ANALYSIS OF THE STUDY OF 2% LIDOCAINE HYDROCHLORIDE SOLUTION HEPATOTOXICITY AT VARIOUS NUMBER OF INJECTIONS IN THE EXPERIMENT

Pohodenko-Chudakova I. O., Maksimovich E. V., Kuznetsov Y. O.

Abstract. The aim of the study was to analyze the differences in morphological preparations of liver tissue with different numbers of injections of 2% lidocaine hydrochloride solution into the head and neck region of experimental animals.

Objects and methods. Experimental studies were carried out on 10 male laboratory white mice, which were injected with a 2% solution of lidocaine hydrochloride according to the technique developed by us into the submandibular region (a variant of mandibular anesthesia with an extraoral access) every 3-4 days (1, 3, 7, 11, 15 days, total 5 injection) in average therapeutic doses, based on the data of clinical pharmacology. Liver tissue was taken from the objects withdrawn from the experiment for pathohistological examination.

Results. In the study of liver preparations, after the first injection of 2% lidocaine hydrochloride, multiple foci of necrosis of hepatocytes with or without perifocal inflammatory reaction, different in shape and size, were revealed. After second injection of local anesthetic, moderate parenchymal and interstitial edema, small foci of necrosis of hepatocytes, mainly centrilobular and near the central veins, with a perifocal cellular inflammatory reaction were observed morphologically. In single portal tracts, an inflammatory reaction and mild cholestasis are noted. After third injections of local anesthetic morphologically, the liver we revealed: plethora, foci of necrosis of hepatocytes with a perifocal inflammatory reaction, focal inflammatory infiltration of many portal tracts, moderate nuclear polymorphism, fatty degeneration of hepatocytes. After fourth injections of a 2% solution of lidocaine hydrochloride in liver preparations, we revealed plethora, small and large foci of necrosis of hepatocytes with a perifocal inflammatory reaction, focal inflammatory infiltration of the portal tracts, moderate nuclear polymorphism, fatty degeneration of hepatocytes. After fifth injections of local anesthetic in the liver, nuclear polymorphism was noted, multiple, mainly large, foci of necrosis of hepatocytes with a perifocal inflammatory reaction, inflammatory infiltration of the portal tracts, intraductal, cholestasis, inflammatory infiltration around the central veins, eosinophilic intranuclear inclusions were detected in some nuclei hepatocytes.

Conclusion. As a result of the study, it was revealed that even after the firstinjection of a 2% solution of lidocaine hydrochloride, hepatotoxicity was detected, and it increases with the number of injections of this local anesthetic in the head and neck region.

Keywords: hepatotoxicity, 2% lidocaine hydrochloride solution, experimental studies.

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COMPARATIVE ASSESSMENT OF DYNAMICS OF INFLAMMATORY INFILTRATE AREA IN PATIENTS WITH BOILS IN MAXILLOFACIAL AREA AND NECK WITH DIFFERENT APPROACHES TO COMPLEX POSTOPERATIVE TREATMENT

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The connection of the publication with planned research works. The topic of scientific research work of the Department of Oral Surgery of the educational institution "Belarusian State Medical University" in 2018-2022 is "Prediction, diagnostics, treatment, prevention of complications and rehabilitation of patients with surgical pathology of the maxillofacial region" (State register No. 20180755 of 25.05.2018).

Introduction. The most common non-endogenous inflammatory diseases of the maxillofacial region include boils [1]. Questions related to the development of this pathology are relevant not only for dental surgeons, maxillofacial surgeons and otorhinolaryngologists, but also for general surgeons and dermatologists [2].

Special attention should be paid to the rehabilitation of patients with boils in the maxillofacial region and neck, since incisions during primary surgical treatment (PST) of the infectious and inflammatory focus are carried out by external access. Taking this into account, it is necessary to strive for the most aesthetic result of surgical treatment in the shortest possible time, in order to prevent psychodogic discomfort in this category of patients [3, 4].

