2. Al-Jobair A, Khounganian R. Evaluating the cariogenic potential of flavored milk: An experimental study using rat model. J Contemp Dent Pract 2015; 16: 42–47.
3. Bachanek T, Hendzel B, Wolańska E, Szybinsky V, Ogonovsky R, Hrynovets V, et al. Prevalence of dental erosion among 18-year-old adolescents in the borderland districts of Lviv (Ukraine) and Lublin (Poland). Annals of Agricultural and Environmental Medicine. 2018; 25, 1, 66–70.
4. Hegde AM, Naik N, Kumari S. Comparison of salivary calcium, phosphate and alkaline phosphatase levels in children with early childhood caries after administration of milk, cheese and GC tooth mousse: an in vivo study. J Clin Pediatr Dent. 2014; 38: 318–325.
5. Hegde AM, Naik N, Kumari S: Comparison of salivary calcium, phosphate and alkaline phosphatase levels in children with early childhood caries after administration of milk, cheese and GC tooth mousse: an in vivo study. J Clin Pediatr Dent. 2014; 38: 318–325.
6. Johansson I_Milk and dairy products: possible effects on dental health Pages 119–122, Published online: 13 Dec 2016; https://doi.org/10.1080/1102648026036324.
7. Kulkarni V, Bhatavadekar NB, Uttamani JR The effect of nutrition on periodontal disease: A systematic review. J. Calif. Dent. Assoc. 2014; 42, 302–311.
8. Kostyrenko OP, Melnyk VL, Shevchenko VK, Sylenko YuI, Yeroshenko GA. Application of nanocrystals in treatment of chronic apical periodontitis. World of medicine and biology. 2020; 3 (73). 61–64. DOI: 10.26724/2079-8334-2020-3-73-61-65
9. Mahlovanyy A, Grygus I, Kunynets O, Hrynovets V, Ripetska O, Hrynovets I, Buchkovska A, Mahlovana G. Formation of the mental component of the personality structure using physical activity. Journal of Physical Education and Sport. 2021; 21,5: 3053–3059. doi:10.7752/jpes.2021.s406.
10. Olczak-Kowalczyk D, Mysiak-Dębska M, Dębska-Łasut K, Grzebieluch W, Kaczmarek U. Food and dental caries. Part 1. Milk and dairy products, Borgis - Nowa Stomatologia 1/2017; 30–38.
11. Savchuk OV, Gasyuk NV, Klytynska OV, Yeroshenko GA, Zaliznyak MS. Clinical and morphological aspects of complex treatment of generalized periodontitis. World of medicine and biology. 2020; 2 (72). С. 115–119. doi: 10.26724/2079-8334-2020-2-72-115-119

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EFFECTIVENESS OF OZONE THERAPY IN THE TREATMENT OF HERPETIC UVEITIS

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The purpose of the study was to learn the impact of ozone therapy on the outcomes of treatment in patients with herpetic uveitis. 80 patients (80 eyes involved) with herpetic uveitis were treated. The resorption of the infiltration of the choroid in the main group (40 patients – 40 eyes), was treated with ozone therapy in combination with conventional treatment terms of resorption of infiltration of the choroid were completed earlier than the compared group (40 patients – 40 eyes), which was treated with the preparation based on a combination of highly active enzymes of plant and animal origin combined with conventional treatment (respectively, 19.4±0.2 and 25.1±0.3; $p<0.05$). The duration of treatment in main group was shorter than in the control group (respectively, 21.1±0.3 and 26.8±0.5; $p<0.05$). The main group, which was treated with ozone therapy, showed a higher therapeutic effect in comparison to the control group of patients, who obtained tablets of preparation based on a combination of highly active enzymes of plant and animal origin, the results were statistically significant.

Key words: ozone therapy; herpetic uveitis; treatment.

