



EFFECT OF OZONE-AIR MIXTURE OBTAINED BY ULTRAVIOLET RADIATION ON LOCAL IMMUNITY INDICATORS IN PATIENTS WITH BISPHOSPHONATE JAW OSTEONECROSIS

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ABSTRACT

Purpose of research is the definition of influence of ozono -air mixture, gained with the help of ultraviolet light, indicators of local immunity in patients with bisphosphonate osteonecrosis of jaws.

First group of research included 38 patients with bisphosphonate osteonecrosis of jaws in the age from 32 to 78 years. To the Patients of this group have been conducted treatment, including monthly courses of ozontherapie in the area of osteonecrosis, consisting of 10 everyday procedures (from 2 to 10).

"Control" group of research included 22 patients with bisphosphonate osteonecrosis of jaws in the age from 49 to 76 years, which were conducted treatment of osteonecrosis, without ozontherapie.

The analysis of indicators of targeted immunity to all patients was conducted before, after treatment, at occurrence at a radiological research of signs of sequestration.

The analysis of indicators of local immunity to the patients after treatment with using local ozontherapie showed strong positive dynamics, which is characterized by increase in activity phagocytosis in 1.2 times. Also it showed increase in quantity of late neutrophils (EN-PO) in 1.2 times ($p < 0.05$). The obtained data confirm increase in products of a S-component ephythelial cells of a mucous membrane of an oral cavity (S-IgA/IgA) and strengthening of a protective role of S-IGA (S-IgA/IgG).

As a result of carried out treatment to 20 patient 1 group (46.7%) has been formed sequesters.

At execution of analysis of ratings local immunity at the patients of the second group decrease of the content 1.2 times protective S-IgA in the saliva in as compared with norm was preserved ($p < 0.05$) that points to decrease of protective role S-IgA in the oral cavity.

As well marginal improvement of activity and rate of phagocytosis is revealed, however their decrease is preserved regarding norm to 1.22 times ($p < 0.05$) and 1.3 times respectively ($p < 0.05$).

KEYWORDS: bisphosphonate, osteonecrosis of jaws, indicators of local immunity, ozontherapie.

INTRODUCTION

The problem of treating patients with osteonecrosis after antiresorptive drugs therapy (bisphosphonates, denosumab) becomes more essential in modern dentistry [Bocci V, 2004; Azarpazhooh A,

Limeback H, 2008; Heufelder M et al., 2014; Zaslavskaya N et al., 2014]. Most patients have a medical history of malignant neoplasms combined treatment and metastatic bone damage. The number of patients with malignant tumors tends to increase annually. Followed somatic pathology in this category of patients is determined by treatment complexity and methods choice limitations. Jaw osteonecrosis has a significant impact on the quality of patient's life: varying pain syndrome se-

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verity, inflammation, risks of developing inflammatory complications in maxillary soft tissues, prosthetics impossibility.

Surgical interventions prior to the formation of sequels in the treatment of this category of patient's often lead to relapses, which leads to the severity of the patient's condition.

Department of maxillofacial and plastic surgery of A Evdokimov Moscow State University of Medicine and Dentistry and Department of therapeutic dentistry of I Sechenov First Moscow Medical University developed an effective, minimally invasive method for patient's treatment using an ozone-air mixture obtained by photochemical method with ultraviolet radiation [Zaslavskaya N et al., 2013, Zaslavskaya N et al., 2014, Makeeva I et al., 2017].

Ozonation can be used with patients with severe concomitant pathology, expressed trophic disorders etc. The use of ozonation in the treatment of hypo- and hyperergic inflammation is particularly effective [Zaslavskaya N et al., 2013]. An advantage of topical application of ozonized solutions or ozone gas is that ozone is able to penetrate deeply into all areas of the treated surface, even with slotted cavities and fistulas. Ozone is a powerful oxidant, much more reactive than diatomic oxygen. Therefore, this gas has a more pronounced effect on metabolic processes.

Ozone therapy mechanism is universal: antimicrobial, anti-inflammatory and immunomodulatory effects, microcirculation and regeneration processes impact and side effects absence provide the possibility of using this method in bisphosphonate jaw osteonecrosis treatment [Azarpazhooh A, Limeback H, 2008; Azarpazhooh A et al., 2009; Chergeshtov Yu et al., 2016; Makeeva I et al., 2017].

There are two main ways to produce ozone by electrical discharge (electrointhesis) and by short ultraviolet rays (photosynthesis).

