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T.V. Horodova-Andrieieva, V.I. Liakhovskiy, A.V. Sydorenko
Poltava State Medical University, Poltava

INFLUENCE OF VACUUM INSTILLATIONS WITH INTRAVENOUS INTRODUCTION OF NITROGEN OXIDE DONATORS ON THE HEALING OF PURULENT SOFT TISSUE WOUNDS

e-mail: gorodova78@gmail.com

The efficacy of vacuum therapy with instillations of L-arginine was studied in combination with its intravenous infusion. Results were in 89 patients, treated for purulent-necrotic soft tissue diseases. Patients were emergency operated on. The main group - 44 patients, got the same therapy and intravenous 100 ml of arginine hydrochloride solution daily. 2-3 courses of vacuum therapy, 3 days each were performed. In the main group, signs of intoxication and body temperature returned to normal by an average of 3.1 days. Normalization of the level of leukocytes was observed in 5.4 days. pH-metry from the wound surface, it was found that significant changes in the average pH of patients in the main group were observed for 7-10 days - the beginning of the regeneration phase. The therapy in the main group in comparison with typical local treatment provided accelerated wound cleansing, reduction of microbial contamination and faster transition of purulent-necrotic phase to regeneration.

Key words: purulent-necrotic diseases, vacuum therapy, instillations, arginine, wound healing.

Т.В. Городова-Андрєєва, В.І. Ляховський, А.В. Сидоренко

ВПЛИВ ВАКУУМІНСТИЛЯЦІЙ З ВНУТРІШНЬОВЕННИМ ВВЕДЕННЯМ ДОНАТОРІВ ОКСИДУ АЗОТУ НА ЗАГОЄННЯ ГНІЙНИХ РАН М'ЯКИХ ТКАНИН

Вивчена ефективність вакуумної терапії інстиляціями L-аргініну в поєднанні з його внутрішньовенним вливанням. Отримано результати у 89 пацієнтів, які проходили лікування з приводу гнійно-некротичних захворювань м'яких тканин. Хворих екстрено прооперували. Основна група - 44 пацієнти, які отримували таку ж терапію та внутрішньовенно вводили 100 мл розчину аргініну гідрохлориду щодня. 2-3 курси вакуум-терапії по 3 дні кожен. В основній групі ознаки інтоксикації та температура тіла нормалізувалися в середньому на 3,1 доби. Нормалізація рівня лейкоцитів спостерігалася через 5,4 доби. рН-метрією з поверхні рани було виявлено, що достовірні зміни середнього рН у пацієнтів основної групи спостерігалися протягом 7-10 днів - початку фази регенерації. Терапія в основній групі в порівнянні з типовим місцевим лікуванням забезпечувала прискорене очищення рани, зменшення мікробного забруднення та швидший перехід гнійно-некротичної фази в регенеративну.

Ключові слова: гнійно-некротичні захворювання, вакуумна терапія, інстиляції, аргінін, загоєння ран.

The study is a part of the research project "Development of modern scientifically based principles of stratification, monitoring and prediction of surgical diseases and injuries", state registration number 0120U101176.

Despite advances in medicine, wounds healing remains one of the main problems of surgery. Depending on the size and causes of their occurrence, a variety of methods are used. One of them is the use of vacuum therapy [2, 8].

In the present day, it's an innovative method of wound healing, which accelerates the terms of the wound-healing process. The anti-inflammatory effect of its use has been proven in studies compared with typical wound healing, the level of the anti-inflammatory cytokine interleukin 10 (IL-10) is slightly higher [8], and microbial contamination is reduced by removing excess exudate [11].

The next stage of treatment is the connection of the drainage-flushing and vacuum systems [3]. Foreign literature calls this method vacuum instillation therapy (Vacuum Instillation Therapy). The arsenal of drugs for such therapy is wide [4, 6]. One of these drugs is L-arginine (L-arginine hydrochloride).

Arginine (α -amino- δ -guanidine-valeric acid) is one of the most polarized, positively charged amino acids. Metabolism occurs in two alternative ways.