At the same time, the issue of wound healing and treatment remains one of the most urgent in modern medicine. The big difficulties in the trratment of these patients are diagnosis, prediction of the course of the pathological process, determination of adequate tactics, subject to strict compliance with the basic principles of treatment of purulent wounds and wound infection. It should be emphasized that the limited possibility of using standard methods of treatment and prevention of complications is associated with an increase in the number of observations of allergic reactions in the population. This fact is the reason for attracting non-drug

therapeutic effects, including acupuncture, to the practice of maxillofacial surgeons [5, 6, 7, 8].

At present, the method of electro-acupuncture therapy (EAT) has found wide application in somatic diseases [9], and has also become widely used in the postoperative treatment and medical rehabilitation of patients with surgical pathology of the maxillofacial region and neck [10, 11], including patients with infectious and inflammatory processes of non-ontogenic origin [12]. EAT has advantages over classical acupuncture, as it is non-invasive, non-traumatic and well tolerated by patients. In addition, most devices designed for electroacupuncture have a number of additional functions that allow to search for acupuncture points (AP), conduct microelectrophoresis of medicinal products in the projection of AP, as well as act on several AP simultaneously, exerting an action in the mode of automatic switching of the current polarity, constant, pulsed and modulated currents [13].

However, in the available sources of special literature, there is no information about studies containing the results of the use of electroacupuncture in the complex treatment of boils of the maxillofacial area and neck. There is no data on the results of comparison when using EAT as part of a complex treatment with the standard complex treatment of this disease.

Each of facts, as well as all of them together justify the expediency of the undertaken research and confirm its relevance.

The aim of the study was to perform a comparative assessment of the area of inflammatory infiltrate in patients with a boil of the maxillofacial region and neck in dynamics during standard postoperative treatment and when used in the treatment and rehabilitation complex of electroacupuncture therapy.

Object and methods of the research. The area of inflammatory infiltrate was measured in 40 patients with a diagnosis of maxillofacial and neck furuncle, whose age ranged from 18 to 58 years. All patients were divided into 2 groups, each of which included 10 men and 10 women.

The study was performed in accordance with the basic bioethical norms of the Helsinki Declaration of the World Medical Association on the Ethical Principles of Medical Research, as amended (2000, as amended in 2008), the Universal Declaration on Bioethics and Human Rights (1997), the Council of Europe Convention on Human Rights and Biomedicine (1997) [14]. All necessary measures were taken to ensure the anonymity of patients.

The study was preceded by a positive conclusion of the bioethical commission of the Belarusian State Medical University.

The conditions for inclusion of patients in the study included the following items: age over 18 years; diagnosis-maxillofacial furuncle; absence of a history of somatic diseases, injuries, operations (except for the PST performed on the maxillofacial furuncle); availability of voluntary informed consent to participate in the study.

The first group received standard complex treatment which included carrying out PST of the infectious and inflammatory focus, followed by daily dressings with drainage replacement, a anti-inflammatory drug therapy (antibacterial, antihistamines, general tonic drugs and antiplatelet agent-acetylsalicylic acid ("Aspirin")). Also, after the acute phase of inflammation was stopped, the wound was cleaned and the growth of granulations began, patients were prescribed physiotherapy [15].

In the second group of patients, the standard course of treatment was carried out in the same volume. However, instead of physical therapy, a course of EAT was prescribed, in which the effect was carried out in accordance with the instructions for use by I. O. Pohodenko-Chudakova, M. S. Fleryanovitch, A. P. Sivakov (2021) [16].

Since the inflammatory process develops around the hair follicle in boils in most cases the infiltrate has the shape of a circle, therefore its area was calculated using the following formula:

$$S=\pi r^2, \quad (1)$$

where S is the area of the circle (cm^2), π is a number equal to 3.14, and r is the radius of the circle (cm). The measurements were carried out using a caliper, pretreated with an antiseptic solution. The data obtained was fixed in square centimeters (cm^2) [17].

