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PROBLEMS OF DIABETIC FOOT SYNDROME TREATMENT AND POSSIBLE WAYS OF THEIR SOLUTION

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Abstract. A number of patients with diabetes mellitus worldwide increases with geometric progression, which means that a number of complications increases as well. Diabetic foot syndrome is the leading cause of early disability of patients. Therefore, the search for new therapeutic tactics is a constant process that motivates surgeons and in turn opens new opportunities in the treatment of various forms of purulent-necrotic processes in patients with diabetes mellitus. Therapy with negative pressure is one of the most promising nowadays. A number of conducted randomized clinical trials have already proved its effectiveness in practice. The use of vacuum therapy as an integral component of the combined treatment of purulent-necrotic lesions in diabetic foot syndrome can significantly accelerate reconvalescence and reduce % of high amputations in the future.

Keywords: diabetes mellitus, diabetic foot syndrome, wound process, vacuum therapy of wounds.

Introduction. Diabetes mellitus (DM) is a widespread multisystem disorder with numerous potential complications and significant socio-economic implications. Attempts in recent years to stop the diabetes pandemic yet to succeed [23]. According to the International Diabetic Federation, the number of patients with diabetes will reach 552 million by 2030. For comparison, it should be noted that in 1980 their number was 108 million. Moreover, according to the WHO by 2030, every seven deaths will be due to the DM complications. In different countries, the growth rate of the diabetic population is changing averaging 2.2-6.1%. Some authors have established that the rate of spread of diabetes depends on the population income level. In the middle and high-income countries, the pace of its dissemination is much higher. Thus, in Japan, there are more than 10% of patients ill with diabetes and in Ukraine their number reaches 9.1% out of the total population [28].

One of the terrible DM complications is diabetic foot syndrome (DFS), depending on age statistics, reaches 30%-80% in patients with persistent hyperglycemia [19]. According to a number of authors, it can be argued that the DFS includes any purulent-destructive processes on the lower extremities. It is a main cause leading to early patients' disability. Up to 85% of all nontraumatic amputations occur in patients with this pathology [13]. So, only in the United States, 82,000 of annually performed extremities amputations are directly related to diabetes. In addition, among patients with DFS a significant place is occupied by trophic ulcers, which account for 85% of all lesions. The prevalence of foot ulcers for different population groups ranges from 2% to 43%. Most of them heal while 10%-15% remain active out of which 5%-24% will eventually lead to limbs' amputation within 6-18 months after their formation. In the remaining 15% of DFS patients there is a pathology such as osteomyelitis, abscess, phlegmon, tendovaginitis, purulent arthritis and so on that may occur either on their own or as a result of a trophic ulcer [34].

According to WHO, estimated 2.5% to 15% of annual national health budgets are spent only on diseases associated with the progression of DM [10]. The cost of treatment for such patients also increases [26, 46], which in the USA ranges from 3959 to 188 thousand dollars [201]. The above socio-epidemic indicators indicate a generally high level of importance of this topic. In Ukraine, the cost of treatment for one such patient varies from 10 thousand hryvnias to hundreds of thousands of hryvnias, in the case of prosthetics.

All of the aforementioned purulent-necrotic lesions are a constant "headache" for surgeons who have been in a constant process of improving their therapeutic and tactical approaches for years to solve the problems of the patient cohort [17].

Main section. The choice of the treatment method for patients with DFS is directly determined by the degree of severity of vascular and neuropathic disorders, the stage and nature of the inflammatory process, the degree of compensation and DM severity [5], activity and the number of concomitant diseases. Initial therapy includes efforts intensification aimed at compensating for hyperglycemic disorders as well as targeted empirical and corrected antibiotic therapy taking into account the features of microbial profile of purulent necrotic processes, minimization of the phenomena of critical limb ischemia, foot discharge, and local use of modern adsorption bandages and treatment of concomitant pathology.

The main obstacle to the normal course of the wound process is hyperglycemia, which directly affects the rate of infection elimination and wound epithelization [6]. Therefore, the main condition for a successful start of conservative treatment is to achieve a normal glycemic profile level. The next equally important component in the treatment of purulent-necrotic DFS lesions is the use of antibiotics. Prior to commencing the antibiotic therapy application, it is necessary to determine the potential microbial associations in the wound. The empirical approach relies on the use of 3-4 generations of cephalosporins and to a lesser extent fluoroquinolones or combinations thereof [15]. According to the latest data, metronidazole should be added to the therapy. In the osteomyelitis treatment, the best results can be obtained with the use of linzamides and high doses of cephalosporins with fluoroquinolones. Etiotropic antibiotic therapy is a result of successive repeated wound cultures and can vary in quantity and quality depending on their results.