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ЕФЕКТИВНІСТЬ ОЗОНОТЕРАПІЇ ПРИ ЛІКУВАННІ ГЕРПЕТИЧНОГО УВЕЇТУ

Метою дослідження було вивчити вплив озонотерапії на результати лікування хворих на герпетичний увеїт. Проведено лікування 80 пацієнтів (залучено 80 очей) із герпетичним увеїтом. Розсмоктування інфільтрату судинної оболонки в основній групі (40 хворих – 40 очей), що лікувалися озонотерапією в поєднанні з традиційним лікуванням (основна група), показало більш короткі терміни розсмоктування інфільтрату судинної оболонки, ніж у групі порівняння (40 хворих – 40 очей), яких лікували препаратом на основі комбінації високоактивних ферментів рослинного та тваринного походження у поєднанні з традиційним лікуванням (відповідно 19,4±0,2 та 25,1±0,3; $p<0,05$). Тривалість лікування в основній групі була коротшою, ніж у контрольній (відповідно 21,1±0,3 та 26,8±0,5; $p <0,05$). В основній групі, яка отримувала озонотерапію, відзначений більш високий терапевтичний ефект порівняно з контрольною групою пацієнтів, які отримували таблетки препарату на основі комбінації високоактивних ферментів рослинного та тваринного походження, результати були статистично значущими.

Ключові слова: озонотерапія, герпетичний увеїт, лікування.

Wide spread among the population, the predominant lesion of active age individuals, recurrences, high incidence of visual impairment make uveitis a highly significant social problem, according to some data, the uveitis is one of the causes of blindness and poor vision in 15–30 % of all patients, who have lost their sight [1, 2].

Herpesvirus infections (HI) are the most widely spread viral infections on the globe, according to WHO data, about 80–90 % of the world's population is infected by one or more types of herpesviruses. An estimated 3.7 billion people under 50 years of age (67 %) worldwide are infected with herpes simplex virus type 1 (HSV-1). [3, 10]. The main biological and pathogenetic features of the herpesviruses are the long persistence in the body of an infected person, polytropism to the various tissues and the ability to reactivate.

These properties of herpesviruses cause polymorphism of the clinical demonstrations, multiple lesions of various organs in generalized forms and a high probability of transition of infection to chronically recurrent. According to the data of various authors, herpetic uveitis is the cause, with probability of (2.5 % to 38.5 %) of all inflammatory diseases of the vascular tract. Diagnosis and treatment of herpesvirus uveitis has a great social significance that is connected with its spreading, severe and recurrent course. Approximately 35 % of uveitis of herpesvirus etiology leads to the disability [1, 9].

The problem of HI therapy, associated with a steady increase in the number of patients, the severity of the course, chronicity, complications and relapses of various forms of herpetic diseases, remains actual and the search for preparations and safe treatment regimens continues [4, 10].

During the recent years, there is an increasing interest of modern medicine to alternative non-drug treatments. Among these methods of treatment ozone therapy has received the greatest recognition [5, 6, 11].

There are two mechanisms of action of ozone: 1) the direct action of ozone, detected mainly in the local application and manifested in the form of chemotherapeutic disinfecting activity, causing a violation of the integrity of the microbial membrane due to the oxidation of phospholipids and lipoproteins; interaction with viruses leading to the damage of proteins of the outer membrane and polypeptide chains of nucleic acids, which creates an obstacle for the ability of viruses to attach to cells; 2) the systemic effect due to the ozone-induced low concentrations of peroxides. The active use of ozone therapy is determined by a variety of therapeutic effects: a wide range of antimicrobial action, anti-inflammatory, immunomodulatory, antioxidant etc. [7].

A wide range of therapeutic ozone action demonstrates positive results of its use in the practice of general medicine (rheumatology, cardiology, general surgery, otorhinolaryngology, oncology, nephrology etc.), the comparative cheapness of the method of application, the absence of side effects and safety give grounds for its wider application in ophthalmology [6, 8].

The purpose of the study was to learn the impact of ozone therapy on the outcomes of treatment in patients with herpetic uveitis.