The simultaneous course of these processes is possible. Hydrolysis by bacteria from arginine forms agmatine, a highly alkaline amine. This explains the antimicrobial effect [1]. Peptides, interacting with the microbial membrane, change its structure and permeability [9]. Their mechanism of action is universal, and as a result of which they are harmful even to microorganisms that got resistant to antibiotics. This reduces the growth of microflora and promotes healing. During the cyclization of the arginine derivative glutamate, proline is formed, which is a component of the connective tissue, and hydroxyproline is synthesized from it [5]. Due to this, the use of arginine in tissues improves the course of the healing process, which is important in the earlier postoperative period.

There are mechanisms by which arginine has a positive effect on wound healing. The compound is metabolized by NO-synthetase to nitric monoxide (NO), and being an active radical, NO interacts with oxygen and forms peroxynitrite (OONO), which has an antimicrobial effect by the attack and destruction of biomolecules. In addition, NO dilates blood vessels, raising blood circulation [9, 10]. At the same time, it is metabolized with the synthesizing of ornithine, which turns into polyamines necessary for cell growth and is the origin of proline and hydroxyproline necessary for collagen synthesis [7].

Both groups of effects restore cells and intercellular substances. Wounds after the occurrence need natural and/or artificial hemostasis, after which healing happens. During the induction phase of inflammation, NO increases the content of chemoattractive cytokines in the wound, such as IL-8, TGF-1, and others. These cytokines have an attractive role for neutrophils and, with some delay, monocytes. The function of neutrophils is reduced to phagocytosis of bacteria and necrotic tissues. Monocytes in the wound turn into macrophages and phagocytize apoptotic neutrophils, which leads to the completion of the inflammation phase. NO increases the proliferation of other fibroblast and keratinocyte cells. This accelerates re-epithelialization and provides faster closure of the skin. NO has the ability to accelerate collagen synthesis, which helps to quickly recover the extracellular matrix.

The foregoing suggests that NO is a regulatory molecule that accompanies healing. Both inducible (iNOS) and endothelial (eNOS) isoforms of NO-synthase are often involved in NO production, although their contribution to wound healing may vary. Therefore, the study of the effect of nitrogen donors on the healing of purulent wounds remains relevant.

The purpose of the study was to evaluate the effectiveness of vacuum therapy with instillations of L-arginine in combination with intravenous infusion of a nitric oxide donor for clearing and healing purulent wounds of soft tissues.

Materials and methods. The study included 89 patients who had purulent-necrotic soft tissue damage and were hospitalized in the surgical department No. 1 of the CE "2nd City Clinical Hospital of the Poltava City Council" during 2018-2021. All patients were received to the department for emergency reasons. When examining patients in both groups, an increase in body temperature, hyperemia and local hyperthermia of the skin, a painful and dense infiltrate were observed. In 34 (38.2 %) patients, the area of softening was clearly defined, that is, a positive symptom of fluctuation was observed.

Before surgery, all patients had a comprehensive examination, which included: an objective examination, laboratory general blood and urine tests, a biochemical blood test, serum glucose, coagulation test and instrumental methods of ECG, the US of soft tissues, radiographs of affected zones.

All patients got surgery on urgently on the day of hospitalization. Surgical treatment, depending on the localization, the prevalence of the pathological process and the expression of the intoxication, was performed with local infiltrative, conduction, spinal anesthesia or intravenous anesthesia. During the intervention, a wide opening, sanitation and drainage of the purulent site was carried out without suturing the postoperative defect. The contents were taken for bacteriological tests and the sensitivity of microorganisms to antibiotics.

Postoperative treatment of patients in both groups included antibacterial therapy (mainly drugs from the groups of cephalosporins and fluoroquinolones in combination with metronidazole), the correction of which, if necessary, was carried after receiving the results of a microbiological study to determine sensitivity to antibiotics, and, according to indications, detoxification therapy was performed.

However, depending on the additional methods of patients treatment in the postoperative period, they were divided into two groups: the main group and the comparison group. The main group included 44 patients who, starting from the second day of treatment, were treated with vacuum therapy with instillations of L-arginine ("Tivortin", solution for infusion 42 mg/ml; "Yuria-Pharm" LLC, Ukraine) according to the method we developed in for 2-3 sessions lasting 3 days each [5] and additionally performed intravenous

infusion of 100 ml of the same solution daily. The comparison group included 45 patients who, in the postoperative period, starting from the second day, got vacuum therapy sessions according to the typically method. Conservative drug treatment in both groups did not fundamentally differ. During treatment, 2-3 courses of vacuum therapy were used, each lasting 3 days.

