

## Ozone therapy effectiveness in patients with ulcerous lesions due to diabetes mellitus

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### ABSTRACT

**Introduction:** Development of purulo-necrotic foot lesions is one of the most dangerous surgical complications of diabetes mellitus, it causes high lethality, early disability, considerable economical expenses on treatment and rehabilitation. Mentioned above determine substantial actuality of diabetic foot problem and condition the necessity of further search of new ways and effective methods of lower extremities lesions complex treatment.

**The aim:** of our research was to study the effectiveness of ozone use in complex therapy among patients with diabetic foot.

**Material and methods:** Under our observation were 47 patients with I and II stages of diabetic foot that correspond to superficial and deep ulcers without involving of subcutaneous tissue, ligaments, tendons and muscles into the process, without bone lesion, phlegmons and abscess forming according to Meggit-Wagner (1978) classification. Depending on treatment every group of patients was divided into subgroups. B group composed patients that received traditional therapy. A group composed patients that along with traditional therapy course received course of systemic and regional ozone therapy for 12–14 days, one session per day. Cytological examination of discharge from wounds was carried, lipid peroxidation state and antioxidant protection state was assessed.

**Results:** Ozone use has more evident clinical effect, significantly affects the phase course of wound process, promotes the improvement of lipid peroxidation and antioxidant protection indexes, reduces the length of hospital stay and term of treatment of patients with diabetic foot.

**Conclusions:** Studies conducted showed that including of ozone therapy into complex surgical treatment has positive effect on wound process.

**Key words:** ozone therapy, diabetic foot, lipid peroxidation, antioxidant system.

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### INTRODUCTION

Diabetic foot remains significantly complicated and urgent problem of modern surgery treatment results of which nowadays can not be satisfactory. Qualitative care after patients with diabetes considerably decreases the frequency of foot lesion emergence but does not prevent it [1, 2]. Diabetic foot develops among 30–80% of such patients and 30–70% of cases are complicated by purulo-necrotic foot lesions [2–4]. Development of purulo-necrotic foot lesions is one of the most frequent and dangerous surgical complications of diabetes mellitus, it causes high lethality, early disability, considerable economical expenses on treatment and rehabilitation [4–6]. Mentioned above determine substantial actuality of diabetic foot problem and condition the necessity of further search of new ways and effective methods of lower extremities lesions complex treatment.

The **aim** of our research was to study the effectiveness of ozone use in complex therapy among patients with diabetic foot.

### MATERIAL AND METHODS

Under our observation were 47 patients with I and II stages of diabetic foot that correspond to superficial and deep ulcers without involving of subcutaneous tissue, ligaments, tendons and muscles into the process, without bone lesion, phlegmons and abscess forming according to Meggit-Wagner (1978) classification [7].

Women made up 31.9 % (15), men – 68.1% (32), the middle age was  $60.06 \pm 1.28$  years.

Depending on treatment every group of patients was divided into subgroups. B group composed patients that received traditional therapy including blood sugar correction, antibacterial therapy, antiaggregatory therapy, anticoagulants, infusion of rheological and detoxicative preparations.

Local treatment included daily dressing with antiseptics. Glycemia correction was carried out using insulin intermittent dosing. A group composed patients that along with traditional therapy course received course of systemic and regional ozone therapy for 12–14 days, one session per day. They were getting 200 ml of physiologic saline ozonized using ozone therapy apparatus “Ozone UM-80” (ozone concentration 1000–1300 mcg/l) intravenously. For regional therapy (application on wound surface) were used ozone, dissolved in 0.9% NaCl solution, and ozonized Sea buckthorn oil of 4000 mcg/l concentration [8]. Cytological examination of discharge from wounds was carried out by smears-imprints method according to the Pokrovska-Makarov technique [9].

Lipid peroxidation state was assessed by lipid peroxidation secondary products level - malondialdehyde (MDA) [10]. For assessment of antioxidant protection state catalase activity by Koroliuk method [11] and ceruloplasmin content in blood serum (by Bestuzhev, Kolb in Revin’s modification) were determined [12].

## RESULTS AND DISCUSSION

After ozone therapy a positive course of clinical signs of main disease as well as its complications was observed in a subgroup A. It was displayed by general condition improvement, disappearance of complaints on thirst, dry mouth and polyuria. Conducted complex treatment including ozone therapy also reduced sensation of burning pain in foot (from 69.57% at the beginning of treatment to 39.13% of cases after conducted therapy), constant coolness of feet (from 30.43% to 8.70%) and paresthesia (from 69.57% to 34.78%). During treatment with ozone improved skin sensitivity, disappeared feeling of feet and toes numbness, emerged pleasing warmth in feet and shins. Deterioration of patients' condition, adverse effects and complications during ozone therapy were not observed.

Surgical treatment of trophic disorders consisted of surgical d-bridement with following antiseptic wound management (boric acid, chlorhexidine, dioxidine). Part of patients were getting local ozone therapy in addition to systemic ozone therapy. Dynamics of wound process was determined by terms of necrotic tissues rejection, granulations emergence, marginal epithelization, wound healing (Tab. I).

From the table 1 it follows that use of local and general therapy promoted swelling reduction and skin hyperemia around the wound on  $10.17 \pm 0.74$ th day accompanied by considerable reduction or disappearance of pain during palpation. Terms of wound cleansing from purulo-necrotic tissue took up  $14.08 \pm 0.43$  days. Granulations emergence was observed precisely in the same terms ( $14.46 \pm 0.40$  days). Filling of wound with granulations and beginning of marginal epithelization were observed on  $19.83 \pm 0.21$ th day from the moment of hospitalization.