Ozone electrosynthesis has become most common as it allows the production of ozone in high concentrations. However, in the production of ozone by this method, there is a significant problem that nitrogen is contained in the air in addition to the oxygen from which ozone is generated. The electrical discharge dissociates not only the oxygen molecules, producing ozone, but also the nitrogen molecules, which then passes into nitrogen oxides and on when reacted with water into nitric acid. Therefore,

it is dangerous to use ozonizers of this type in a moist oral environment, since the resulting nitric acid can have a damaging effect on tissues.

In order to avoid nitric acid formation, it is necessary to use special filters absorbing nitrogen oxides or to use pure oxygen. This complicates the design of the apparatus and significantly increases its cost.

Another negative side of electric discharge ozone generators is the formation of ozone at high concentrations, which are many times higher than the MPC (maximum permissible concentration) of ozone in the inhaled air, which in our country is 0, 1mg/m³. Therefore, the use of this type of oral ozonator is not safe, as ozone in high concentrations can have a damaging effect on the airways and lungs by accidental inhalation.

Another method of producing ozone is photochemical. This method is based on the dissociation of an oxygen molecule by short-wave ultraviolet radiation. Synthesis under the influence of ultraviolet radiation is easier to implement, it consists in the fact that air is passed through a special chamber, where under the influence of short-wave ultraviolet radiation the oxygen molecule dissociates into two atoms and then ozone is formed by fusion of the atom and the whole oxygen molecule.

An important feature of ozone production by short-wave ultraviolet radiation is that the action of ultraviolet rays doesn't lead to dissociation of nitrogen molecules and nitric acid is not being formed. More over this type of ozone generators allows obtaining ozone in a concentration sufficient to provide a therapeutic effect and not to have a negative effect on the respiratory system [Heufelder M et al., 2014; Chergeshtov Yu et al., 2016; Makeeva I et al., 2017; Dikopova N et al., 2019]. Thus, while treating bisphosphonate jaw necrosis it is advisable to use ozone generators that produce ozone using ultraviolet radiation. However, unfortunately, domestic and foreign industry does not produce ozone generators with parameters of our interest at the present time. Regarding that we have designed an ozone generator that produces ozone using ultraviolet radiation based on available medical devices. The device portable bio-irradiator "BOP - 01/27" («Novoanninsky plant electromedical equipment», Russia) emits shortwave ultraviolet spectrum was used as a source of ultraviolet radiation. This ozone generator is equipped with a compressor for pumping and ozone-air mixture sup-

plying, abductive and adductive silicone tubes system and standard interchangeable nozzles (Ultradent Mini Tip (USA)).

The objective is: to determine the effect of ozone-air mixture obtained with ultraviolet radiation on the local immunity indicators in patients with bisphosphonate jaw osteonecrosis.

MATERIAL AND METHODS

The first group of the "conservative treatment using local ozone therapy" study consisted of 38 patients with bisphosphonate jaw osteonecrosis, age from 32 to 78 years old. The patients of this group underwent conservative treatment which included monthly courses of ozone therapy in the field of osteonecrosis. It consisted of daily procedures from 2 to 10 minutes (depending on the prevalence of the pathological process). Intervals between repeated courses of ozone therapy were at least 5 weeks.

The second "control" group of the study included 22 patients with bisphosphonate jaw osteonecrosis at the age of 49 to 76 years old that underwent conservative treatment of osteonecrosis without ozone therapy. It included an antiseptic treatment of osteonecrosis zones with antiseptic solutions: solution of 0.05% chlorhexidine digluconate, Miramistin solution; dressings with hydrophilic-based ointment levomekol and general strengthening treatment were used. When inflammation appeared antibacterial and anti-inflammatory therapy was prescribed for up to 10 days (Amoxiclav 625 mg 1 tab. 3 times per day and also this therapy was supplemented with drugs based on metronidazole - Tiberall 1 tab. 2 times per day for 5 days).

The analysis of indicators of targeted immunity to all patients was conducted before treatment and after treatment, at occurrence at a radiological research of signs of sequestration. For the research we used 3-5 ml of unstimulated mixed saliva which was collected in a plastic tube 1 hour after a meal. In order to obtain rinse from the oral cavity the patient was asked to rinse the oral cavity with 10 ml of a 0.9% sodium chloride solution for 2-3 minutes. The rinse was collected in a plastic tube. The test tube with the rinse cells was centrifuged, precipitate was washed with Hanks solution, then Hanks solution was being added until the cell con-

centration reached 2×10^6 cells/ml. Cell viability was checked by 0.3% solution of trypan blue staining (only dead cells are stained). Reaction was performed only with a rinse, which included at least 60% of viable neutrophils.