Materials and methods. Our work involved 80 patients (80 eyes, 1 affected eye per patient) with herpetic uveitis (HU). The etiologic diagnosis of HU was carried out in the Virology laboratory of NCO, named after acad. Z. Aliyeva, by detecting the antigen of herpes virus in scrapings from the conjunctiva (FAM), determination of serum IgM and IgG antibodies to structural antigens of HSV–1 and HSV–2, as well as the determination of serum IgG antibodies to the early non-structural regulatory antigens of HSV–1 and HSV–2 (ELISA).

For differential diagnosis of patients, the antibodies of blood were tested for other infections: cytomegalovirus, toxoplasmosis, tuberculosis, chlamydia, brucellosis, and rheumatism. The results were negative. The diagnosis was established according to the clinical and anamnestic data.

Clinical data included pathognomonic for herpetic uveitis (pigmented precipitates, which were mistaken for old, hyphema, and secondary hypertension (for uveitis of another etiology hypotension is more characteristic).

Before the treatment, anamnestic data was collected in the course of which they clarified: the etiology and circumstances of the eye disease; complaints of patients and their dynamics depending on the terms of the disease; the results of diseases expressed in changes of visual acuity; types and means of the previously used treatment.

During the examination and observation of patients, methods that were used are generally accepted in the clinical practice of ophthalmologists: visometry; biomicroscopy; esthesiometry: optical coherence tomography of the anterior segment; ophthalmoscopy; tonometry; A-B scan.

The research involved 41 men and 39 women, the age ranged from 24 to 67 (40.3±11.5) years. The patients were divided into two groups equal by severity of clinical symptoms (respectively, 23.15±0.34 and 22.57±0.4). The severity of the clinical picture was evaluated by the point system. The number of patients included in the main group was 40 (40 eyes), in the comparison group there also were 40 patients (40 eyes).

The main group (40 patients – 40 eyes) received complex treatment which included the conventional traditional treatment in combination with ozone therapy. Traditional treatment included selective both anti-herpetic treatment and pathogenetic symptomatic treatment. Patients received ozone therapy in the form of intravenous drip of ozonated physiological solution (ozone dose in each case was selected individually and ranged from 4 to 9 mg/l), for a course of 7–12 procedures. The control group consisted of 40 patients (40 eyes), they obtained traditional medicine treatment with Wobenzym® (Mucos, Germany), content: Pancreatin 300 Prot. units (100 mg); papain 90 FIP-Unit. (18 mg), bromelain 225 FIP-U. (45 mg), triacylglycerol lipase 34 FIP-U. (10 mg); amylase 50 FIP-Units (10 mg); trypsin 360 FIP-Unit. (12 mg) chymotrypsin 300 FIP-U. (0.75 mg); rutoside 50 mg.

Antiherpetic treatment:

– 3 % eye ointment Zovirax® (GLAXO WELLCOME OPERATIONS, Great Britain; content: aciclovir), *or*

– 1.5 % Virgan gel® (content: ganciclovir), Valtrex® tablets (GLAXO WELLCOME OPERATIONS, Great Britain; content: valaciclovir), *or*

– Zovirax, eye drops Ophthalmoferon® (“Firn M”; content: interferon alpha-2b human recombinant + Diphenhydramine) and Poludan (“Veropharm”; content: biosynthetic polyribonucleotide complex of polyriboadenylic and polyribouridylic acids) for subconjunctival or parabulbar injection.

Eye ointment Zovirax or Virgan gel was used every 4 hours 5 times a day, Valtrex was taken 1 tablet (500 mg) 2 times daily or Zovirax – 1 tablet (200 mg) 5 times a day during 5–10 days depending on the severity and dynamics of the process. Ophthalmoferon was taken by patients as 2 drops every 2 hours during the acute stage of the disease, then after subsiding of symptoms the quantity of drips had reduced to 3–4 times a day, Poludan 50 U subconjunctivaly 1 time a day during 7–10 days. As a symptomatic treatment patients received steroidal and non-steroidal anti-inflammatory drugs both locally and generally, mydriatics etc.

