



CLINICAL AND EXPERIMENTAL VALIDATION OF THE OZONE THERAPY EFFECTIVENESS IN CASE OF ACCIDENTAL EXPOSURE OF THE DENTAL PULP

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ABSTRACT

An experimental study was conducted on rabbits of the "Soviet chinchilla" breed. Iatrogenic pulpitis was modeled in animals, in the first group only a direct coating with the material "Trioxidant" was used, 12 animals, in the second group, 12 animals, before covering the pulp with the material "Trioxidant", the opened tooth pulp was blown with an ozone-air mixture. A study was conducted in 18 patients with an accidental opening of the pulp of the tooth aged 20 to 45 years. The first group consisted of 9 patients, who were treated with ozone therapy in order to preserve the viability of the pulp, after the pulp was directly coated with "Trioxidant" material. In the second group of 9 patients ozone therapy was not prescribed, but a direct coating of the pulp with "Trioxidant" material was also performed. The experiment revealed that ozone therapy combined with direct coating of the pulp with material "Trioxidant" has anti-inflammatory effect on the structure of the tooth pulp, and also stimulates dentin formation and regeneration of the pulp. Macrophage and the intensity of reaction with S100 on the 14th day of treatment of iatrogenic pulpitis and formation of thin, high-density dentin bridges and structuring odontoblasts in a single layer on the 35th day.

The result of studying the effectiveness of ozone therapy in case of accidental opening of the tooth pulp in clinical practice proved that in the group where ozone therapy was not used, two of nine patients had irreversible pathological changes in the pulp. In the group where ozone therapy was used, and after direct coating of the pulp with "Trioxidant" material was performed, all patients managed to preserve the viability of the pulp.

KEYWORDS: direct coating of the pulp, tooth pulp, vital pulp therapy, ozone therapy.

INTRODUCTION.

The preservation of dental pulp vitality after the accidental exposure during the dental procedure is a pressing issue in the field of dentistry. Vital pulp therapy (VPT) is a biological and conservative treatment modality to preserve the vitality and function of the coronal or remaining radicular pulp tissue in vital permanent teeth. Vital pulp therapy

(VPT) is also defined as "treatment aimed at preserving and maintaining pulp tissue that has been compromised but not destroyed by extensive dental caries, dental trauma, and restorative procedures or for iatrogenic reasons", offers several advantages over traditional endodontic root canal treatment. The benefits of having a live tooth pulp, which serves as the most effective barrier against microbial invasion in cases of dental caries and prevents the pathological microorganisms from entering the periodontium, have long been recognized [Alexandrov M.T. et al., 2018; Doroshina V. Yu. et al., 2019;]. At the same time, the dental

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practitioner that carries out the procedures aimed at preserving pulp vitality has to be confident in the predictability of the result, as well as be able to monitor the state of the pulp, which helps prevent the development of periodontitis. A significant amount of scientific research is devoted to the study and development of materials used for direct pulp capping [Akhlaghi N., Khademi A.K., 2015; Hanna SN et al., 2020]. Although in various research has taken a different approach, with most studies showing favorable treatment outcomes. The Mineral Trioxide aggregate (MTA) appears to be more effective than calcium hydroxide (Ca (OH) 2) in maintaining long-term pulp viability after indirect and direct pulp capping. However, it seems that the success rate for partial pulpotomy and pulpotomy with Ca (OH)2 is similar to MTA. The biocompatibility, cytotoxicity of different materials and their effect on the reparative processes of dental pulp have been thoroughly examined in the experimental studies [Paula AB et al., 2019] as well as in clinical practice [Nikolskaya I.A et al., 2013]. According to the majority of researchers, the 'gold standard' among the materials currently used for direct pulp capping is the mineral trioxide aggregate [Li M et al., 2019; Paula AB et al., 2019]. However, the sufficiency of using it as the only material for high treatment efficacy without any additional treatment methods is debatable. A group of authors suggested using pulp regeneration materials for direct capping in combination with the method of ozone therapy [Nikolskaya IA et al., 2013]. However, neither mineral trioxide aggregate nor its alternative has been used for direct pulp capping. The therapeutic efficacy of ozone therapy has been linked to the ozone's high oxidation-reduction potential that provides the disinfecting effect against bacteria, viruses and fungi, as well as induces activation of metabolic processes in tissues. Ozone interacts with protein-lipid complexes of cell membranes and blood plasma which facilitates the transformation and synthesis of biologically active substances, enhances the activity of immunocompetent cells and improves the rheology and oxygen-carrying capacity of the blood [Seidler V. et al., 2008].