The following indicators were determined:

- Total number of neutrophils in the mouth rinse, %
To determine the number of neutrophils rinse cytology with cells counting was performed.
- Subpopulation composition of neutrophils:
 - ✓ Late neutrophils (EN-PO), %. These are mature neutrophils that possess the highest phagocytic activity and have a set of bactericidal proteins and enzymes involved in destruction of damaged cells and tissues during inflammation.
 - ✓ Double neutrophils (DEN), %. These are the precursors of late neutrophils number of which increases with a decrease of late neutrophils and accordingly a decrease of cellular defense mechanisms.

Evaluation of neutrophil subpopulation was performed with erythrocyte markers in rosetting reactions [Petrova I et al., 1984] with identification of EN-PO number in reaction of spontaneous rosetting and DEN number in reaction of the complementary rosetting.

Immediately prior to reaction performing a suspension of erythrocyte markers was prepared. To prepare it washing of sheep erythrocytes with a physiological solution was performed by centrifugation until the supernatant became colorless. 0.5% erythrocytes suspension was prepared from the washed precipitate on the substrate 199.

Late neutrophil amount (EN-PO) determination by spontaneous rosette formation reaction.

There are receptors for sheep erythrocytes (SE receptors) on neutrophils surface. When they fix sheep erythrocytes a "socket" is being formed. 0.1 ml of a 0.5% solution of sheep erythrocytes was added to 0.1 ml of the cell sediment. The mixture was incubated at $t = 37^\circ\text{C}$ for 5 minutes then kept for 2 hours in the refrigerator to form rosettes.

Then 0.05 ml of 0.6% glutaraldehyde solution was added to fix the rosettes and left for 20 minutes at room temperature. It was washed from further glutaraldehyde exposure with saline 2 times by centrifugation. Then smears were made, dried, fixed in alcohol, dyed by Romanovsky-Giemsa and we counted the number of rosette-forming

neutrophils (E - erythrocyte, N - neutrophil, RO - rosetting). A rosette is a cell that has attached at least 3 red blood cells.

Determination of double neutrophils number (DEN) was performed in the reaction of complementary rosetting formation. In addition to sheep erythrocytes receptors early neutrophils also have receptors for complement (C) on their surface and, therefore, are referred to as double neutrophils (DEN). In addition to sheep erythrocytes standard hemolytic serum with antibodies (A) to sheep erythrocytes was used at a dilution of 1: 200 in reaction of complementary rosetting formation. 2.0 ml of hemolytic serum was combined with 2.0 ml of sheep erythrocytes (E), incubated at $t = 37^{\circ}\text{C}$ for 30 minutes to form a complex (EA). The standard dry complement of the mouse was diluted 1:10 and 2.0 ml of complement (C) was added to 2.0 ml of EA, incubated at $t = 37^{\circ}\text{C}$ to form the EAC complex. The mixture was washed twice to decrease an excess of complement in medium by centrifugation. Then 0.1 ml of the EAC complex was combined with neutrophil sediment, incubated at $t = 37^{\circ}\text{C}$ for 30 minutes and centrifuged for 5 minutes to plant the EAC on neutrophils. The following steps did not differ from the spontaneous rosette reaction.

➤ **Neutrophils phagocytic function:**

- ✓ Phagocytic index is the percentage of phagocytic neutrophils which indicates the phagocytosis activity.
- ✓ Phagocytic number is an average number of microbes phagocytized by one neutrophil. It reflects phagocytosis intensity.

To determine neutrophils phagocytic function a test was conducted with a bacterial culture according to the method of I.Y. Serebriysky et al. (1950): 0.1 ml of bacterial test culture suspension containing 2 billion microbial cells in 1 ml of saline was added to 0.1 ml of rinse cells sediment. The mixture was incubated at 37°C for 30 minutes, smeared, dried, fixed in alcohol and stained according to Romanowsky-Giemsa stain at 1:20 dilutions. Percentage of phagocytic neutrophils in smears and the number of microbes phagocytized averagely by one neutrophil were calculated.