The efficiency of treatment in the research was evaluated according to the terms of resorption of infiltration of the vascular membrane (i.e., resorption of signs of inflammation of the vascular membrane: swelling of the vascular membrane, precipitates, inflammatory cells in the anterior chamber, hypopion, hyphema and opacity of the vitreous body), the duration of treatment, the dynamics of visual acuity.

Results of the study and their discussion.

The results of treatment in the main and control groups of patients are presented in Table 1.

Table 1

Comparative clinical indices of treatment in patients of main and control groups

Groups of investigation	Severity of clinical characteristics	Resorbtion of infiltration	Duration of treatment	Visual acuity	
				before	after
Main group	23.15±0.34	19.4±0.2	21.1±0.3	0.03±0.02	0.72±0.08
Control group	22.57±0.4	25.1±0.3	26.8±0.5	0.04±0.03	0.64±0.06
Coefficient of significance (p)	>0.05	<0.05	<0.05	>0.05	>0.05

Terms of resorption of infiltration of the vascular membrane varied from14 days (1 patient – 2.5 %) to 22 days (1 patient – 2.5 %), the average period was 19.4±0.2 days. At 36 (90 %) patients the clinical signs of inflammation of the vascular membrane of the eye (precipitates, inflammatory cells in the anterior chamber, in the vitreous body) were completely resorbed at the 18-20 days of treatment. 2 (5 %) patients had uveitis, which was accompanied by hypopion, at 1 patient (2.5 %) hypopion of 3 mm in height was resolved on the 16th day of treatment, at the 2-nd patient the hypopion was resolved on the 19th day of treatment. At 4 patients (10 %) uveitis was accompanied by hyphema and hemophthalmos, resorption was observed on the 17-18th days of treatment. Visual acuity increased at all patients from 0.04±0.02 to 0.72±0.08. Herewith, 39 (97.5 %) patients obtained the visual acuity above 0.2. The total duration of treatment was 21.1±0.3 days. At 2 (5 %) patients by the 28th day of treatment residual infiltration of the vascular membrane (single precipitates and opacity of the vitreous body) was registered, the patients were related to the group with improvement.

The efficiency of treatment is evaluated as follows: recovery – 38 patients (95 %); improvement – 2 patients (5 %). In the analysis of the side effect no signs of toxic-allergic irritation were observed. The results of the general clinical examination (subjective feelings of the patient, temperature reaction, urine and blood tests) reflect good tolerability of complex treatment. The results of immunological blood tests with determination of the level of specific immunoglobulins revealed a more significant decrease in the level of IgG and IgM HSV-I after treatment in the main group in comparison to the control group.

Results of treatment in the control group of patients, receiving conventional treatment with Wobenzyme tablets.

Terms of resorption of infiltration of the vascular membrane ranged from 18 days (1 patient – 2.5 %) to 27 days (1 patient – 2.5 %), the average period was 25.1±0.3 days. 29 (72.5 %) patients had clinical signs of inflammation of the eye's vascular membrane (precipitates, inflammatory cells in the anterior chamber, in the vitreous body) were resorbed by 24–26 days of treatment. Uveitis was accompanied by hypopion at 2 (5 %) patients. 1 (2.5 %) patient had hypopion of 3 mm in height was resolved on the 19th day of treatment, in 1 patient by the 23th days of treatment. 4 patients (10 %) had uveitis that was accompanied by hyphema and hemophthalmos resorption was observed on the 22th days of treatment. Visual acuity was increased in all patients on average from 0.04±0.03 to 0.64±0.06. Herewith, 32 (80 %) patients obtained visual acuity – higher 0.2. The total duration of treatment was 26.8±0.5 days. 12 (30 %) patients by the 28th day the residual infiltration of the vascular membrane (single precipitates and vitreous opacity) was registered, and the patients were related to the group with improvement.

The efficiency of treatment was evaluated as follows: recovery – 28 patients (70 %); improvement –12 patients (30 %) (Fig. 1).

