

**PECULIARITIES OF THE USE OF DRUGS WITH ANTIOXIDANT AND IMMUNOSTIMULATING ACTION IN THE COMPLEX TREATMENT OF PATIENTS WITH ODONTOGENIC PHLEGMONS**<sup>1</sup>Zaporizhzhia State Medical University (Zaporizhzhia, Ukraine)<sup>2</sup>Kharkiv National Medical University (Kharkiv, Ukraine)<sup>3</sup>Bogomolets National Medical University (Kyiv, Ukraine)

li4man@i.ua

*The problem of conservative treatment of patients with odontogenic phlegmon is not only a medical, but also a medical and social problem, despite the large number of studies in this field of maxillofacial surgery. A special place is occupied by studies that are carried out in order to establish the features of the use of drugs that have antioxidant and immunostimulating effects as part of conservative therapy for phlegmon. The aim of this work was to increase the effectiveness of conservative treatment of patients with odontogenic phlegmon by including phosphatidylcholine nanocapsules in the complex therapy. The study involved 60 patients who were divided into two groups of 30 people: in the 1st group, the treatment was carried out according to the standard protocol, in the 2nd - according to the protocol with the addition: conservative therapy included intravenous injections of the effectiveness of conservative treatment of patients with odontogenic phlegmon by including phosphatidylcholine nanocapsules in complex therapy. The obtained results constituted a clinical and laboratory evidence base for the effectiveness of applying the effectiveness of conservative treatment of patients with odontogenic phlegmons by including phosphatidylcholine nanocapsules in complex therapy as part of complex therapy in patients with odontogenic phlegmons: an improvement in all clinical indicators of purulent wound regeneration and laboratory blood parameters was recorded.*

**Key words:** odontogenic phlegmon, complex treatment, conservative treatment, regeneration of a purulent wound, antioxidants and immunostimulants.

**Connection of the publication with planned research works.**

The work is a fragment of the complex NDR of the Kharkiv National Medical University of the Ministry of Health of Ukraine "Optimization of methods of diagnosis and treatment of major dental diseases" (state registration number O119U002899).

**Introduction.**

The problem of developing modern methods and techniques for the treatment of purulent-inflammatory diseases of the maxillofacial region, prone to a sluggish, protracted course, has become particularly relevant due to an increase in the number of such patients, an increase in local and general complications [1-3]. Odontogenic phlegmons are characterized by a long development, a sluggish torpid course, they present significant difficulties for diagnosis, which is primarily due to the variety of clinical manifestations and the low efficiency of traditional therapy [4, 5].

Currently, data on the immune status of the body with sluggish phlegmon of the maxillofacial region are quite scattered and contradictory [2, 4, 6]. However, all studies indicate immune disorders expressed to varying degrees, causing an atypical course of inflammation and the complexity of treatment [3, 5-7]. Therefore, in case of sluggish, poorly amenable to traditional therapy, purulent-inflammatory diseases, direct or indirect activation of the immune system is necessary by including immunomodulators in complex therapy [8, 9].

**The aim of the study.**

To improve the efficiency of conservative treatment of patients with odontogenic phlegmon by including phosphatidylcholine nanocapsules in complex therapy.

**Object and methods of research.**

A survey with surgical and conservative treatment of 60 patients (32 male and 28 female, age 19-63) with odontogenic phlegmons were carried out in the department of maxillofacial surgery of the Municipal non-profit enterprise of the Kharkov Regional Council "Regional Clinical Hospital". The study excluded patients who had comorbidities that could have an impact on the clinical picture of the disease and the results of treatment. All concomitant chronic diseases that were present in patients included in the study were in remission for at least 3 months.

The patients were divided into 2 groups: the first (control) – 30 people, whose treatment was carried out by traditional generally accepted methods, and the second – 30 people, in the scheme of complex treatment of which additionally included the immunomodulator drug "Lipin" with nanocapsules of phosphatidylcholine.