This examination was carried out in dynamics three times during daily dressings of patients with boils of the maxillofacial region and neck: the 1st study – before the surgical stage of treatment; the 2nd study – on the 3rd day after the PHO of the infectious and inflammatory focus; the 3rd study – on the 5th day after the operation.

The obtained data were subjected to statistical processing using the application software package "Statistica 10.0" and "Exel". The median (Me), lower 25th and upper 75th quartiles were calculated. The Wilcoxon test (T) and the Friedman test – $\chi 2$ (chi-square) were used to compare the differences in the dependent variables in dynamics. Based on the Mann-Whitney test (U-test), two samples of quantitative data were compared. The obtained result was considered statistically significant if the probability of differences did not exceed 5% ($p<0.05$) [18].

The results of the study and their discussion. In the course of the study, it was found that the average age of patients in the first group was 31.0 (26.0-35.0) years, and the second – 22.0 (20.0-32.0), with $\chi^2=3.42$; $p=0.038$. Thus, these groups had no significant differences in age.

In the 1st study in patients of the first group, the size of the infiltrate was 4.5 (3.9-5.0) cm^2, in patients of the second group it was 4.3 (3.9-5.1) cm^2. Using the Kruskal-Wallis test ($H=0.0018$; $p=0.97$), there were no significant differences between the selected groups.

In the 2nd study, patients of the same group showed a decrease in the average value of the infiltrate area to 4.10 (3.9-4.6) cm^2, but it was not reliable relative to the Wilcoxon test when compared with the results of the 1st study.

In the 3rd study, the area of the inflammatory infiltrate decreased to 2.9 (2.0-3.0) cm^2, which was significant ($T2\text{-}3=0.0$; $p<0.001$). At the same time, assessing the dynamics of the indicator from the 1st study to the 3rd in the first group, based on the Friedman criterion, where $\chi^2=35.74$; $p<0.001$, a significant decrease in the area of the infectious and inflammatory focus was found.

In patients of the second group, the median value of the infiltrate area in the 2nd study was 3.5 (3.0-4.0) cm^2 and was characterized by a significant decrease in com-

parison with the 1st study according to the Wilcoxon criterion (T1-2=0.0; p<0.001).

In the 3rd study, the size of the infiltrate was 2.9 (2.0-3.0) cm^2, which also indicated a significant decrease in its area

(T2-3=0.0; p<0.001). Assessing the dynamics of the indicator from the 1st study to the 3rd in the second group, based on the Friedman criterion, where χ^2=40.0; p<0.001, there are grounds to conclude that the dynamics was directed towards a decrease in the area of infectious and inflammatory infiltrate.

At the same time, when comparing the results of two groups of patients with a boil of the maxillofacial region and neck, in the 2nd study, a significant difference was found in the indicators with a predominance of positive changes in persons belonging to the second group (U=73.0; p=0.001).

The achieved result in the second group was stable, as evidenced by the comparative assessment carried out in the 3rd study according to the Mann-Whitney criterion (U=52.0; p<0.001).

The results of the performed studies in patients with boils of the maxillofacial region and neck demonstrate a significant reduction in the area of inflammatory infiltrate in both selected groups of patients. At the same time, in the first group, a directed decrease in the value of the infiltrate area was observed only on the 5th day of observation in the postoperative period. At the same time, in patients of the second group, similar changes were detected in the 2nd study – 2 days earlier. Taking into account the fact that the groups of patients were comparable in terms of gender, age, somatic status and the standard set of treatment and rehabilitation measures, the positive result obtained in the second group of patients can be fully attributed to the use of electroacupuncture in the treatment. This is consistent with the results of experimental studies [19] and does not contradict the information presented in the available specialized literature [2, 20].

Conclusion. A comparative comparison of the dynamics of the area of inflammatory infiltrate in patients with furuncles of the maxillofacial region and neck during standard postoperative treatment and when used in the treatment and rehabilitation complex of electroacupuncture revealed the advantage of using the latter, providing the ability to stop the inflammatory infiltrate two days earlier. This will improve both immediate and long-term treatment outcomes, improve the patient's quality of life, and increase the level of specialized medical care provided to the general population.

