TREATMENT OF PYOINFLAMMATORY COMPLICATIONS WITH INDIVIDUALLY SELECTED OZONE DOSE IN PATIENTS WITH DIABETES

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Studies concerning the local and systemic use of ozonotherapy confirm its effectiveness compared to other physical methods. Therapeutic ozone concentrations (in a physiological solution from 1 mg/l to 6 mg/l, on average 3-4 mg/l with a single dose of 1.2-1.6 mg) activate the immunomodulatory function of the body. When administering ozone on the membranes of phagocytic cells (leukocytes, monocytes, macrophages) hydrophilic compounds are adsorbed. Ozonides stimulate cytokines, which, in their turn, promote activation of cellular and humoral immunity, and increases the rate of body's nonspecific protection system.

However, the effect of ozone on pyoinflammatory state of the soft tissues, depending on the administered dose and severity of the process [1-3,8,10], have not been adequately evaluated in patients with diabetes mellitus.

Therefore, the need emerged to find out the cellular mechanisms of wound healing regulation impairment, disease course characteristics and treatment superiority with the use of ozonotherapy during pyoinflammatory complications of soft tissues secondary to diabetes mellitus. Moreover, our study is significant, as from theoretical, so from the practical view [4-7,9,10].

The aim of our study is to improve management of pyoinflammatory processes in patients with diabetes mellitus with individually selected dose of ozonotherapy.

Material and methods. In total, 124 patients with diabetes and pyoinflammatory complications were enrolled in the study. Depending on the severity of the diabetes course, patients were divided into two groups: first group consisted of patients with severe stage – 76 (61.2%) and second group consisted of patients with moderate stage – 48 (38.7%).

Enrolled patients were also divided into two groups depending on treatment option. The main group - 53 (42.7%) was treated with individually selected dose of ozone therapy, while control group - 71 (57.2%) received only conventional treatment. Most patients in the main group - 76 (61.2%) had severe conditions, including diabetic gangrene in the distal regions of the foot - 17 (13.7%), phlegmone of the foot - 25 (20.16%), phlegmone of the ankle - 5 (4.03%), phlegmone of the perineum - 1 (0.8%), as well as isolated cases of phlegmone of the anterior abdominal wall (0.8%) and thigh (0.8%), purulent omphalitis (0.8%) and purulent wounds of the forearm (0.8%).

Pyoinflammatory lesions of the right lower limb in the study population were observed in 71 (57.2%) patients, and lesions of the left limb – in 53 (42.7%) patients.

During the treatment period, conservative therapeutic procedures and various surgical interventions were performed in most study participants: the primary surgical treatment of the wound - in 33 (26.6%) patients; exarticulation of the fingers of the lower extremities in 37 (29.8%) patients (including exarticulation of the I^{st} finger in 11 (8.9%) cases, II^{nd} finger – in 10 (8.1%) cases, III^{rd} finger – in 5 (4.0%) cases, IV^{th} finger – in 4 (3.2%) cases, V^{th} finger – in 7 (5.6%) cases); disclosure and drainage of soft tissues ulcers in 30 (24.2%) patients.

Amputation of the lower extremities at the level of the lower third of the thigh was performed in 15 (12.1%) patients; reamputation of the lower limb at the level of the lower third of the thigh was performed in one (0.8%) patients; foot amputation according to the Chopart method was performed in one (0.8%) patient; autodermoplasty was performed in 7 (5.6%) patients after the elimination of purulent-inflammatory processes of soft tissues on large and sluggishly granulating wounds.