The main group included 19 (43.2 %) men and 25 (56.8 %) women, mean 48 ± 0.9 years, body mass index 27.2 ± 2.35 . The comparison group included 21 (46.6 %) men and 24 (53.4 %) women with an average body mass index of 28.4 ± 2.74 and an average age of 51.89 ± 0.8 years.

Purulent-necrotic processes were localized on the hand in 4 (9.0 %) patients of the main group and in 4 (8.8 %) of the comparison group. On the buttock in 11 (25 %) patients of the main group and in 10 (22.2 %) of the comparison group. In addition, abscesses were located on the thigh in 8 (18.2 %) persons of the main group and in 9 (20.0 %) of the comparison group. Below knee in 12 (27.3 %) patients of the main group and in 14 (31.8 %) of the comparison group. On the foot in 9 (20.5 %) patients of the main group and in 8 (17.8 %) of the comparison group. The duration of the disease during hospitalization averaged 3.4 ± 0.66 days. However, the majority of patients (86.4 % of the main group and 88.9 % of the comparison group) were hospitalized within 2 to 3 days from the beginning of illness.

Statistical analysis is performed using the "Statistica" 6.0 software (StatSoft Ins, USA). To assess the statistics, the Mann-Whitney U-test and Student's t-test, the results of the assessment are significant at $p < 0.05$.

Results of the study and their discussion. The proposed methodics for the use of vacuum therapy with instillations of L-arginine with additional intravenous infusion of 100 ml of arginine hydrochloride solution once a day, compared with the traditional treatment of purulent wounds of soft tissues, had a more favorable effect on the course of the postoperative period. Thus, in patients of the main group, clinical signs of intoxication and body temperature returned to normal on an average of 3.1 ± 0.34 days, while in the comparison group, subfebrile temperature was observed on average for 5.7 ± 0.68 days ($p < 0.05$) after the surgery. The same changes happened with local signs of inflammation. Thus, in patients of the main group, such local signs as skin hyperemia and edema gone on average by 4.2 ± 0.46 days, and in persons of the comparison group - by 7.4 ± 0.82 days ($p < 0.05$) after the surgery. There was no next spread of the purulent-inflammatory process in patients of both study groups.

In addition, in patients of the main group, there was a faster, compared with patients in the comparison group, normalization of the parameters of general blood test. Thus, a decrease in the number of leukocytes in general blood test of patients of the main group began on average from 2.9 ± 0.38 days, and in patients of the group compared with 5.2 ± 0.54 days ($p < 0.05$). Normalization of blood leukocytes in patients of the main group was observed on average from 5.4 ± 0.74 days, and in patients of the group compared with 7.8 ± 0.86 days ($p < 0.05$). Also, the indicators of the leukocyte index of intoxication decreased, which were in patients of the main group, starting on average from 3.5 ± 0.48 days, significantly ($p < 0.05$) lower than in patients of the comparison group.

A microbiological study of contents from the surgical wound showed that in all patients of both study groups, the level of microbial contamination before the start of local treatment was in the range of 106-107 per 1 g of tissue, which significantly exceeded the critical level. So, in case of opening abscesses in patients of the main group, the average value of colony forming units per 1 g of tissue (CFU/g) was $2.3 \pm 0.74 \times 10^7$, and in patients of the comparison group this value was $9.6 \pm 0.74 \times 10^6$ ($p > 0.05$). In the study of the composition of the microflora of purulent wounds in patients of the main group on the first day, a significant increase in *S. aureus*, isolated in 30 (68.2 %), and *Enterobacter* in 10 (22.8 %), *Proteus* in 2 (4.5 %), *Accinetobacter* in 2 (4.5 %) people. In patients of the main group, combinations of *Enterobacter* and *E. fecalis* prevailed in microbial associations, which were sown in 30 (68.2 %) patients. In patients of the comparison group, monoculture was obtained in 31 (68.9 %), and microbial associations were similar to those found in patients of the main group. In 29 (64.4 %) people, *St. aureus*, 9 (20 %) *Enterobacter*, 5 (11.1 %) *Accinetobacter* and 2 (4.5 %) *Proteus*.