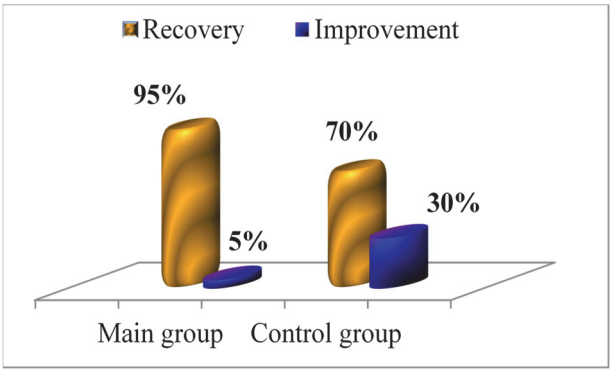

Fig. 1. Therapeutic efficacy in main and control groups

The average terms of resorption of infiltration of the vascular membrane were in the main group – 19.4±0.2 days, and in the comparison group 25.1±0.3 days. At 36 (90 %) patients of the main group with clinical signs of inflammation of the vascular membrane of the eye - the precipitates completely resolved, clouding of the vitreous body and chorioretinal edema resorbed by 18–20 days of treatment, in the control group 29 (72.5 %) of patients – by the 24–26 day of treatment. Visual acuity increased at patients of the main group from an average of 0.04±0.02 to 0.72±0.08, in the control group from 0.04±0.03 to 0.64±0.06. At the same time 39 (97.5 %) patients of the main group obtained a visual acuity – above 0.2, in the control group 32 (80 %) patients obtained visual acuity – higher than 0.2.

The total duration of treatment of patients of the main group was 21.1±0.3 days, of patients of the control group – 26.8±0.5 days. The efficiency of treatment is evaluated as follows: in the main group recovery – 38 patients (95 %); improvement – 2 patients (5 %). The effectiveness of treatment was the control group was evaluated as follows: recovery – 28 patients (70 %); improvement – 12 patients (30 %).

Thus, resorption of infiltration of the vascular membrane (i.e. resorption of signs of inflammation of the vascular membrane) at patients of the main group was completed earlier, in compare with the control group (respectively, 19.4±0.2 and 25.1±0.3; $p<0.05$). The duration of treatment of the main group is shorter than the duration of treatment in the control group (respectively, 21.1±0.3 and 26.8±0.5; $p<0.05$). The effect of increasing of the visual acuity was, respectively, 0.72±0.08 and 0.64±0.06 ($p>0.05$). In both groups the high therapeutic activity was noted recovery in 95 % and 70 %, improvement in 5 % and 30 % of cases, accordingly, deterioration and lack of effect was not observed in any case.

The main group receiving ozone therapy in combination with traditional treatment according to some parameters (terms of resorption of infiltration of the vascular membrane and duration of treatment) showed a higher therapeutic effect than in the control group of patients receiving conventional treatment with Wobenzyme tablets. The results are statistically reliable.

During the analysis of the side effect, no signs of toxic-allergic irritation were observed in any case. The results of the general clinical examination (subjective feelings of the patient, temperature reaction, urine and blood tests) indicated good tolerability of complex treatment with the use of the method of ozone therapy.

Using antiviral preparations is one of the important parts of herpesvirus infection treatment of ophthalmic pathologies, which were confirmed in our study. Wang X, et al with aim to explore the clinical efficacy of oral ganciclovir (GCV) in the prevention of recurrent herpes simplex keratitis (HSK). A multicenter, prospective, randomized, single-blind, and controlled clinical trial was conducted from April 2010 to June 2013. 173 eyes involved with the diagnosis of recurrent HSK definitely, including stromal keratitis and corneal endotheliitis. The results showed that short-term oral GCV could cure

recurrent HSK and endotheliitis, shorten the course, reduce recurrent rate of HSK and have confirmed safety [9].

Kaya A, et al with the purpose to investigate efficiency of ozone therapy in uveitis observed 24 albino Wistar rats and evaluated vitreous cytokine levels. The authors revealed that clinical and histopathologic examination results indicate that systemic application of ozone may be efficient in the treatment of uveitis. These results support our data about efficacy ozone therapy in treatment of inflammatory process [3].