Conservative treatment included the following medications: infusion therapy (5% glucose solution, Ringer-Locke's solution, 0.9% sodium chloride solution, Reosorbilact and others), vasoactive medications (Trental, Vasaprostan), nicotinic acid and medications containing nicotinic acid: Teonicol, Complamine, xanthinol nicotinate, reocorrectors (Rheopolyglukin), anticoagulants and antiagregants (Heparin, Fraxiparine, Aspirin, a wide range of antibiotics), antispasmodic medications (No-Spa, Spasmalgon, Platyphylline), Vitamins A, C, E, of B group, biological stimulants, anabolic steroid medications (Retabolil, Nerobol), antagonists of calcium ions (Verapamil, Cinnarizinum, Corinfar), cocarboxylase, ATP, desensitizing medications (Dimedrol solution, Suprastin, Loratadine), diuretics (Lasix, Furosemide), anti-inflammatory medications (Nimesil, Diclofenac, Naklofen), cardiological medications, medications for lipid metabolism correction – lipoic acid, Berlithion.

All patients from the main group received individually selected dose of ozone therapy in addition with traditional treatment and surgical interventions. Individual doses of ozone was determined using lymphocytotoxic test and was delivered by catheter into the ulnar vein (Table 1) for 6 day-period.

Ozone was delivered by automated ozone device "Boson" produced by the Scientific and Production Enterprise "Econika" in Odessa, Ukraine. The technological process of manufacturing ozone-containing saline solution was carried out in accordance with the standard method of preparation of ozone-containing saline solution for parenteral administration based on the methodological recommendations of the Ministry of Health of Ukraine.

Table 1. An individual ozone dose selection method using a lymphocytotoxic test

Ultimate ozone concentration	Cytotoxicity, %					
	1 stage of severity		2 stage of severity		3 stage of severity	
	control	main	control c	main	control c	main
10 mg/l	42	34	34	32	41	47
20 mg/l	42	38	34	28	41	34
40 mg/l	42	31	34	21	41	55

Table 2. Dynamics of blood glucose changes during the treatment process

Group of patients		Glucose levels, mmol/l	
	3rd day	6th day	14th day
Main group (n=53)	10.4 ±4.5	8.4 ±1.3	8.2 ±1.2
Control group (n=71)	10.8 ±4.2	11.6 ±1.5	8.8 ± 2.2

The criteria for patient's discharge from the clinic were the following: cessation of the spread of purulent-necrotic focus, the development of granulation tissue in the wound and the onset of marginal epithelization.

Statistical processing of the material was carried out using methods of variation statistics with standard techniques.

Results and their discussion. In medicine ozone is used as an ozone-oxygen mixture for local and systemic use. The selective effect of ozone having double and triple bonds on compounds is already determined. They include proteins, amino acids and unsaturated fatty acids that form part of the plasma lipoprotein complexes and the lipid biological layer of cell membranes. Reactions with these compounds make the basis of biological effects of ozonotherapy and have pathogenetic significance in various diseases.

The concentrations of ozonation are proposed by various authors: they are different and depend on many factors. [2,4,8].

It is appropriate to use an ozone-oxygen mixture with a concentration of 0.2 to 80 mg of ozone per liter of oxygen, since different types of metabolic reactions arise in different pathologies.

To achieve the overall metabolic effect, a technique, which gives good clinical results and eliminates the complications, is used; the concentration of ozone at the outlet of the ozonator is assigned at a rate of 20 μg per 1 kg body weight of the patient.

Selecting individual dose of ozone is very important for the patients with different types of metabolic reactions in various pathologies.

In our study participants with diabetes mellitus predominantly had severe inflammatory complications., For all study subjects the concentration of ozone was selected individually by the lymphocytotoxic test [8]; the ultimate concentration of ozone in vitro was 40 mg/l (Table 1).

The dose of ozone in the amount of 55 mg/l led to the destruction of lymphocytes and was ineffective for therapeutically use. Our study showed that patients who received ozone therapy in addition with traditional or surgical treatment had less pain complaints than subjects from the control group. In addition to pain relief, regression of edema, infiltration and hyperemia around the wound were observed in these patients. Moreover, after 2-3 procedures body temperature decreased and sleep and appetite normalized.

Interestingly, for the subjects from the control group all above-mentioned features normalized only on the 12-14th day of inpatient treatment.