➤ **Correlations for secretory defense mechanisms evaluation:**

- ✓ S-IgA / IgG is the ratio of secretory S-IgA

level formed in oral cavity as a result of B-lymphocytes (synthesizing IgA subunits) interaction with epithelial cells producing secretory component (S) to IgG. This parameter indicates either the predominance of protective secretory S-IgA or the predominance of the inflammatory component (IgG).

- ✓ S-IgA/IgA is the ratio that indicates ability of oral mucosa epithelial cells to synthesize secretory S-component required for S-IgA synthesis.

➤ **Correlation for assessing the relationship between secretory, humoral and cellular oral cavity protection components:**

- ✓ IgG/Phagocytic index
- ✓ IgG/Phagocytic number

Immunoglobulins concentration in saliva was determined by radial immunodiffusion in a gel according to Mancini G and co-authors (1965) using monospecific antiserum to S-IgA, IgA, IgM, and IgG. Since the concentration of immunoglobulins in secreted fluids is significantly lower than in serum, antisera dispersed in agar at concentrations 3-4 times lower than in the determination of serum immunoglobulins.

RESULTS

When analyzing obtained indicators of local immunity all examined patients showed a decrease of protective S-IgA in saliva; the first group patients by 1.5 times ($p < 0.05$) compared to normal values, the second group patients by 1.3 times ($p < 0.05$), which indicates protection decrease of S-IgA in the oral cavity. In contrast IgA and IgG levels slightly exceeded the norm. That's why in 1st and 2nd groups of patients a decrease compared to the normal S-IgA/IgG was by 1.65 times and by 1.5 times respectively ($p < 0.05$) as well as S-IgA/IgA by 1.6 times and 1.9 times ($p < 0.05$). This indicates an insufficient production of the S-component by oral mucosa epithelial cells (S-IgA / IgA) as well as a protection decrease of S-IgA (S-IgA / IgG).

As for cellular immunity, neutrophils increase in oral cavity rinses was revealed with a change in their subpopulation composition: decreasing the number of both late (EN-PO) neutrophils by 1.4 (group 1 patients) and by 1.3 times (group 2 patients) and early double neutrophils (DEN) by 1.3

times, which indicates the absence of compensatory reactions and deep inhibition of local defense mechanisms in the oral cavity ($p < 0.05$).

Activity decrease of phagocytosis in both groups of the study by 1.2 and 1.25 times was also revealed respectively compared to the norm ($p < 0.05$). Phagocytosis intensity was also reduced by 1.85 times in the 1st group patients and by 1.4 times in the 2nd group ($p < 0.05$).

Table 1 presents obtained values of local immunity indicators in 1st and 2nd patients study groups before the treatment start.

Analysis of local immunity indicators in patients after treatment with local ozone therapy revealed pronounced positive trend in immunity cellular component (Table 2), which is followed by the phagocytosis activity increase by 1.2 times and the number approximation to normal. Intensity of phagocytosis increased by 1.7 times ($p < 0.05$). Late neutrophils increase (EN-PO) by 1.2 times ($p < 0.05$) was also detected.

Protective S-IgA in saliva increased by 1.25 times ($p < 0.05$) compared to the pretreatment val-

ues, thus the amount of S-IgA in saliva approached to normal values. IgA and IgG levels decreased by 1.15 and 1.1 times, respectively ($p < 0.05$), thus it approached to normal values. Also S-IgA/IgG (increased by 1.4 times) and S-IgA/IgA (increased by 1.25 times) approached to normal ($p < 0.05$). The obtained data indicates an increase in S-component production by oral mucosa epithelial cells (S-IgA/IgA) and the strengthening of S-IgA protective role (S-IgA/IgG).

As a treatment result the formation of sequestrers occurred in 20 patients of the 1st group (46.7%). Sequestration terms varied from 6 to 15 months. When identifying signs of formed sequestrer (according to x-ray and clinical examination data - sequestration motility during sensing) sequestrectomy was performed.

When analyzing local immunity indicators in the second group of patients any significant positive dynamics according to ongoing conservative treatment was not revealed.

There was a decrease of protective S-IgA in saliva by 1.2 times compared to the normal ($p < 0.05$) which indicates a decrease of protective role of S-IgA in oral cavity. It was also revealed elevated levels of IgA and IgG in saliva, a decrease of S-IgA/IgG by 1.4 times ($p < 0.05$) compared to normal and S-IgA/IgA by 1.6 times ($p < 0.05$). Therefore we can conclude the insufficient production of S-component by the oral mucosa epithelial cells (S-IgA/IgA) as well as a decrease of S-IgA protective role (S-IgA/IgG).