Conducted a comprehensive immunological examination, which included the following tests: determination of the level of T- and B-lymphocytes in the blood, %; determination of classes and amount of immunoglobulins in blood and saliva (IgA, IgG, IgM). The obtained data were statistically processed on a personal computer by conventional methods using the programs "Microsoft Excel 2016" and "Primer of Biostatistics, Vers. 9.03. To determine the significance of differences between the compared means, Student's t-test was used. Differences were recognized as significant at  $p < 0.05$ .

The study was conducted in accordance with the principles of the Helsinki Declaration on the Protection of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, and the provisions of the relevant laws of Ukraine. The study protocol was approved by the Local Ethics Committee for all participants.

Written informed consent was obtained from all patients who participated in the study.

#### Research results and their discussion.

The inclusion of phosphatidylcholine nanocapsules in the complex therapy of odontogenic phlegmon had a beneficial effect on changes in peripheral blood parameters.

At the time of hospitalization, there were no significant differences in all hemogram parameters between clinical groups, however, the use of phosphatidylcholine nanocapsules led to a faster and more significant decrease in most indicators compared to the initial level and the control group.

During hospitalization, the number of erythrocytes and the level of hemoglobin in the peripheral blood in patients of the main and control groups were comparable and significantly reduced compared to similar indicators in the group of healthy individuals ( $p < 0.05$ ).

The number of erythrocytes in peripheral blood during treatment tended to increase by 11% only in patients of the main group.

On the 7th day, this indicator approached the level of healthy individuals and was significantly higher than the average value of the number of erythrocytes in patients in the control group. The level of hemoglobin concentration in patients of the main group also slightly increased, but these changes were not statistically significant. The dynamics of changes in the value of the color index in patients in both clinical groups was also not statistically significant.

The average number of leukocytes in patients with atypically current phlegmon of the maxillofacial area upon admission to the hospital significantly exceeded ( $9.7 \pm 0.7 \times 10^9$  g/l) the values determined by us for a group of healthy individuals. At the same time, there were no significant differences in this indicator between clinical groups at the time of hospitalization.

The use of phosphatidylcholine nanocapsules in the complex therapy of patients led to a more significant decrease in the number of leukocytes in the peripheral blood compared to the control group. So on the 7th day, their average value for patients of the main group was  $5.9 \pm 0.6 \times 10^9$  g/l, which is 32% lower than the number of leukocytes at admission and lower than the corresponding indicator for the control group. Changes in the percentage of eosinophils and basophils in the peripheral blood of patients in both groups were not statistically significant.

The use of phosphatidylcholine nanocapsules in the complex treatment of patients of the main group led to a more rapid decrease in the number of stab neutrophils ( $2.5 \pm 0.1\%$ ) and a more significant increase in the content of lymphocytes ( $24.3 \pm 0.4\%$ ). The erythrocyte sedimentation rate (ESR) in patients upon admission to the hospital was 5-6 times higher than in the group of healthy individuals. The inclusion of phosphatidylcholine nanocapsules in the complex therapy of patients of the main group led to a more rapid normalization of this indicator and by the 8th day the ESR value reached  $9.7.0 \pm 1.2$  mm/h, which significantly differed from the value of this indicator in the control group.

The initial concentration of immunoglobulins A and G in saliva was reduced in all patients, and the concentration of immunoglobulin M was increased by 2.7-4.2%. In patients of the control group, these changes persisted

until the 9th day, while in patients of the main group they reached the normal range by 5 days after the administration of phosphatidylcholine nanocapsules and by 9-10 days their level was already within the physiological limits. At the same time, in patients of this group, the IgA concentration slightly exceeded the physiological level, which, in turn, suggests a favorable clinical course of the disease.

In the course of treatment in patients of the control group, immunoglobulin G remained at the level of the initial concentration up to 10 days of observation, while in patients of the main group, starting from the 5th day, a tendency to increase its level was recorded. The concentration of immunoglobulin M in patients of the control group remained unchanged, and in patients of the main group there was a significant decrease in concentration by the 8th day to  $3.2 \pm 0.2$  g/l.