In 10 (22.7 %) patients of the main group, bacteria were isolated on the 4th day of the postoperative period, and as a monoculture in 6 (13.6 %, *St. Aureus*), and associations (combination of *St. epidermidis* and *E. Fecalis*) in 4 (9.1 %) people. Their number averaged $4.6 \pm 1.48 \times 10^4$ CFU/h. In the same period of the study, 10 (22.2 %) patients of the comparison group had isolated bacteria as a monoculture with a microbial number, which averaged $6.9 \pm 2.07 \times 10^5$ CFU/g ($p < 0.05$), and 5 (11.1 %) patients of this group experienced the formation of new bacterial mixed associations by the addition of new strains (*Klebsiella*, *E. coli*, *S. Epidermidis*). On the 7th day of the study, no microflora was gotten from wounds in patients, and in patients of the comparison group, monoculture was found in 7 (15.6 %) patients, and microbial associations in 3 (6.7 %) patients.

When conducting pH-metry from wounds, it was based that before the start of vacuum therapy, it averaged 5.54 ± 0.37 in patients of the main group, and in patients of the comparison group 5.22 ± 0.29 ($p > 0.05$). After the first session of vacuum therapy on day 4, the average pH did not change significantly

in patients of both groups. On the 7th day after the second session of vacuum therapy, an increase in the average pH of the wound to 6.73 ± 0.31 was observed in patients of the main group, while in patients of the comparison group there was a slight increase in this indicator to 5.98 ± 0.28 ($p > 0.05$). At the end of the course of vacuum therapy, on the 10th day of monitoring, in patients of the main group, there is an increase in the pH of the wound content below the initial value, and on average it is 7.33 ± 0.36 , and in the comparison group this average indicator reached the level of $6,42 \pm 0.32$ ($p < 0.05$). Significant changes in the average values of pH-metry in patients of the main group were observed on days 7-10, which corresponded to the beginning of the regeneration phase of the wound process.

Consequently, in patients of the main group the wound cleaning with the forming of granulations, were observed starting on average from 3.6 ± 1.87 days of the postoperative period, and in patients of the comparison group, such changes began to form on average from 5.3 ± 2.05 days. The average hospital-day in the surgical department of patients in the main group was 12.57 ± 1.32 , and in patients of the comparison group 15.93 ($p < 0.05$).

Thus, the data of our study prove that the local use of vacuum therapy with L-arginine instillations with additional intravenous infusion of 100 ml of arginine hydrochloride solution daily, significantly refines the course of the postoperative period compared to traditional methods of healing soft tissue purulent wounds. At the same time, the signs of intoxication decreased and no further spread of the purulent-inflammatory process was observed. These data completely coincide with the data of O.V. Storozhenko and authors [8]. By reducing the exudation by purulent wounds, the level of contamination of microorganisms is reduced, which also confirms the opinion of other scientists [11]. In addition, at the end of the proposed course of treatment with the use of vacuum instillation therapy, patients showed a significant increase in the pH of the wound content below the initial value, which corresponded an earlier onset of the regeneration phase and the forming of granulations in the wounds, compared with patients who underwent traditional local and general treatment. And the average hospital-day of inpatient treatment was significantly less in patients of the main group compared to patients in the comparison group. These data suggest that in case of purulent wounds of soft tissues under the effect of vacuum therapy with instillations of L-arginine with intravenous infusion of 100 ml of arginine hydrochloride solution daily, processes occur that reduce the growth of microflora and help the wound healing, and by the cyclization of the arginine derivative-glutamate, proline is formed, which is a component of connective tissue, hydroxyproline is formed from it, which better the course of the wound process, confirmed by other researchers [1, 5]. Arginine is also metabolized by NO-synthetase with the formation of an active radical - nitric monoxide, which dilates blood vessels and make the local improvement in blood circulation, which improves the wound healing. Such an effect of arginine was described in scientific works by other scientists [9, 10].