Difference was observed also in the appearance of granulations between main and control groups: granulation appeared on average after 3-9th day of treatment in the main group and after 10-17th days in the control group In 44 (83%) patients from the main group the wound process was not complicated by the formation of necrotic changes in tissues after surgery. On the second day from surgery, in most cases from the main group, there was no need of narcotic anesthetic medications.

The addition of ozone therapy positively affected the duration of the hospital stay. Patients from the main group stayed in the hospital on average 9-12 days, while prolonged average stay was observed in patients from the control group -15-19 days.

Blood glucose levels were evaluated at baseline and on 3rd, 6th and 14th day after surgery in both study groups. At baseline the glucose levels did not differ between two groups. After 6 days of treatment glucose values in the main group was decreased and clinically significant difference was observed between the groups Although we have to admit that after 14 days of treatment the glucose levels decreased in both groups and reached almost similar values (Table 2).

The value of the leukocyte index of intoxication in norm equals to 1.04±0.5. The dynamics of the leukocyte index of intoxication in study population was as follows: In the main group 3.6±0.3, 2.8±0.2 and 1.8±0.1 - at the time of admission, after 6 and 14 days of treatment, respectively. In the control group leukocyte index of intoxication was 3.6±0.2, 3.7±0.2 and 2.6±0.2 - at the time of admission, after 6 and 14 days of treatment, respectively.

The baseline and after treatment results of other general

and biochemical blood tests did not differ significantly between the main and control groups.

Conclusions. Our study showed that the dose of ozone should be selected individually for each patient according to the lymphocytotoxic test and depending on the severity of the course of diabetes complication.

In patients who underwent ozone therapy with individually selected dose, the proliferation of purulent necrotic focus, development of the granulation tissue in the wound and the onset of border epithelization occurred faster then those who received only traditional treatment. Moreover, their period of hospital stay was 3 days shorter compared to the control group. In adittion, glucose levels and leukocyte index of intoxication was markedely lower after ozone therapy.

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SUMMARY

TREATMENT OF PYOINFLAMMATORY COMPLICATIONS WITH INDIVIDUALLY SELECTED OZONE DOSE IN PATIENTS WITH DIABETES

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The severity of purulent-inflammatory process in patients with diabetes mellitus is determined by lymphocytotoxic test. The test shows that application of intravenous ozone therapy with individually selected ozone dose significantly decreases the spread of necrotic suppurative focus already on the third day of treatment. Granulation tissue and marginal epithelization in the wound develops on the 6-8th day of hospitalization; normalization of glycemic levels shorten of the period of the hospital stay up to 3-5 days, compared to the control group.

Keywords: pyoinflammatory complications, diabetes mellitus, ozonotherapy.

РЕЗЮМЕ

ЛЕЧЕНИЕ ГНОЙНО-ВОСПАЛИТЕЛЬНЫХ ОСЛОЖНЕНИЙ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ С ИНДИВИДУАЛЬНЫМ ПОДБОРОМ ДОЗЫ ОЗОНА

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Применение у больных сахарным диабетом с гнойно-воспалительными осложнениями в лечении, внутривенной озонотерапии с индивидуальным подбором дозы озона, в зависимости от тяжести течения гнойно-воспалительного процесса по лимфоцитотоксическому тесту, значительно способствует снижению распространения гнойно-некротического очага уже на третьи сутки. Развитие в ране грануляционной ткани и краевой эпителизации происходит на 6-8 сутки стационарного пребывания больных, а также снижение показателей уровня сахара в крови, сокращению срока стационарного пребывания больных до 3-5 суток, в сравнении с контрольной группой.