Modern pharmacotherapy for critical lower limb ischemia involves the use of drugs from the groups of glucosamineglycans, prostaglandins and pentoxifylline and low molecular weight heparins in the treatment of neuropathic DFS forms are less effective [34]. In addition, in the treatment of diabetic polyneuropathy, the drugs that improve the nervous tissue metabolism and support the fight against paresthesia and pains are used. In this case, the best results are noted with the use of a-lipoic acid, vitamins B, gabapentin and tricyclic antidepressants. An important component in the treatment of purulent-necrotic

DFS lesions is a complete discharge of the limb [36]. An active use of non-removable unloading bandages from polymeric fixing materials allows almost no limitation of motor freedom of the patient and if necessary allows applying bandages through special openings [10]. Such bandages can reduce up to 90% of the pressure on wound soft tissue [66, 68]. However, the use of local stage surgical wound treatment can significantly activate and enhance the effectiveness of planned conservative therapy. The essence of the consistent approach to the purulent-necrotic processes treatment is prompt abscesses disclosure, permanent wound cleansing, quality control and the amount of exudates, perseverance against microbial contamination [4].

Today, special interactive coatings that have a number of advantages over a classic gauze bandage and antiseptic are actively used in the treatment of purulent DFS complications. They are well ventilated and are atraumatic, provide thermal insulation and maintain moisture in the wound, remove excess of exudate and create a bacterial barrier, prevent injury to the wound [21]. A higher rate of purulent wounds healing after their disclosure in surgical hospitals is achieved by means of minimizing surgical intervention, conducting local treatment on a wet basis, preventing the onset of intradermal wound infection and stimulating reparative processes [27]. The challenges of purulent-necrotic DFS lesions treatment unfortunately cannot be solved solely by surgical invasion [20]. Many discussions have been prompted on the back of the cooperation of doctors from different specialties, which will eventually allow to significantly reducing the number of trophic ulcers of the feet and the lower extremities amputations [16].

The choice of surgical tactics depends on the DFS form, the nature and distribution of purulent-necrotic complications and the general condition of a patient [11]. Timely interventions are aimed at preserving the lower limbs [3]. At the same time, most specialists adhere to the principles of stage treatment. The first stage involves a disclosure and drainage of abscesses with non-cresecastrectomy while the next (its scope will depend on the results of the previous one) - may be in the form of stage sanation or reconstructive-plastic interventions [29]. In the presence of necrotic tissues, all non-chic keratomy is performed within healthy tissues [4].

The latest option for surgical treatment is amputation of the gangrene of the lower extremities. However, different authors' opinions on the level is divided into those who consider the optimal level of amputation of the thigh in moist and organ-saving operations in dry gangrene [12]. It should be noted that the five-year survival after such operations is less than 50% [7]. All amputations are conventionally divided into "low" and "high" the boundary of which is the joint of Lesfranca. When choosing the level of amputation the presence of occlusion or stenosis of the major artery is determined. Depending on conditions, endovascular revascularization is conducted [7].

However, it is not possible to significantly reduce a number of amputations of the lower extremities despite a standardized multidisciplinary approach to solving the problem of purulent necrotic DFS lesions treatment [1]. A relatively new method is the use of nitric oxide (NO-therapy). The basis of NO-therapy is the effect on tissues of the air plasma flow to obtain a surgical effect (sterilization, destruction of non-viable tissues, coagulation). Flow of gas formed because of air plasma cooling and contains nitrogen oxide molecules (NO) gives a therapeutic effect due to bactericidal action, anti-aggregate and anticoagulant action. In addition, nitric oxide activates antioxidant defense, regulates apoptosis, stimulates proliferation of fibroblasts and synthesizes collagen, regulates immune disorders, promotes secretion of cytokines and induces phagocytosis [33]. One of the main advantages of NO therapy is the influence of polyfunctional NO on all phases of the wound process. NO therapy accelerates vascular proliferation and creates favorable conditions for the formation of granulations. The use of plasma flow has a pronounced antibacterial effect in an experiment with staphylococcus and blue-purulent rod, and the treatment with its purulent wounds reduces the cost of treatment and improves the quality of life of patients without unnecessary surgical intervention. Nitric monoxide and ozonotherapy accelerates the formation of fibroblast cells, increases the activity of collagenase, increases the number of cells of the basal layer of the epithelium 1, 5-2 times and reduces the number of infectious postoperative complications threefold. NO-containing air-plasma streams and ozone therapy have a pronounced bactericidal effect and reduce the bacterial contamination of the wound surface [22].

According to some authors, the use of NO-therapy improves the results of a comprehensive treatment of soft tissue infections of the lower extremities in patients with diabetes mellitus. At the same time wound healing is accelerated, their repair, microbial contamination decreases, which leads to a shortening of treatment periods [32]. Other scientists point out that wound healing from the deviated tissues takes place after the application of nitric oxide in patients with purulent wounds; the emergence of granulations and marginal epithelization occurred 3.2 ± 1.1 days sooner compared to traditional methods of treatment [4].

Nowadays, one of the new methods of treatment of purulent wounds in DFS patients is a use of vacuum therapy [2]. Vacuum therapy can be used at any stage of purulent complications treatment [8]. Every year this methodology acquires a wider application in surgical practice, although positive effects are not always confirmed at the cellular level [36]. Preliminary data on the effectiveness of this method can be divided into the following components: 1) extracellular (increased blood flow, decreased edema), 2) cellular (granulation tissue formation and cellular synthesis), 3) complex (wound healing and infection control). When conducting scientific literature analysis at the Kochran library starting from 2011 and AWMA (Association of the Scientific Medical Societies in Germany) from 2006, M. Augustinb and M. Herberger discovered more than 650 original publications that proved the effectiveness of the use of negative pressure therapy in a treatment of DFS patients [37]. Of these, more than 350 studies had 1b level of evidence. The World Wound Study Organization developed the first clear recommendations regarding the use of vacuum therapy in early 2008 [38].