The application of ozone therapy in dental practice currently appears to be of high interest. Ozone therapy is used in the treatment of inflammatory

diseases of the maxillofacial region, in particular, inflammatory processes in soft tissues and in bone structures, in the treatment of bisphosphonate osteonecrosis of the jaws, in the treatment of osteomyelitis, as well as in the complex of treatment of periodontal diseases. There are known works devoted to the use of ozone therapy in the treatment of diseases of dental hard tissues [Huth K.C. et al., 2011; Makeeva I.M. et al., 2017; Gloria JCR et al., 2020; Sadatulla S. et al., 2012; Leewananthawet A et al., 2019; Srinivasan S.R. et al., 2019, Volkov A.G. et al., 2020]. As a result, the idea to continue research in this direction using the combination of modern direct pulp capping material and direct exposure of the pulp to the ozone-air mixture.

MATERIAL AND METHODS

The first part of the study was experimental. Its goal was to examine the regenerative capacity of dental pulp as a result of applying the MTA alternative "Trioxident" as a direct capping material in combination with the direct pulp exposure to ozone in an experiment.

The experimental study was carried out on rabbits of the "Soviet Chinchilla" breed -24 specimens.

Alongside premedication with a 2% xylazine hydrochloride solution, a dose of 7.0 mg/kg of a 5% zoletil solution was administered intravenously to ensure painless experiment conduction. It was followed by the installation of the palate expander and mechanical cleaning of teeth under examination. The spherical dental bur #2 was used on the facial surface of the incisors and the morsal surface of the premolars and molars in order to simulate iatrogenic pulpitis.

Laboratory animals were randomly divided into 2 groups, depending on treatment method. In the first group of 12 specimens the direct pulp capping procedure was performed using the MTA alternative "Trioksident" (produced in Russia by the "VladMiVa" company), which contains fine particles of calcium oxide, silicon, alumi-



*To overcome it
is possible, due to the
uniting the knowledge and
will of all doctors in the world*



FIGURE 1. *Blowing of exposed tooth pulp with ozone-air mixture*

num, copper-calcium hydroxide and bismuth oxide. This group did not undergo ozone therapy. The second group of 12 specimens received a 1 minute long ozone-air mixture blowing procedure on the exposed pulp before pulp capping with the same “Trioksident” material (fig. 1). The UV irradiator OKUF-5m (“Ema”, Russia) was used as the source of ozone. The final stage of the treatment included the placement of a permanent filling “Twinky Star” (Voco, Germany).

The animals were withdrawn from the experiment on days 7, 14, 21 and 35. The isolated rabbit jaw samples underwent mild decalcification, then the area of the postoperative opening was cross-sectioned and layer by layer sections were made through the neck and the root of the tooth. Further, the histological samples were stained with hematoxylin-eosin, according to Masson’s trichrome. An additional immunohistochemical study with CD3, CD20, Ki-67, S100, Macrophage, CD34 was conducted.

The second part of the experiment was aimed at the examination of the ozone therapy effectiveness in case of accidental pulp exposure in clinical practice.

The treatment was carried out on 18 patients aged 20 to 45 years old (10 women, 8 men). An accidental pulp exposure occurred during the preparation of patients’ deep carious cavities. The patients were divided into two groups depending on the treatment.

The first group consisted of 9 patients who received ozone therapy followed by the direct pulp capping with “Trioksident” to preserve the pulp vitality after its accidental exposure. The ozone was generated by the OKUF-5m equipment which

synthesizes ozone using ultraviolet radiation. The duration of the dental pulp exposure to the ozone-air mixture was 1 min.