The prospect of further research. The presented results are the actual justification for the study of the clinical effectiveness of the use of electroacupuncture as part of a complex of therapeutic and rehabilitation measures in patients with boils of the maxillofacial region and neck both at the end of the course of inpatient treatment and in the long-term period which will be the basis for recommending a wider introduction of the method into clinical practice for providing specialized medical care to patients of this category.

References

1. Shallcross LJ, Hayward AC, Johnson AM, Petersen I. Incidence and recurrence of boils and abscesses within the first year: a cohort study in UK primary care. Br. J. Gen. Pract. 2015;639(65):668-76. doi: 10.3399/bjgp15 X686929.
2. Bakshi SS. Image diagnosis: nasal furunculosis – a dangerous nose infection. Perm J. 2018;22:17-076. doi: 10.7812/TPP/17-076.
3. Hay RA, Shalaby K, Zaher H, Hafez V, Chi ChChi, Dimitri S, et al. Interventions for acne scars. Cochrane Database Syst. Rev. 2016;4:CD011946. doi: 10.1002/14651858.CD011946.pub2.
4. Afra TP, Razmi TM, Narang T, Dogra S, Kumar A. Topical tazarotene gel, 0.1%, as a novel treatment approach for atrophic postacne Scars: a randomized active-controlled clinical trial. JAMA Facial Plast. Surg. 2019;21(2):125-32. doi: 10.1001/jamafacial.2018.1404.
5. Naik PN, Kiran RA, Yalamanchal S, Kumar VA, Goli S, Vashist N. Acupuncture: an alternative therapy in dentistry and its possible applications. Med. Acupunct. 2014;26(6):308-14. doi: 10.1089/acu.2014. 1028.
6. Gemma M, Nicelli E, GioiaL, MoizoE, BerettaL, Calvi MR. Acupuncture accelerates recovery after general anesthesia: a prospective randomized controlled trial. J. of Integrat. Med. 2015;13(2):99-104. doi: 10.1016/S2095-4964(15)60159-5.
7. Park JiY, Namgung UK. Electroacupuncture therapy in inflammation regulation: current perspectives. J. Inflamm. Res. 2018;11:227-37. doi: 10.2147/JIR.S141198.
8. Mi JP, He P, Shen F, Yang X, Zhao MF, Chen XY. Efficacy of acupuncture at the sphenopalatine ganglion in the treatment of persistent allergic rhinitis. Med Acupunct. 2020;32(2):90-8. doi: 10.1089/acu.2019.1373.
9. Kong JTi, Puetz Ch, Tian L, Haynes I, Lee E, Stafford RS, et al. Effect of electroacupuncture vs sham treatment on change in pain severity among adults with chronic low back pain: a randomized clinical trial. JAMA Netw Open. 2020;10(3):e2022787. doi: 10.1001/jamanetworkopen.2020.22787.