Conclusion

Thus, the use of vacuum therapy with instillations of L-arginine for the local treatment of pyoinflammatory processes and additional intravenous infusion of 100 ml of arginine hydrochloride solution daily, compared with typical local treatment using the generally accepted course of vacuum therapy, contributed to accelerated injury. Their microbial contamination and a faster transition of the purulent-necrotic phase of the wound process into the regeneration phase, which caused the decreasing of the hospital treatment of patients of the main group.

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V.V. Horokhovskiy, O.V. Dienha¹, A.E. Dienga¹, T.O. Pyndus², A. Jenča Jr.²,
S.A. Shnaider¹, I.O. Tsushko¹

Odessa National Medical University, Odessa,

¹State Establishment "The Institute of stomatology and maxilla-facial surgery National academy of medical sciences of Ukraine", Odessa,

²Pavol Jozef Safarik University and Academy of Kosice, Košice, Slovakia

ANALYSIS OF THE FREQUENCY AND STRUCTURE OF NON-CARIOUS LESIONS OF HARD TISSUES OF TEETH IN CHILDREN

e-mail: oksanadenga@gmail.com

The study is devoted to determining the prevalence and structure of non-carious lesions of the hard tissues of the teeth in children 6–15 years of Odessa. The study involved 720 children aged 6 to 15 years. They were divided into 3 age groups. The dental examination was performed in a dental office. As a result of the conducted researches the high prevalence of non-carious lesions of the hard tissues of the teeth in children of the city of Odessa was established. It is concluded that children with non-carious lesions of the hard tissues of the teeth need dispensary supervision at the dentist and timely treatment. It is necessary to develop new modern methods to prevent the development and prevention of complications of non-carious lesions of the hard tissues of the teeth in children.

Key words: children, oral health, teeth eruption, dental care, hard tissues of teeth.

V.V. Гороховський, О.В. Дєньга, А.Е. Дєньга, Т.О. Пиндус, А. Єнча,
С.А. Шнайдер, І.О. Цушко

АНАЛІЗ ЧАСТОТИ ТА СТРУКТУРИ НЕКАРІОЗНИХ УРАЖЕНЬ ТВЕРДИХ ТКАНИН ЗУБІВ У ДІТЕЙ

Дослідження присвячено визначенню поширеності та структури некаріозних уражень твердих тканин зубів у дітей 6–15 років міста Одеса. В дослідженнях приймали участь 720 дітей віком від 6 до 15 років. Вони були розподілені на 3 вікові групи. Стоматологічний огляд було проведено в умовах стоматологічного кабінету. В результаті проведених досліджень було встановлено високу поширеність некаріозних уражень твердих тканин зубів у дітей міста Одеси. Зроблено висновок, що діти з некаріозними ураженнями твердих тканин зубів потребують диспансерного нагляду у стоматолога та своєчасного проведення лікувальних заходів. Необхідна розробка нових сучасних методів запобігання розвитку та профілактики ускладнень некаріозних уражень твердих тканин зубів у дітей.

Ключові слова: діти, стан порожнини рота, прорізування зубів, стоматологічна допомога, тверді тканини зубів.

The work is a fragment of the research project "Correction of pathogenetic mechanisms of carbohydrate disorders and lipid metabolism in the body and tissues of the oral cavity in patients depending on environmental and nutritional factors affecting carbohydrate and lipid metabolism", state registration No. 0118U006966.

Modern epidemiological studies of the oral cavity in children and adolescents indicate a high level of dental morbidity in this age group of Ukraine. Unfortunately, so far the prevalence of major dental diseases is much higher than in other European countries [2, 7, 11]. High prevalence and intensity of caries of permanent teeth in children indicate the need for more thorough diagnosis of all risk factors for its occurrence. Given that the main complication of non-carious lesions is dental caries, the study of hard tissues of teeth of non-carious origin in children is an urgent task of modern medicine [13].

Ameloblasts are known to be secretory cells that are involved in the formation of tooth enamel and are very sensitive to endogenous and exogenous factors [1, 5, 14]. Since enamel is formed only during a certain period of tooth development, the dysfunction of these cells at the stage of emalegenesis can lead to permanent irreversible morphological defects of its development. Such defects can manifest themselves in the form of structural disorders or lack of enamel in a certain area. These areas can be additional retention points for microorganisms, food debris and soft dental plaque, which can be factors that can cause tooth