The second group of 9 patients underwent the direct pulp capping with the “Trioksident” material, but did not receive the ozone therapy.

The final stage of treatment in both groups involved temporary restoration of the hard tooth tissues defect using a light-cured compomer (“Twinky Star”, Voco, Germany). The final restoration was performed after 6 months in the absence of inflammatory symptoms.

Patients were examined one day after the treatment, as well as 14 days, 2, 6 and 12 months after the treatment. The patient’s dental status was assessed using clinical and additional research methods.

The follow-up began with a survey, which included the identification of complaints and the presence or absence of concomitant pathology. It was followed by the examination, probing and percussion testing. This included the assessment of the dental crown, the oral mucosa in the examination area, and the presence or absence of a percussion reaction.

Additional research methods included electroodontodiagnostics, laser doppler flowmetry (LDF) and X-ray imaging.

Electroodontodiagnostics was used to assess the status of the dental pulp’s nerve elements and was carried out using the digital domestically-produced device “IVN-01 Pulptest-Pro”. Electroodontodiagnostics was performed on incisors – from the middle of the incisal edge; on premolars – from the buccal cusp; on molars – from the anterior buccal cusp.

A domestically-produced device - the laser blood flowmeter “LAKK-02” (NPO “Lasma”, Russia) - was used to study microcirculation in the dental pulp.

The pulp microcirculation assessment was preceded by the hardware compensation of the signal level affected by the tooth color and thus having an impact on the magnitude of the signal received directly from the pulp. In order to do this the light guide in a black elastic nozzle was installed in the upper third of the examined tooth’s crown and the biological zero was obtained in the device by automatic subtraction. After that, the light guide probe was installed perpendicularly to the tooth facial or buccal surface in the neck area 2 mm above the

gingival margin in the crown portion of the pulp. It was followed by finding a desired signal of blood flow fluctuations in the pulpal microcirculatory bed and recording an LDF-gram for 3-5 min with its subsequent automatic processing.

The status of microcirculation was assessed using the microcirculation parameter (M). The characteristic of erythrocyte flow " σ " (standard deviation of the amplitude of blood flow fluctuations) was also assessed. The ratio between the tissue perfusion and its variability (flux) was assessed by calculating the coefficient of variation - Kv (%), which characterizes the vasomotor activity of microvessels. Additionally, the indicators characterizing the active mechanism of blood flow modulation were registered. Those included myogenic and neurogenic activity - ALF/ σ , microvascular tone - σ /ALF. Passive modulation mechanism was measured by heart rate fluctuations - ACF/ σ , and respiratory rate fluctuations - AHF/ σ . The integral characteristic of the ratio of active and passive blood flow modulation mechanisms was determined using the fluxmotion index. Intravascular resistance was determined by the ACF/M ratio.

The state of the periapical tissues was assessed on the basis of data collected using the spot/enlargement dental X-ray and computer visiography during the X-ray examination which was conducted 2, 6 and 12 months after the treatment.

RESULTS

Experimental results. On the 7th day of the experiment all cross-sections showed minimal inflammatory infiltration in the tooth cavity and root canal. The cells observed were represented by an insignificant number of CD3+/CD20+ small lymphocytes and a large number of macrophages. Dentin bridges were not visible (Fig. 2).

On the 14th day, the group where ozone therapy was not used showed minor proliferation of odontoblasts, alongside the still significant colonization by macrophages and a moderate amount of lymphocytes. The results of the group that was subjected to the ozone therapy displayed a small number of macrophages, a few lymphocytes, and a significant proliferation of fibroblasts (Fig. 3).

The histologic pattern on the 21st day of the experiment in the group, whose treatment did not include ozone therapy showed no significant changes

compared to that of the 14th day. The samples of the ozone therapy group showed small-caliber vessels with less pronounced hyperemia, as well as the absence of endothelial edema. Numerous dentin bridges in the early stages of development were observed (Fig. 4).