რეზიუმე

შაქრიანი დიაბეტით და ჩირქოვან-ანთებითი გართულებებით ავადმყოფების მკურნალობა ოზონის ინდივიდუალურად შერჩეული დოზით

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უკრაინის სახელმწიფო უმაღლესი განათლების დაწესებულება
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შაქრიანი დიაბეტით და ჩირქოვან-ანთებითი გართულებებით ავადმყოფების მკურნალობაში ოზონოთერაპიის გამოყენება ოზონის ინდივიდუალურად შერჩეული დოზით და ჩირქოვან-ანთებითი პროცესის სიმძიმის გათვალისწინებით ლიმფოციტოტოქსიკური ტესტის მეშვეობით უზრუნველყოფს ჩირქოვან ნეკროზული კერის გავრცელების შემცირებას. ჭრილობის გრანულაციური ქსოვილის და ნაპირების ეპითელიზაციის განვითარება ხდება ავადმყოფის სტაციონარში ყოფნის მე-6-8 დღეს. ასევე მიმდინარეობს სისხლში შაქრის მაჩვენებლის და ავადმყოფების სტაციონარში ყოფნის პერიოდის შემცირება 3-5 დღე-ღამით შედარებით იმ ავადმყოფებთან, რომლებსაც არ ჩაუტარდათ ოზონოთერაპია.

РОЛЬ НЕКОТОРЫХ ВАЗОАКТИВНЫХ ПЕПТИДОВ В ПАТОГЕНЕЗЕ РАННИХ ФОРМ РОЗАЦЕА И СОСТОЯНИЕ СИСТЕМЫ ГЕМОСТАЗА

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Розацеа представляет собой хроническое кожное заболевание неизвестной этиологии, поражающее преимущественно центральную область кожи лица (щеки, подбородок, нос и лоб), характризуется периодами ремиссий и обострений. Актуальность проблемы розацеа очевидна в силу широкого распространения, отсутствия четкого представления об этиологии, резистентности к терапии, а также наличия не только медицинских, но и косметологических аспектов, которые усугубляются психоэмоциональными расстройствами [1].

Большинство исследователей существенную роль в патогенезе отводят сосудистым нарушениям [2,3,5]. Патология капилляров кожи связана с несколькими факторами, которых объединяет один результат - стойкое расширение сосудов кожи и в последующем стаз крови [5], что клинически проявляется эритемой и телеангиэктазиями. В последнее время в патогенезе розацеа все чаще обсуждается значение вазоактивных пептидов желудочно-кишечного тракта (пентагастрин, вазоактивный кишечный пептид - VIP) и медиаторных веществ, таких как эндорфины, брадикинин, серотонин, гистамин и субстианция Р [4]. Ключевая роль в механизме вазодилатации, увеличения проницаемости сосудов, развития воспаления, ангиогенеза принадлежит сосудистому эндотелиальному фактору роста (vascular endothelial growth factor - VEGF). VEGF, является одним из членов семейства структурно близких между собой белков - лигандов для семейства рецепторов одноименного цитокина, который связывается с двумя близкими по строению мембранными тирозинкиназными рецепторами (VEGF-1 и VGTF-2) и активирует их, способствуя повышению уровня IL-8, играющего значительную роль в развитии воспаления [7]. VEGF синтезируется активированными кератиноцитами в результате воздействия различных факторов, в частности, ультрафиолетовое облучение провоцирует выработку цитокинов IL-1 и TNF-α, которые стимулируют кератиноциты к синтезу VEGF [2,9]. Последний влечет за собой продукцию энзимов (матриксных металлопротеаз), вызывая деградацию волокон дермы, поддерживающих кровеносные сосуды, провоцируя атонию стенок сосудов и повышая их хрупкость [6]. Полагают, что именно этот фактор имеет этиологическое значение при розацеа. Проведено изучение экспрессии VEGF у больных розацеа, выявлена повышенная экспрессия VEGF и его рецепторов клетками эпидермиса. В биоптатах кожи обнаружены периваскулярные и перифолликулярные лимфогистоцитарные инфильтраты и расширенные кровеносные сосуды. Данные, касающиеся состояния свертывающей системы у больных розацеа, свидетельствуют о наличии сдвига функциональной активности гемостаза