The level of IgA was reduced during hospitalization: in patients in both groups, but with traditional treatment, it recovered only by 9-10 days, and in patients of the main group, stabilization of the IgA concentration began on days 3-4 after the start of treatment ( $4.55 \pm 0.44$  g/l).

Indicators of cellular immunity are the most demonstrative for characterizing the degree of damage and complications of purulent-inflammatory processes of the face and neck. First of all, this concerns the content of T- and B-lymphocytes in the peripheral blood of patients. In our observations, the ratio of T- and B-lymphocytes in patients of both groups upon admission to the hospital was destabilized quite significantly.

At the same time, the changes persisted until the end of the observation in both groups. However, in patients of the main group, after the appointment of phosphatidylcholine nanocapsules, the recovery of indicators was faster than in patients who received only traditional treatment. In patients of the main group, by day 8, the content of T- and B-lymphocytes was closer to physiological –  $41.2 \pm 0.5\%$  and  $56.7 \pm 0.5\%$ , respectively, which, in turn, led to normalization of humoral immunity in the form of restoration of the levels of immunoglobulins G, M and A in peripheral blood.

An indirect indicator of such a positive shift is the leukocyte index of intoxication. In patients of the control group, it remained at a high level until the end of the observation ( $1.8 \pm 0.1$  conditional units), while in patients of the main group, the trend towards its significantly more significant decrease begins to be traced already from the 6th day of treatment ( $1.5 \pm 0.2$  conditional units), which indicates the normalization of self-regulatory mechanisms that restore the body's immune status.

#### Conclusions.

Thus, the conducted clinical and laboratory studies in the postoperative period showed that the inclusion of phosphatidylcholine nanocapsules in the treatment regimen for patients with odontogenic phlegmon allows to normalize the state of general and local immunity, as a result of which the general condition of patients noticeably improves and the effectiveness of the treatment increases.

#### Prospects for further research.

In further studies, it is planned to investigate the effect of antihypoxants on the mechanisms of regeneration of a purulent wound in patients with odontogenic phlegmon.

## References

1. Böttger S, Zechel-Gran S, Schmermund D, Streckbein P, Wilbrand JF, Knitschke M, et al. Odontogenic Cervicofacial Necrotizing Fasciitis: Microbiological Characterization and Management of Four Clinical Cases. *Pathogens*. 2022 Jan 9;11(1):78. DOI: [10.3390/pathogens11010078](https://doi.org/10.3390/pathogens11010078).
2. Ferjaoui M, Kolsi N, Bergaoui E, Naouar M, Bouatay R, Harrathi K, et al. Odontogenic cervical-facial cellulitis: report of 87 cases. *J. Rev Med Liege*. 2022 Mar;77(3):181-186.
3. Bègue L, Schlund M, Raoul G, Ferri J, Lauwers L, Nicot R. Biological factors predicting the length of hospital stay in odontogenic cellulitis. *J Stomatol Oral Maxillofac Surg*. 2022;123(3):303-308. DOI: [10.1016/j.jormas.2021.07.007](https://doi.org/10.1016/j.jormas.2021.07.007).
4. Stevens DL, Bryant AE, Goldstein EJ. Necrotizing Soft Tissue Infections. *Infect. Dis. Clin. N. Am.* 2021;35:135-155. DOI: [10.1016/j.idc.2020.10.004](https://doi.org/10.1016/j.idc.2020.10.004).
5. Chou PY, Hsieh YH, Lin CH. Necrotizing fasciitis of the entire head and neck: Literature review and case report *Biomed. J.* 2020;43:94-98. DOI: [10.1016/j.bj.2019.08.002](https://doi.org/10.1016/j.bj.2019.08.002).
6. Kusumoto J, Iwata E, Huang W, Takata N, Tachibana A, Akashi M. Hematologic and inflammatory parameters for determining severity of odontogenic infections at admission: a retrospective study. *BMC Infect Dis*. 2022 Dec 12;22(1):931. DOI: [10.1186/s12879-022-07934-x](https://doi.org/10.1186/s12879-022-07934-x).
7. Zemplyeni K, Lopez B, Sardesai M, Dillon JK. Can progression of odontogenic infections to cervical necrotizing soft tissue infections be predicted? *Int J Oral Maxillofac Surg*. 2017;46:181-188. DOI: [10.1016/j.ijom.2016.09.016](https://doi.org/10.1016/j.ijom.2016.09.016).
8. Prabhu SR, Nirmalkumar ES. Acute fascial space infections of the neck: 1034 cases in 17 years follow up. *Ann Maxillofac Surg*. 2019;9:118-123. DOI: [10.4103/ams.ams\\_251\\_18](https://doi.org/10.4103/ams.ams_251_18).
9. Stathopoulos P, Igoumenakis D, Shuttleworth J, Smith W, Ameerally P. Predictive factors of hospital stay in patients with odontogenic maxillofacial infections: the role of C-reactive protein. *Br J Oral Maxillofac Surg*. 2017;55:367-370. DOI: [10.1016/j.bjoms.2016.11.004](https://doi.org/10.1016/j.bjoms.2016.11.004).