Smith NL, et al have conducted a comprehensive review of ozone therapy, investigating its contraindications, routes and concentrations of administration, mechanisms of action, disinfectant properties in various microorganisms, and its medicinal use in different pathologies. They explored the therapeutic value of ozone in pathologies of the cardiovascular system, gastrointestinal tract, genitourinary system, central nervous system, head and neck, musculoskeletal, subcutaneous tissue, and peripheral vascular disease [7]. Despite the fact that in this study there were no evidences about impact ozone therapy in ophthalmology, the general mechanisms are the same. In addition, our study presented the significant data, which support thesis mentioned above.

Conclusion

Due to the result of clinical studies it was established that the use of ozone therapy in the treatment of herpetic uveitis allows to increase the effectiveness of treatment and improves the basic clinical parameters (terms of resorption of infiltration of the vascular membrane and the duration of treatment). Summarizing the aforementioned we can say that the method of ozone therapy opens new opportunities for ophthalmologists in the effective treatment and prevention of complications of recurrent herpetic uveitis.

References

1. De-la-Torre A, Valdes-Camacho J, Foster CS. Bilateral Herpes Simplex Uveitis: Review of the Literature and Own Reports. Ocul Immunol Inflamm. 2017 Aug;25(4):497–502. doi: 10.3109/09273948.2016.1142572.

2. Katerenchuk IP, Tkachenko LA, Yarmola TI, Talash VV, Rustamyan ST, Pustovoyt AL, et al. Churg-strauss syndrome: clinical case and its features. Wiadomosci Lekarskie. 2019. 72(4): 723–726.

3. Kaya A, Sonmez M, Kar T, Haholu A, Yildirim Y, Müftüoğlu T, et al. Efficiency of Ozone Therapy in a Rat Model of Experimental Uveitis. Ocul Immunol Inflamm. 2017 Oct;25(5):695–700. doi: 10.3109/09273948.2016.1161057.

4. Reynaud C, Rousseau A, Kaswin G, M'garrech M, Barreau E, Labetoulle M. 2017. Persistent impairment of quality of life in patients with herpes simplex keratitis. Ophthalmology. 2017.124(9):160–169.

5. Shamim T. Ozone therapy in dentistry: Revisited. Medical Gas Research. 2018; 7. 278. doi:10.4103/2045-9912.222453

6. Siniscalco D, Trotta MC, Brigida AL, Maisto R, Luongo M, Ferraraccio F, D'Amico M, Di Filippo C. Intraperitoneal Administration of Oxygen/Ozone to Rats Reduces the Pancreatic Damage Induced by Streptozotocin. Biology (Basel). 2018 Jan 11;7(1):10. doi: 10.3390/biology7010010.

7. Smith NL, Wilson AL, Gandhi J, Vatsia S, Khan SA. Ozone therapy: an overview of pharmacodynamics, current research, and clinical utility. Med Gas Res. 2017 Oct 17;7(3):212–219. doi: 10.4103/2045-9912.215752.

8. Tezcan AH, Ozturk O, Ustebay S, Adali Y, Yagmurdur H. The beneficial effects of ozone therapy in acetaminophen-induced hepatotoxicity in mice. Pharmacol Rep. 2018 Apr;70(2):340–345. doi: 10.1016/j.pharep.2017.11.003.

9. Wang X, Wang L, Wu N, Ma X, Xu J. Clinical efficacy of oral ganciclovir for prophylaxis and treatment of recurrent herpes simplex keratitis. Chin Med J (Engl). 2015 Jan 5;128(1):46–50. doi: 10.4103/0366-6999.147808.

10. WHO. Herpes simplex virus. https://www.who.int/ru/news-room/fact-sheets/detail/herpes-simplex-virus

11. Zanardi I, Borrelli E, Valacchi G, Travagli V, Bocci V. Ozone: A Multifaceted Molecule with Unexpected Therapeutic Activity. Curr Med Chem. 2016;23(4):304–14. doi: 10.2174/0929867323666151221150420.

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