On the 35th day of the experiment the histological samples of all groups showed no signs of in-

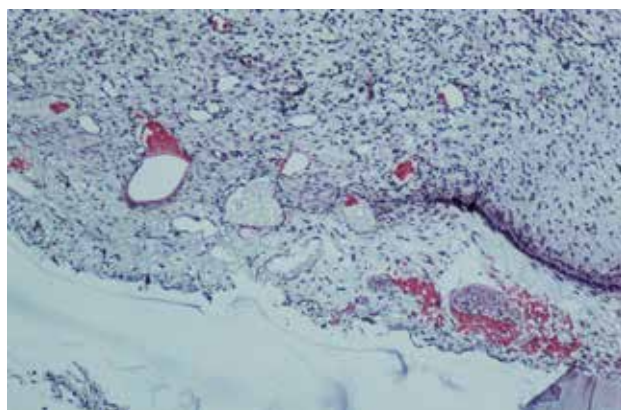


FIGURE 2 Exposed pulp with congested vessels, fibroblast proliferation, lymphoid infiltration. Hematoxylin-eosin staining (X400)

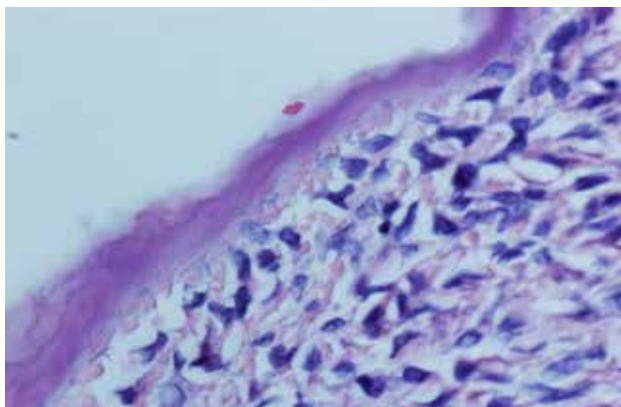


FIGURE 3 Insignificant proliferation of odontoblasts, a tendency to formation of dentinal bridges. Hematoxylin-eosin staining (X600)

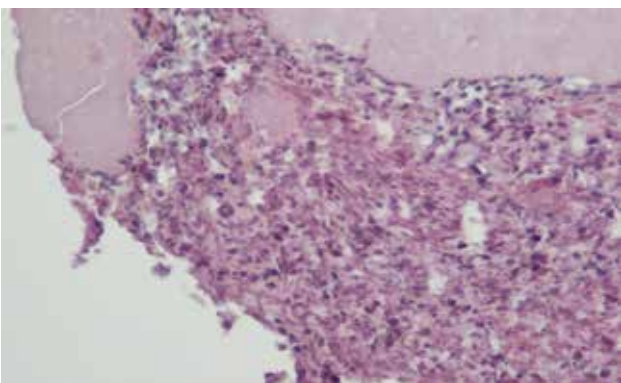


FIGURE 4. Multiple dentinal bridges in early stages of development. Hematoxylin-eosin staining (X400)

flammatory infiltration; numerous newly formed blood and lymph vessels were visible. In the area of emerging dentin bridges the aforementioned elements were structured in a multi-row layer (fig. 5).

The most beneficial changes were observed in the group where ozone therapy was utilized. The histological samples displayed thin, higher density dentin bridges. Numerous odontoblasts which produce reparative dentin substance were observed forming a single layer structure (Fig. 6).

Clinical study results. 24 hours after the treatment, the patients of the first group that underwent ozone therapy had no complaints. The electroodontodiagnostics readings ranged from 14 μA to 23 μA . The LDF indicated the development of inflammatory hyperemia. In all the examined teeth microcirculation measurements were increased by 32% on average and the standard deviation of the amplitude of blood flow fluctuations showed an increase of 19%, compared to the measurements of intact teeth.

Two weeks after the treatment, the teeth electroexcitability increased to 8 - 17 μA . Pulp hyperemia remained present: microcirculation index was 39% higher than that in the intact pulp, the

standard deviation of the amplitude of blood flow fluctuations was also 22% higher than normal.