### ОСОБЛИВОСТІ ЗАСТОСУВАННЯ ПРЕПАРАТІВ З АНТИОКСИДАНТНОЮ ТА ІМУНОСТИМУЛЮЮЧОЮ ДІЄЮ У КОМПЛЕКСНОМУ ЛІКУВАННІ ПАЦІЄНТІВ З ОДОНТОГЕННИМИ ФЛЕГМОНАМИ

Варжапетян С. Д., Григоров С. М., Маланчук В. О.

**Резюме.** Натепер проблема консервативного лікування пацієнтів з одонтогенними флегмонами є не лише медичною, а й медико-соціальною проблемою, незважаючи на велику кількість досліджень у цій галузі щелепно-лицевої хірургії. Особливе місце займають дослідження, які проводяться з метою встановлення особливостей застосування у складі консервативної терапії флегмон препаратів, які мають антиоксидантну та імуностимулюючу дію. На сьогодні існує багато робіт як вітчизняних, так і закордонних вчених, в яких міститься інформація щодо застосування антиоксидантів та імуностимуляторів в якості монотерапії, а дані щодо їх комбінованого використання поодинокі та суперечливі. Метою даної роботи стало підвищення ефективності консервативного лікування хворих на одонтогенні флегмони шляхом включення до комплексної терапії нанокапсул фосфатидилхоліну. У дослідженні взяло участь 60 пацієнтів, які були поділені на дві групи по 30 осіб: у 1 групі лікування проводилося згідно стандартного протоколу, у 2-й – за протоколом з доповненням: до складу консервативної терапії входили внутрішньовенні ін'єкції ефективності консервативного лікування хворих з одонтогенними флегмонами шляхом включення до комплексної терапії нанокапсул фосфатидилхоліну. У процесі роботи були використані лабораторні методи дослідження. Доведено, що застосування нанокапсул фосфатидилхоліну в комплексному лікуванні пацієнтів 2-ї групи призводить до достовірного зниження кількості паличкоядерних нейтрофілів ( $2,5 \pm 0,1\%$ ) і підвищення вмісту лімфоцитів ( $24,3 \pm 0,4\%$ ). Слід також відмітити, що у пацієнтів другої групи на восьму добу післяопераційного періоду вміст Т- та В-лімфоцитів фіксується найближчим до норми, а саме  $41,2 \pm 0,5\%$  та  $56,7 \pm 0,5\%$  відповідно, що, призводить до оптимізації роботи імунної системи та є доказом ефективності використання авторської методики лікування.