10. Razakov DH, Konnov VV, Arushanjan AR, Pichugina EN, Popko ES. Rol' dinamicheskoj jelektronejrostimuljacii v kompleksnom lechenii myshechno-sustavnoj disfunkcii pacientov s deformacijami zubnyh rjadov i prikusa. Sovremennyye problemy nauki i obrazovaniya. 2015;6:1. Available from: http://science-education.ru/ru/article/view?id=23542. [in Russian].
11. Pohodenko-Chudakova IO, Surin AV. Izmenenie biohimicheskih pokazatelej rotovoj zhidkosti pri ispol'zovaniij elektrorefleksoterapii v sostave kompleksnogo lechenija hronicheskogo odotogennogo sinusita verhnecheljustnoj pazuhi. Meditsinskiye novosti. 2018;12:45-7. [in Russian].
12. Pohodenko-Chudakova IO, Avdeeva EA. Sovremennye vozmozhnosti kompleksnogo lechenija travmaticheskih povrezhdenij periphericheskih vetvej trojnichnogo nerva. Novosti Khirurgii. 2010;18(2):123-32. [in Russian].
13. Sivakov AP, Podsadchik LV, Mankevich SM, Grekova TI. Vnekanal'nye tochki akupunktury: ucheb.-metod. posobie. Minsk: BelMAPO; 2018. 32 s. [in Russian].
14. Kotlyarov II, Kozlova AA. Mezhdunarodnoe pravovoe regulirovanie zashhity prav cheloveka v sfere biomediciny v ramkah Soveta Evropy. Vestnik Moskovskogo universiteta MVD Rossii. 2020;7:200-4. doi: 10.24411/2073-0454-2020-10415. [in Russian].
15. Durnovo EA. Klinicheskaja diagnostika i algoritm lechenija vospalitel'nyh zabolevanij i travmaticheskih povrezhdenij cheljustno-licevoj oblasti: ucheb.-metod. posobie. N. Novgorod: NizhGMA; 2016. 124 s. [in Russian].
16. Pohodenko-Chudakova IO, Fler'janovich MS, Sivakov AP, izobretatel'; BSMU, patentoobladatel'. Metod lechenija pacientov s furunkulami cheljustno-licevoj oblasti i shei s ispol'zovaniem jelektroakupunktury. Patent Respubliki Belarus' № 192-1220. 2021 Yanv 28. [in Russian].
17. Balajan JeN. Repetitor po geometrii dlja 7-9 klassov. Rostov-na-Donu: Feniks; 2021. 359 s. [in Russian].
18. Truhacheva NV. Medicinskaja statistika: uchebnoe posobie. Rostov na Donu: Feniks; 2017. 324 s. [in Russian].
19. Pohodenko-Chudakova IO, Fler'janovich MS, Moiseeva AM. Dinamika immunologicheskih pokazatelej syvorotki krovi u jeksperimental'nyh zhivotnyh s model'ju furunkula v oblasti golovy ishei pri razlichnyh podhodah k kompleksnomu lecheniju. Sovremennaya stomatologiya. 2021;82(1):59-62. [in Russian].