As for cellular immunity it was a slight increase of late (EN-PO) neutrophils and early double neutrophils (DEN), however, in comparison to the normal it was reduced by 1.28 times ($p < 0.05$) and 1.04 times ($p < 0.05$) respectively. The obtained data indicates continuing depression of local defense mechanisms in the oral cavity after the treatment. A slight improvement of phagocytosis activity and intensity was also detected, however, remains its decrease by 1.22 times ($p < 0.05$) and 1.3 times, respectively ($p < 0.05$).

Among the second group of patients sequestrers formation was detected in 9 patients (40.9%) according to MSCT, however, it was no clinically sequestrers mobility. Sequestration appearance ranged from 13 to 36 months (Table 2).

Table 3 represents local immunity indicators in

TABLE 1
Initial average local immunity indices in patients with bisphosphonate jaw osteonecrosis

Indicator	Groups		
	1 st group	2 nd group	Normal
S-IgA (mg %)	17.94±1.8*	20.57±2.56*	26.5±2.6
IgA (mg %)	13.29±1.2*	13.79±1.65*	10.2±1.0
IgG (mg %)	15.23±1.6*	15.57±1.43*	13.1±1.1
Total number of neutrophils in rinse (%)	57.3±1.96	60.43±2.28*	55.0±1.6
DEN (%)	37.3±1.8*	31.0±1.62*	32.5±1.7
EN-PO (%)	46.7±4.61*	44.14±4.31*	58.2±4.0
PI (%)	63.6±5.87*	60.71±5.9*	76.0±5.0
PN	4.37±0.46*	5.78±0.62*	8.1±0.6
S-IgA/IgG	1.18±0.15*	1.32±0.12*	2.0±0.1
S-IgA/IgA	1.35±0.18*	1.49±0.12*	2.6±0.2
EN-PO/DEN	1.25±0.12*	1.42±0.13*	1.8±0.1
DEN/IgG	2.45±0.29*	1.99±0.2*	2.5±0.2
IgG/PI	0.24±0.01*	0.26±0.01*	0.17±0.01
IgG/PN	3.5±0.95*	2.7±0.04*	1.6±0.1

NOTE: * - reliability of obtained values difference compared to the normal $p < 0.05$ which corresponds with the probability of a correct forecast of 95.5

TABLE 2

Dynamics of average local immunity indices in the first and second groups of patients before and after ozone therapy

Indicator	first group		second group		Normal
	Before	After	Before	After	
S-IgA (mg %)	17.94±1.8	25.02±2.34*	20.57±2.56	21.23±2.2*	26.5±2.6
IgA (mg %)	13.29±1.23	11.6±1.15*	13.79±1.65	12.89±1.33*	10.2±1.0
IgG (mg %)	15.23±1.63	13.67±1.33*	15.57±1.43	15.3±1.44*	13.1±1.1
Total number of neutrophils in rinse (%)	57.3±1.96	57.6±1.28*	60.43±2.28	58.5±2.5*	55.0±1.6
DEN (%)	37.3±1.8	36.6±1.72*	31.0±1.62	31.2±1.8*	32.5±1.7
EN-PO (%)	46.7±4.61	54.8±4.11*	44.14±4.31	45.2±4.2*	58.2±4.0
PI (%)	63.6±5.87	73.8±6.5*	60.71±5.9	62.1±5.8*	76.0±5.0
PN	4.37±0.46	7.6±0.5*	5.78±0.62	6.2±0.7*	8.1±0.6
S-IgA/IgG	1.18±0.15	1.83±0.15*	1.32±0.12	1.39±0.1*	2.0±0.1
S-IgA/IgA	1.35±0.18	2.15±0.2*	1.49±0.12	1.65±0.2*	2.6±0.2
EN-PO/DEN	1.25±0.12	1.5±0.12*	1.42±0.13	1.45±0.13*	1.8±0.1
DEN/IgG	2.45±0.29	2.68±0.25*	1.99±0.2	2.04±0.2*	2.5±0.2
IgG/PI	0.24±0.01	0.18±0.01*	0.26±0.01	0.25±0.01*	0.17±0.01
IgG/PN	3.5±0.35	1.8±0.15*	2.7±0.04	2.47±0.1*	1.6±0.1

NOTE: * - reliability of obtained values difference after treatment compared to initial $p < 0.05$ which corresponds to the probability of correct prediction of 95.5%

oral cavity in patients of groups 1 and 2 after the treatment. Local immunity indicators of group 1 are close to normal whereas a significant deviation of normal values remains in the second group of patients. These results show continuing disorder in cellular, secretory and humoral defense mechanisms in oral cavity.