Отримані результати склали лабораторну доказову базу ефективності застосування ефективності консервативного лікування хворих з одонтогенними флегмонами шляхом включення до комплексної терапії нанокапсул фосфатидилхоліну у складі комплексної терапії у пацієнтів з одонтогенними флегмонами.

**Ключові слова:** одонтогенна флегмона, комплексне лікування, консервативне лікування, регенерація гнійної рани, антиоксиданти та імуностимулятори.

### PECULIARITIES OF THE USE OF DRUGS WITH ANTIOXIDANT AND IMMUNOSTIMULATING ACTION IN THE COMPLEX TREATMENT OF PATIENTS WITH ODONTOGENIC PHLEGMONS

Varzhapetian S. D., Grigorov S. O., Malanchuk V. O.

**Abstract.** Currently, the problem of conservative treatment of patients with odontogenic phlegmons is not only a medical, but also a medical and social problem, despite the large number of studies in this field of maxillofacial surgery. A special place is occupied by studies conducted with the aim of establishing the specifics of the use of drugs that have antioxidant and immunostimulating effects as part of the conservative therapy of phlegmon. Today, there are many works of both domestic and foreign scientists, which contain information on the use of antioxidants and immunostimulants as monotherapy, and data on their combined use are isolated and contradictory. The aim of this work was to increase the effectiveness of conservative treatment of patients with odontogenic phlegmons by including phosphatidylcholine nanocapsules in complex therapy. 60 patients participated in the study, who were divided into two groups of 30 people each: in the 1st group, the treatment was carried out according to the standard protocol, in the 2nd – according to the protocol with an addition: the conservative therapy included intravenous injections of the effectiveness of the conservative treatment of patients with odontogenic phlegmons by including phosphatidylcholine nanocapsules in complex therapy. Clinical and laboratory research methods were used during the work. It was established that in group 2, the main indicators visualizing the dynamics of purulent wound healing decrease already on the 5-7th day of the postoperative period, with the appearance of granulations already on the  $6.8 \pm 0.3$  day. We recorded a complete cleansing of the wound in  $9.9 \pm 0.5$  days, and the average length of stay of the patient in the hospital was  $10.2 \pm 0.6$  days. It has been proven that the use of phosphatidylcholine nanocapsules in the complex treatment of patients of the 2nd group leads to a significant decrease in the number of rod-shaped

neutrophils ( $2.5 \pm 0.1\%$ ) and an increase in the content of lymphocytes ( $24.3 \pm 0.4\%$ ). It should also be noted that in patients of the second group, on the eighth day of the postoperative period, the content of T- and B-lymphocytes is recorded as the closest to the norm, namely  $41.2 \pm 0.5\%$  and  $56.7 \pm 0.5\%$ , respectively, which leads to optimize the work of the immune system and is proof of the effectiveness of using the author's method of treatment.

The obtained results formed a clinical and laboratory evidence base for the effectiveness of conservative treatment of patients with odontogenic phlegmons by including phosphatidylcholine nanocapsules in complex therapy as part of complex therapy in patients with odontogenic phlegmons.

**Key words:** odontogenic phlegmon, complex treatment, conservative treatment, purulent wound regeneration, antioxidants and immunostimulators

**ORCID and contributionship:**

Varzhapetian S. D.: [0000-0001-5649-1126](https://orcid.org/0000-0001-5649-1126)<sup>ADF</sup>

Grigorov S. O.: [0000-0001-9527-8408](https://orcid.org/0000-0001-9527-8408)<sup>BCE</sup>

Malanchuk V. O.: [0000-0001-8111-0436](https://orcid.org/0000-0001-8111-0436)<sup>EF</sup>

Conflict of interest:

The conflict of interests is absent in this article.

---

Corresponding author

Grigorov Sergiy Mykolayovych

Kharkiv National Medical University

Ukraine, 61022, Kharkiv, 4 Nauky av.

Tel.: +380951266514

E-mail: [li4man@i.ua](mailto:li4man@i.ua)

---

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

**Received 15.08.2022**

**Accepted 02.02.2023**