecalis	3 (16.7)	1 (6.7)
Staphylococcus aureus	3 (16.7)	2 (13.3)
Staphylococcus epidermidis	2 (11.1)	2 (13.3)

maintaining pulp viability has other benefits, as it supports dentin deposition and immunological response [1]).

In our work, we studied the effect of modern materials, namely calcium hydroxide paste and Biodentin, in restoring pulp tissue. Our results showed the highest percentage of effective treatment in patients treated with a therapeutic and prophylactic complex with Biodentin. It was found that in 93.3% of cases, clinical and overall success was achieved, respectively, compared to patients who underwent pulp tissue restoration using the traction method (77.8% and 83.3%, respectively), which is consistent with the data obtained by other researchers [25, 26].

For decades, calcium hydroxide has been the most commonly used antimicrobial to disinfect contaminated root canals [27]. Still, its effectiveness against specific pathogens such as Enterococcus faecalis, Actinomyces naeslundii, and Candida albicans is limited. In addition, the overall efficacy of calcium hydroxide in dentinal tubules seemed unreliable. Therefore, other intracanalicular medications (e.g. antibiotics) or a combination of different agents seemed to be of primary importance for maximum microbial eradication. Despite this, topical application of antibiotics can lead to some adverse side effects (e.g., bacterial resistance, cellular toxicity, etc.), which makes it essential to continue searching for an effective and biologically safe method of drug delivery.

Ruiz-Linares et al.[28] describe the results of *in vitro* studies that determined the antimicrobial effect of calcium silicate cement and other endodontic materials against a small number of microorganisms; the authors showed the practicalimpact of Biodentin *in vitro* on reducing the number of microorganisms (*Lactobacillus rhamnosus* and *Streptococcus sobrinus*) compared to calcium hydroxide and mineral trioxide [28]. Poggio et al. [29], confirmed the most robust antibacterial activity of Biodentin against *Streptococcus sanguis* strains, significantly higher than that of mineral trioxide cement and intermediate restorative material *in vitro*. In an *in vivo* study by Al-Ahmad et al. [27], a moderate antimicrobial effect was observed when Biodentin was applied to residual carious dentin. Our study showed that Biodentin has a higher antimicrobial effect than calcium hydroxide paste in the form of a decrease in the frequency of sowing microorganisms of the genus *Streptococcus spp*. with α-haemolytic activity, *Enterococcus faecalis*, *Enterobacter aerogenes* and fungi of the genus *Candida spp*. which is consistent with the results of other authors [30].

5.1. Restrictions and Recommendations

There are several limitations in biological treatment, such as the patient's age over 35 years, generalised somatic diseases, pain for more than 48 hours, and absence of changes in the periodontium and multiple caries. If the above factors are present and there is no effect after the conservative (biological) treatment method, surgical methods of tooth pulp restoration are prescribed.

6. CONCLUSIONS

Despite numerous publications in regenerative endodontics, pulp restoration remains a pressing issue

due to the lack of modern diagnostic tools, targeted biomaterials, and scientific evidence exploring new treatment methods. The balance between inflammation and healing is essential for restoring and maintaining the viability of the dentin-pulp complex, as the elimination of irritation and successful restoration lead to the recovery of pulp tissue.

The use of biological methods of pulp treatment with Biodentin contributed to a positive clinical success of treatment and had a higher antimicrobial effect, allowing us to recommend this method in general dental practice for restoring pulp tissues of the tooth.

Prospects for future research are to study the introduction of modern techniques and materials for restoring pulp tissues after vital extirpation (vital pulpectomy) as one of the surgical methods of treating pulpitis to study the effectiveness of treatment and prevention measures in the long term.

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