Two patients of the second group, in which ozone therapy was not part of the treatment, made complaints about a short-term pain (up to 10 seconds) from cold water on the next day after the procedures. No complaints were received from the rest of the patients. The teeth electroexcitability ranged from 18 μA to 27 μA . Four patients of this group experienced a more significant inflammatory pulp hyperemia than patients in the first group. The blood flow level (M) and its intensity (σ) increased on average by 41% and 26% respectively compared with intact teeth. One of the patients in the second group showed a decrease in microcirculation parameters by 62% and a decrease in standard deviation of the amplitude of blood flow fluctuations by 49%.

Two patients from the group with no ozone therapy included in their treatment were experiencing a short-term pain reaction to temperature stimuli for 2 weeks after the treatment. The teeth electroexcitability of these two patients ranged from 25 μA to 27 μA . The rest of the patients showed an increase in electroexcitability up to 14-22 μA . Four patients had a higher level of inflammatory hyperemia compared to the first group in the same time period. Microcirculation indicator was 54% higher, and the standard deviation of the amplitude of blood flow fluctuations was 33% higher than those of intact teeth.

In contrast, a lower level of microcirculation in comparison with the pulp of intact teeth was observed during the follow-up of one of the patients from the second group. The blood flow level and its intensity were 67% and 52% lower respectively.

In the long-term period (2,6 and 12 months after the treatment) none of the first group patients had any complaints. Their teeth electroexcitability ranged from 2 μA to 12 μA . The LDF readings two months after the treatment matched those of intact pulp. X-ray imaging conducted in the long-term period after the treatment did not reveal any pathological changes in the periapical tissues of the examined teeth.

One of the patients from the second group registered complaints about the hot temperature sensitivity and sensation of pressure in the affected tooth 1,5 months after the treatment. The electroexcitabil-

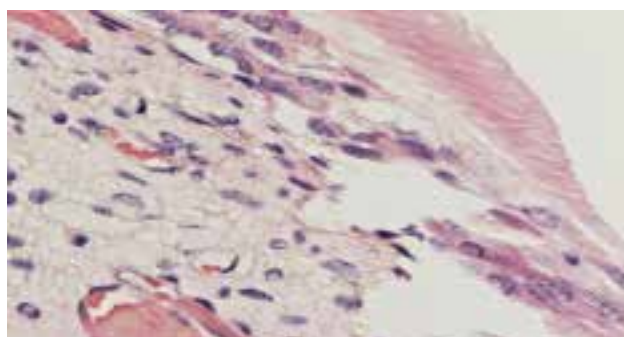


FIGURE 5. Odontoblasts in condition of reactive proliferation. Hematoxylin- eosin staining (X600).

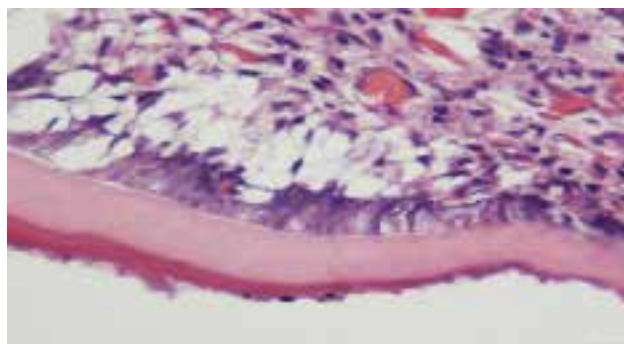


FIGURE 6. Dentine bridges in the pulp of the tooth 35 days after the experiment (second group). Hematoxylin- eosin staining (X400).

ity was reduced to 75 μ A. The LDF showed the absence of blood circulation in the tooth crown, which indicated the presence of crown pulp necrosis and the need for endodontic treatment.

Two months after the treatment another patient from this group noted the onset of spontaneous dull pain sensations intensified by temperature stimuli. Electroodontodiagnostics demonstrated that the pulp electroexcitability was reduced to 45 μ A. The LDF data corresponded to a high degree of dental pulp inflammatory hyperemia. The blood flow level and its intensity were 47% and 26% higher in comparison with the blood circulation indicators in intact teeth. Analysis of clinical and additional research methods determined the presence of a chronic inflammatory process and the development of irreversible changes in the pulp that required endodontic treatment.