20. Kovalevskiy AM, Bocharnikov AA. Vozmozhnost' primenenija refleksoterapii, girudoterapii v lechenii posleoperacionnyh oslozhnenij v cheljustno-licevoj hirurgii. Obzor literatury. Institut stomatologii. 2017;76(3):88-92. [in Russian].

ПОРІВНЯЛЬНА ОЦІНКА ДИНАМІКИ ПЛОЩІ ЗАПАЛЬНОГО ІНФІЛЬТРАТУ У ПАЦІЄНТІВЗ ФУРУНКУЛАМИ ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ ТА ШИЇ ПРИ РІЗНИХ ПІДХОДАХ ДО КОМПЛЕКСНОГО ПІСЛЯОПЕРАЦІЙНОГО ЛІКУВАННЯ

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Резюме. *Вступ.* До найбільш часто виникаючих неодонтогенних запальних захворювань щелепно-лицевої ділянки відносять фурункули. *Мета* дослідження – здійснити порівняльну оцінку площі запального інфільтрату у пацієнтів з фурункулом щелепно-лицевої ділянки та шиї в динаміці при проведенні стандартного лікування і при використанні в його складі електрорефлексотерапії (ЕРТ). *Об'єкти і методи***.** Дослідження проводили у 40 пацієнтів з діагнозом фурункул щелепно-лицевої ділянки та шиї, віком 18-58 років. Всі пацієнти були розділені на дві групи, кожна з яких включала 10 чоловіків і 10 жінок. Перша группа отримувала стандартнее комплексне лікування (первинну хірургічну обробку інфекційно-запального вогнища, з подальшими щоденними перев'язками із заміною дренажу, курсом протизапальної лікарської терапії, фізіотерапією). Пацієнтам другої групи у складі курсу лікування замість фізіотерапії призначали ЕРТ. Оскільки при фурункулах запальний інфільтрат має форму кола, то його площу обчислювали за формулою площі кола. Обстеження проводили тричі: до операції, на 3 добу і на 5 добу після операції. Отримані дані опрацьовувалися статистично. *Результати* демонструють достовірне зменшення площі запального інфільтрату в осіб обох груп. При цьому у першої групи, спрямоване зменшення площі інфільтрату було відзначено на 5 добу після операції. У той же час у пацієнтів другої групи подібні зміни були виявлені на дві доби раніше. З урахуванням того, що групи пацієнтів були порівнянні за статтю, віком, соматичним статусом і проведеним стандартним лікуванням, отриманий позитивний результат у осіб другої групи може бути віднесений на рахунок ЕРТ. *Висновок.* Порівняльна оцінка динаміки зміни площі запального інфільтрату у пацієнтів з фурункулом щелепно-лицевої ділянки і шиї при проведенні стандартного післяопераційного лікування і при використанні в його складі ЕРТ виявило перевагу застосування останньої, що забезпечує можливість на дві доби раніше купірувати запальний інфільтрат, покращує безпосередній і віддалений результати лікування, підвищує якість життя пацієнтів. *Перспектива подальших досліджень.* Представлені результати є фактичним обґрунтуванням для дослідження клінічної ефективності застосування ЕРТ у складі комплексу лікувально-реабілітаційних заходів у пацієнтів з фурункулами щелепно-лицевої ділянки та шиї як при завершенні курсу стаціонарного лікування, так і у віддаленому періоді, що буде підставою для рекомендації більш широкого впровадження методу в клінічну практику для надання спеціалізованої медичної допомоги хворим зазначеної категорії.

Ключові слова: запальний інфільтрат, фурункул, щелепно-лицьова ділянка, післяопераційне лікування, площа інфільтрату.

COMPARATIVE ASSESSMENT OF DYNAMICS OF INFLAMMATORY INFILTRATE AREA IN PATIENTSWITH BOILS IN MAXILLOFACIAL AREA AND NECKWITH DIFFERENT APPROACHES TO COMPLEX POSTOPERATIVE TREATMENT

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Abstract. The aim of the work is to carry out a comparative assessment of the area of inflammatory infiltrate in patients with furuncles in the maxillofacial area and neck in dynamics during standard treatment and when using electro-acupuncture therapy (EAT) in its composition. **Objects and methods.** The study was carried out in 40 patients with diagnosis of furuncle of the maxillofacial region and neck, aged 18-58 years. All patients were divided into two groups, each consisting of 10 men and 10 women. The first group received standard complex treatment (primary surgical treatment of an infectious and inflammatory focus followed by daily dressings with drainage replacement, a course of anti-inflammatory drug therapy, and physical therapy). The second group has EAT instead of physiotherapy. Since the inflammatory infiltrate in boils has the shape of a circle, its area was calculated using the formula of the area of the circle. The examination was performed three times: before the operation, on the 3rd day and on the 5th day after the operation. The obtained data were subjected to statistical processing. **The results** show a significant reduction in the area of inflammatory infiltrate in both groups. At the same time, in the first group, a directed decrease in the area of the infiltrate was noted on the 5th day after the operation. At the same time, in patients of the second group, such changes were found 2 days earlier. Taking into account the fact that the groups of patients were comparable in gender, age, somatic status and standard treatment, the positive result obtained in the second group can be attributed to EAT. **Conclusion.** Comparative assessment of the dynamics of the area of inflammatory infiltrate in patients with a boil of the maxillofacial region and neck during standard postoperative treatment and when using EAT in its composition revealed the advantage of using the latter which provides an opportunity to stop the inflammatory infiltrate two days earlier, improves the immediate and long-term results of treatment, improves the quality of life of patients.

Keywords: inflammatory infiltrate, furuncle, maxillofacial area, postoperative treatment, infiltrate area.

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