Complex surgical treatment including local and systemic ozone therapy promoted phase acceleration of wound process course. From the scheme 2 it is clear that reduction of extremity swelling and hyperemia around the wound passed on  $7.52 \pm 0.62$ th day (in comparison with traditional therapy) and were accompanied by reduction or disappearance of pain during palpation. Under treatment with ozone therapy wound cleansing from fibrin and purulo-necrotic mass was in average 4,47 days faster and granulations emergence in the wound was 4.68 days faster. At the same time granulations were fine-grained, plethoric, easy bleeding. All these accelerated emergence of marginal epithelization signs by 5.4 days in average (in comparison with traditional therapy). Thus, in the first phase due to ozone influence inflammatory process is stopped earlier, swelling and hyperemia around the wound are reduced, and in the second and third phases processes

of wound cleansing, granulations filling, emergence of marginal epithelization are considerably accelerated.

When analyzing cytologic picture of wound smears-imprints at the moment of hospitalization was detected that the latter were characterized by degenerative type of cellular reaction. Degenerative neutrophils prevalence of segmental and stab form (13.0%) on the background of mass cell necrosis ( $82.7 \pm 3.4\%$ ) accompanied by cytolysis ( $32.4 \pm 6.3\%$ ), rugosity and destruction ( $46.7 \pm 4.3\%$ ) was observed. Sharp decrease of phagocytosis process was detected, while macrophages contained only from 10 to 15 bacteria. Phagocytosis was incomplete.

On the 3–5th day of local ozone applications cytograms, received by smears-imprints method, were characterized by regenerative type of cellular reaction. General number of neutrophils decreased with prevalence of regenerative forms (76.0%) compared with degenerative forms (3.0%), number of neutrophils with normal nuclear structure increased to 79.4–83.7%. Percentage of macrophages distinctly increased, monocytes were mainly of large and medium sizes. Ozone activation of wound regeneration, as evidenced by an increase of polyblasts and young conjunctive cells (profibroblasts and fibroblasts), should be noted. On the background of inflammatory subsiding noticeable was decreasing migration of neutrophils from blood vessels (up to 15 in sight) and in 27.3% of patients at the same time migration of neutrophils was 5–8 neutrophils in sight. Microorganisms were detected in small amounts in an active stage of phagocytosis.

Duration of patients' hospital stay was: in a comparison subgroup (B) –  $23.42 \pm 0.45$  days, in a main subgroup (A) –  $17.09 \pm 0.27$ . It should be noted that at the moment of discharge a tendency to full wound healing was registered in both subgroups. So, as it follows from received results of study, average duration of treatment in a subgroup where in complex treatment was used ozone therapy decreased by 6.33 days compared with patients that received a traditional course of treatment.

As a consequence of positive effect of complex treatment using ozone therapy on wound process course indexes, we thought that it would be reasonable to study the influence of this therapy on lipid peroxidation and antioxidant system indexes. It is known that excessive increase in lipid peroxidation process activity while organism antioxidant system exhaustion is one of the main factors that promote development and progression of foot destructive processes. Dynamics of lipid peroxidation processes changes with traditional treatment is shown in the table II.

**Table. I.** Indexes of wound process course depending on conducted treatment.

Groups of patients	Terms of swelling reduction and hyperemia, days	Terms of necrotic tissues rejection, days	Terms of granulations emergence, days	Beginning of marginal epithelization, days
Subgroup A (traditional therapy+ozone), n=23	$7.52 \pm 0.62$	$9.61 \pm 0.39$	$9.78 \pm 0.35$	$14.43 \pm 0.21$
Subgroup B (traditional therapy), n=24	$10.17 \pm 0.74^*$	$14.08 \pm 0.43^*$	$14.46 \pm 0.40^*$	$19.83 \pm 0.21^*$

\* – accuracy of differences between subgroups  $p < 0,05$ .

**Table II.** Dynamics of lipid peroxidation and antioxidant system indexes under conducted treatment.

Index	II group			
	Traditional therapy (Subgroup B) n=24		Traditional therapy+ozone therapy (Subgroup A) n=23	
Malondialdehyde, nmol/L	4.72±0.40	4.63±0.39	4.73±0.39	4.01±0.31
p		p>0.05		p<0,02
Ceruloplasmin, mmol/L	1.577±0.08	1.636±0.09	1.597±0.10	1.847±0.09
p		p>0,05		p<0,02
Catalase, mcat/L	18.47±0.89	18.98±0.67	18.64±0.73	21.89±0.68
p		p>0.05		p<0.02

p – degree of differences accuracy in comparison with control.

According to received data, when using traditional treatment in patients with diabetic foot there were no sizeable changes in lipid peroxidation indexes. Malondialdehyde level at the beginning of treatment was 4.72±0.40 nmol/L and at the end of treatment 4.63±0.39 nmol/L. At the same time, while additional including of ozone therapy, a decrease of malondialdehyde content by 15.22% was observed (from 4.73±0.39 nmol/L).

Analysis of dynamics of antioxidant system indexes in patients with diabetic foot under conducted treatment did not detect any considerable changes in serum catalase as well as in ceruloplasmin level in blood serum. At the same time inhibitory action on lipid peroxidation processes condition in patients with diabetic foot, which was observed during complex treatment with ozone therapy, was accompanied by positive dynamics of antioxidant protection blood system components activity. Thus, an increase of catalase activity from 18.64±0.73 mcat/L at the beginning of treatment to 21.89±0.68 mcat/L at the end of treatment in patients with diabetic foot was observed, and also ceruloplasmin content – from 1.597±0.10 to 1.847±0.09 mmol/L.

## CONCLUSIONS

Thus, studies conducted showed that including of ozone therapy into complex surgical treatment has positive effect on wound process course which appears in substitution of degenerative processes by regenerative ones, improvement of lipid peroxidation and antioxidant system indexes and, as a result, reduces duration of hospital stay.

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