The rest of the second group patients had no complaints in the long-term period after the treatment. The electroodontodiagnostics readings ranged from 11 μ A to 18 μ A. The LDF indicated that the inflammatory reaction in the pulp subsided and the local blood flow was normalized. X-ray imaging revealed no pathological changes in the periapical tissues of the patients' teeth.

DISCUSSION

As a result of the imunohistochemical study of medicine obtained in the treatment of iatrogenic pulpitis in the experiment, it was found that in those groups where ozone therapy was not used, the regenerative ability of the pulp was less evident than in groups where the complex of therapeutic measures included blowing the opened pulp with an ozone-air mixture followed by laying a pad made of "Trioxident" material. On day 14, histological materials of these groups showed a decrease in the level of macrophagical activity: individual macrophages expressed Macrophage. Collagenization of the pulp stroma with compaction and thickening of the fibers was determined. Fibroblasts that completed the stage of proliferation and secreted collagen had a smaller volume of cytoplasm, which correspondingly reduced their size compared to similar elements in the material that was not exposed to ozone. The swelling of the endothelium of the blood vessels of the pulp remained, but less evident compared to the seventh

day of the study.

On the 35th day of the study, in the material of the second and the fourth experimental groups, where ozone therapy was used, the distinctive features, in comparison with the other group, were the visualization of thin, high-density dentine bridges. When Masson trichrome was applied, the tertiary dentin was characterized by a homogeneous intense color. Odontoblasts producing the substance of dentin substitution were structured in a single layer. Their peripheral processes were tightly embedded in the dentin synthesized by them, while their proximal processes were visually lost among the dense connective tissue that replaced the necrotic pulp matrix.

The experiment revealed that ozone therapy in combination with a direct coating of the pulp with the material "Trioxident" has an anti-inflammatory effect on the structures of the tooth pulp, and also stimulates the processes of dental formation and pulp regeneration. In addition, ozone therapy has a detoxifying effect, affecting only pathologically altered tissues and microbial cells, as ozone unlike many antiseptics does not destroy or irritate healthy tissues due to the fact that the cells of a multicellular organism have an antioxidant defense system. The data obtained are consistent with the data obtained in the work [Arakawa S. et al., 2019].

The result of studying the effectiveness of ozone therapy in case of accidental opening of the tooth pulp in clinical practice proved that in the group where ozone therapy was not used, two of nine patients had irreversible pathological changes in the pulp. The use of ozone therapy has improved the quality of treatment. In the group where ozone therapy was used, and after direct coating of the pulp with "Trioxident" material was performed, all patients managed to preserve the viability of the pulp when it was accidentally opened. In these patients the symptoms of inflammation subsided faster and were less evident, as performed the data of electroodontodiagnostics and laser Doppler flowmetry.

The results of the clinical application of ozone therapy in case of accidental opening of the tooth pulp are fully consistent with the results of an experimental study on the efficacy of ozone therapy in the treatment of iatrogenic pulpitis. It is reliably established that the use of ozone therapy in combination with the method of direct coating of the

pulp with trioxide material “Trioxident” improves the quality of treatment of reversible forms of pulpitis. The developed method allows maintaining the viability of the pulp, helps eliminate inflammation, normalizes microcirculation in the pulp and increases the regenerative potential of the pulp. It should also be noted that the treatment of such patients requires quality control using the method of electroodontodiagnostics, which allows assessing changes in the pulp in the early stages of pathology [Makeeva I.M. et al., 2017; Makeeva I.M et al., 2018]. This is the prevention of periodontitis.

CONCLUSION

The results of the clinical application of ozone therapy in case of accidental opening of the tooth pulp are fully consistent with the results of an experimental study on the efficacy of ozone therapy in the treatment of iatrogenic pulpitis. It is reliably established that the use of ozone therapy in combination with the method of direct coating of the pulp with material “Trioxident” (analog of MTA) improves the quality of treatment of reversible forms of pulpitis. This method allows maintaining the viability of the pulp, helps eliminate inflammation, normalizes microcirculation in the pulp and increases the regenerative potential of the pulp.

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