DISCUSSION

When analyzing local immunity indices in 1st group of patients after courses of local ozone therapy treatment positive dynamics were revealed as an increase of phagocytosis activity and intensity by 1.2 and 1.7 times ($p < 0.05$) respectively. These values approximated to normal, which indicated cellular immunity increasing.

The improvement was also revealed in humoral immunity: the amount of protective S-IgA in saliva increased by 1.25 times ($p < 0.05$) and also approached to the normal. An increase of S-IgA/IgG by 1.4 times ($p < 0.05$), S-IgA/IgA by 1.25 times ($p < 0.05$) was revealed which indicates an increase in the production of the S-component by epithelial cells of oral mucosa.

When analyzing the local immunity indices in

TABLE 4

Average local immunity indices in patients with bisphosphonate osteonecrosis after treatment

Indicator	Groups		
	1 st group	2 nd group	Normal
S-IgA (mg %)	25.02±2.34	21.23±2.2	26.5±2.6
IgA (mg %)	11.6±1.15	12.89±1.33	10.2±1.0
IgG (mg %)	13.67±1.33	15.3±1.44	13.1±1.1
Total number of neutrophils in rinse (%)	57.6±1.28	58.5±2.5	55.0±1.6
DEN (%)	36.6±1.72	31.2±1.8	32.5±1.7
EN-PO (%)	54.8±4.11	45.2±4.2	58.2±4.0
PI (%)	73.8±6.5	62.1±5.8	76.0±5.0
PN	7.6±0.5	6.2±0.7	8.1±0.6
S-IgA/IgG	1.83±0.15	1.39±0.1	2.0±0.1
S-IgA/IgA	2.15±0.2	1.65±0.2	2.6±0.2
EN-PO/DEN	1.5±0.12	1.45±0.13	1.8±0.1
DEN/IgG	2.68±0.25	2.04±0.2	2.5±0.2
IgG/PI	0.18±0.01	0.25±0.01	0.17±0.01
IgG/PN	1.8±0.15	2.47±0.1	1.6±0.1

NOTE: * -reliability of obtained values difference after treatment compared to initial $p < 0.05$, which corresponds to the probability of correct prediction of 95.5%

the second group of patients no significant positive dynamics was found. As for cellular immunity there was a slight increase of late (EN-PO) neutrophils and early double neutrophils (DEN). However, it was remaining decrease in comparison to the normal values by 1.28 and 1.04 times ($p < 0.05$) respectively. Insignificant improvement of phagocytosis activity and intensity was found. However, its reduction by 1.22 and 1.3 times ($p < 0.05$) respectively remained.

Decrease of protective S-IgA in saliva by 1.2 times ($p < 0.05$) remained indicating a decrease of S-IgA protective function in the oral cavity. High levels of IgA and IgG in saliva were also detected, which is followed by decrease in S-IgA/IgG by 1.4 times ($p < 0.05$) and S-IgA/IgA by 1.6 times ($p < 0.05$). This indicates an insufficient production of S-component by oral mucosa epithelial cells (S-IgA/IgA), as well as decrease of S-IgA protective function (S-IgA/IgG). The obtained data indicates the persistent inhibition of local protection mechanisms in oral cavity in patients that underwent conservative treatment without ozone therapy.

CONCLUSION

Application of ozone-air mixture received by photochemical way with the aid of ultraviolet radiation, at treatment of bisphosphonate osteonecrosis results in improvement of local immunity in the oral cavity (increase of activity and rate phagocytosis in 1.2 and 1.67 times respectively, as well as increase of the content S-IgA in the saliva to 1.25 times is revealed), as well as to acceleration of formation of budget cuts. It also accelerates the sequesters formation. Accompanying somatic pathology of this category of patients determine complexities and limitations in choosing the method of treatment. Our experience demonstrated, that the priority at the treatment of bisphosphonate osteonecrosis of jaws must be given to conservative methods, which is consistent with foreign works [Agrillo A et al., 2007; Muller P et al., 2007], to rise results of treatment and speed up dates for the formation of sequesters will allow local using of ozontherapie.

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