These are as follows:

1. Firstly, it is necessary to pay attention to the etiology of the process, as well as the presence of concomitant pathology, which will be the basis for stabilizing the process physiology. This will allow establishing individual therapy to a maximum extent.

2. Prior to the vacuum therapy appointment, goals, priorities and possible clinical effects need to be identified. In parallel, symptomatic therapy is performed allowing minimizing complications.

3. The main vacuum therapy goals are as follows:

- strengthening of microcirculation in soft tissues;
- Reduction of around-red edema and elimination of excessive exudates from a wound;
- Reduction of the wound size and depth;
- Activation of granulation tissue growth;
- reducing the number of possible complications and reducing further surgical activity in the wound area.

4. Vacuum therapy supports a damp wound healing principle that increases patients comfort and mobility.

5. Ahead of vacuum therapy application, it is necessary to clean the wound to the maximum extent by mechanical means and to determine its depth.

6. An important element of therapy is constant monitoring of the wound size.

7. Indicators of the effectiveness of vacuum therapy are

- no increase in the wound area;
- the appearance of epithelium in the boundary zone of the defect;
- the appearance of "juicy" granulations in the wound. Daily amount of granulations should increase on average by 3%-5%.

An example of a successful vacuum therapy use is a reduction of the wound size by 15% on a weekly basis [26]. If the healing rate slows down, the treatment should be stopped or replaced by an alternative method [30].

Vacuum therapy cannot be used as a monotherapy [18]. When applied, permanent monitoring of the wound condition, its bottom, monitoring of the quantitative and qualitative state of the exsudate is required. Should the infectious process tend to increase when applying vacuum therapy, the procedure should be stopped and another approach should be applied [31]. To date, the greatest experience in the application of vacuum therapy according to the literature is based on the example of treatment of patients with DFS, but it is necessary to take into account the clinical form of the syndrome. Vacuum therapy is not recommended should there be deep neuroishemic defects of soft tissues [25].

Conclusions. Thus, based on the available literature, it can be concluded that vacuum therapy is an effective remedy for a number of purulent-necrotic DFS complications and may be useful in the complex treatment of such patients. However, it is necessary to continue studying the mechanisms of vacuum therapy influence on different parts of the wound process with specific purulent-necrotic complications, and to improve the schemes with the use of negative pressure therapy.

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ПРОБЛЕМЫ ЛЕЧЕНИЯ СИНДРОМА ДИАБЕТИЧЕСКОЙ СТОПЫ И ВОЗМОЖНЫЕ ПУТИ ИХ РЕШЕНИЯ

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Резюме. Количество пациентов с сахарным диабетом во всем мире увеличивается с геометрической прогрессией, а это означает, что также увеличивается ряд осложнений. Синдром диабетической стопы является основной причиной ранней инвалидизации пациентов. Поэтому поиск новой терапевтической тактики – это постоянный процесс, который мотивирует хирургов и, в свою очередь, открывает новые возможности для лечения различных форм гнойно-некротических процессов у пациентов с сахарным диабетом. Терапия отрицательного давления является одной из самых перспективных в наше время. Ряд проведенных рандомизированных клинических испытаний уже доказал свою эффективность на практике. Использование вакуумной терапии в качестве неотъемлемого компонента комбинированной терапии гнойно-некротических поражений при синдроме диабетической стопы может значительно ускорить реконвалесценцию и снизить в будущем количество высоких ампутаций.

Ключевые слова: сахарный диабет, синдром диабетической стопы, раневой процесс, вакуумная терапия ран.

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ПРОБЛЕМИ ЛІКУВАННЯ СИНДРОМУ ДІАБЕТИЧНОЇ СТОПИ ТА МОЖЛИВІ ШЛЯХИ ЇХ ВИРІШЕННЯ

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Резюме. Кількість пацієнтів із цукровим діабетом у всьому світі збільшується з геометричною прогресією і це означає, що збільшується і кількість ускладнень. Синдром діабетичної стопи є провідною причиною ранньої інвалідизації пацієнтів. Тому пошуки нової терапевтичної тактики є постійним процесом, який мотивує хірургів і, у свою чергу, відкриває нові можливості для лікування різних форм гнійно-некротичних процесів у хворих на цукровий діабет. Терапія негативного тиску є однією з найбільш перспективних в наші дні. Проведені рандомізовані клінічні випробування вже довели її ефективність на практиці. Використання вакуумної терапії як невід'ємної складової комбінованого лікування гнійно-некротичних уражень при синдромі діабетичної стопи може значно прискорити реконвалесценцію та зменшити відсоток високих ампутацій у майбутньому.

Ключові слова: цукровий діабет, синдром діабетичної стопи, рановий процес, вакуумна терапія ран.

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