

КЛІНІЧНА МЕДИЦИНА

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УДК 616.378-008.64-08

DOI <https://doi.org/10.31718/mep.2019.23.5-6.02>

OPTIMIZATION OF THE VACUUM-ASSISTED TREATMENT FOR COMPLICATIONS OF DIABETIC FOOT SYNDROME*

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Досліджено характер репараційних та морфологічних змін в ранах на фоні проведення вакуумної терапії при комплексному лікуванні гнійно-некротичних уражень синдрому діабетичної стопи. Проведене комплексне обстеження та лікування 107 хворих на СДС з II-IV ст. за Meggit-Wagner. Середній вік пацієнтів становив 53,2±4,3 роки, чоловіків було 39 (36,4%), а жінок – 68 (63,6%). У залежності від методів місцевого лікування пацієнти були поділені на дві групи. Основна група включала 55 (51,4%) осіб, яким при проведенні місцевого лікування застосовували вакуумну терапію, а у групу порівняння було 52 (48,6%) пацієнта, які отримували стандартизоване місцеве лікування у залежності від перебігу ранового процесу. Крім клінічного дослідження, усім хворим проводили комплексне лабораторне і інструментальне обстеження, а також вимірювання площі та рН-метрію ран на 1, 4, 7, 10, 13 добу після операції. У результаті проведеного аналізу отриманих результатів встановлено, що при певному рівні рН має місце відповідна цитологічна картина. Широкий діапазон коливань рН ранового середовища у хворих з гнійно-некротичними ураженнями синдрому діабетичної стопи призводить до відповідних змін у клітинах, що проявляється довготривалим запальним процесом. У основній групі швидкість зменшення рани була найбільшою на 8-10 добу, а в групі порівняння – на 14-15 добу. Термін стаціонарного лікування склав 14,2 ліжко-днів в основній групі та 23,5±2,9 у групі порівняння (p < 0,05). Отже, відмічається прискорення позитивних змін клінічних проявів, цитологічної, морфологічної та рН-метричної картини на фоні проведення ВТ у середньому на 5-7 діб. Використання вакуумної терапії дає можливість прискорити перехід до другою фази ранового процесу, що впливає не тільки на терміни лікування, але й на кінцевий результат – збереження нижньої кінцівки у хворих на синдрому діабетичної стопи.

Ключові слова: гнійно-некротичні ураження, синдром діабетичної стопи, вакуумна терапія

The nature of reparative and morphological changes in wounds was examined against the background of vacuum therapy in the comprehensive treatment of purulent and necrotic lesions of diabetic foot syndrome. We conducted comprehensive examination and treatment of 107 patients with DFS of grade II-IV according to Meggit-Wagner. The average age of patients was 53.2-4.3 years; there were 39 (36.4%) male and 68 (63.6%) female patients. Depending on the methods of topical treatment, patients were divided into two groups. The main group consisted of 55 (51.4%) subjects who underwent vacuum therapy during the topical treatment, and the comparison group comprised 52 (48.6%) patients who received standardized local treatment depending on the course of the wound process. In addition to the clinical studies, all patients underwent a comprehensive laboratory and instrumental examination, as well as measuring the area and pH of wounds on the 1st, 4th, 7th, 10th and 13th day after surgery. The analysis of the obtained results gives ground to establish that at a certain level of pH, there is a corresponding cytological pattern. The wide range of fluctuations in the pH of the wound medium in patients with purulent and necrotic lesions of diabetic foot syndrome leads to corresponding changes in cells, which is manifested by a long-lasting inflammatory process. In the main group, the rate of wound reduction was greatest on the 8th-10th days, and in the comparison group – on the 14th-15th days. Inpatient treatment was 14.2 bed-days in the main group and 23.5 ± 2.9 in the comparison group (p < 0.05), respectively. Therefore, there is an acceleration of positive changes in clinical manifestations, cytological, morphological and pH-metric pattern against the background of conducting VT for an average of 5-7 days. The use of vacuum therapy makes it possible to accelerate the transition to the second phase of the wound process, which affects not only the time of treatment but also the outcome – preservation of the lower extremity in patients with diabetic foot syndrome.

Keywords: purulent and necrotic lesions, diabetic foot syndrome, vacuum therapy

* To cite this english version: V.I. Liakhovskiy, O.O. Kyzymenko, O.H. Krasnov, O.I. Krasnov, T.V. Horodova-Andrieieva. Optimization of the vacuum-assisted treatment for complications of diabetic foot syndrome. // The Medical and ecological problems. - 2019. - Vol 23, № 5-6. - P. 15-19.

Introduction

Purulent and necrotic (PN) foot lesions in patients with diabetes mellitus (DM) constitute a significant medical, social and economic problem all over the world. The risk of developing purulent ulcer in diabetic patients during lifetime is up to 25%, and the frequency of nontraumatic amputation of the lower limb is almost by 22 times higher in patients with DM than in those without it [4, 10]. Diabetic foot syndrome (DFS) is one of the most common complications of DM, which occurs in 15% of diabetic patients [8]. In 30% of patients with this pathology, amputations of the other limb are performed 3 years after the first one, and in 5 years they are performed in almost 54% of patients [7, 12].

The complicated multifactorial pathogenesis of DFS still does not allow researchers to find adequate treatment methods [3, 11]. Trophic changes in the DFS create favorable conditions for the development of infection with the onset of PN processes on the foot, while the inflammation phase is prolonged, resulting in the secondary necrosis; the formation of granulation bank also slows down, which together with the uncompleted phagocytosis facilitates the multiplying of microorganisms in the wound [8, 13].

Morphological features of the wound process in patients with diabetes and DFS are increased exudative phase of inflammation and inhibition of proliferative processes in the tissues [2, 4]. Against the background of treatment of such patients, secondary necroses of infectious or vascular genesis can be formed, which are mainly localized in the granulation tissue, which complicates the course of the wound process [8, 11].

The most complex tasks of the surgeon in the treatment of DFS are the improvement of surgical debridement of purulent focus, effective treatment of purulent wounds, prevention of the infection generalization [3, 8, 13]. In order to improve tissue reparation and resistance to microflora, methods of local influence are constantly developing for these patients [4, 9]. Vacuum therapy (VT) is one of the modern methods for treating wound defects in patients with DFS [1, 15]. The scientific literature highlights the treatment of DFS using comprehensive techniques that include VT, but scholarly papers containing contradictory data on their results have also been published [5, 14, 15]. Furthermore, reparative effects and morphological changes, occurring in the wounds with VT, have not been sufficiently investigated.

Consequently, the question of the most rational composition of the highlights treatment for DFS and the feasibility of incorporating some of the new techniques remains debatable and requires additional research [1, 6].

The aim of the research was to study and investigate the nature of reparative and morphological changes in the wounds against the background of vacuum therapy as a part of comprehensive treatment of PN lesions in DFS.

Materials and methods

We conducted the comprehensive examination and therapy of 107 patients with DFS, stages II-IV by Meggit-Wagner, who were treated at the surgical department No.1 of Poltava City clinical hospital No.2 during 2015-2018. The average age of patients was 53.2 ± 4.3 years, for men – 39 (36.4%), and women – 68 (63.6%). 89 patients (83.2%) suffered from type 2 DM, 18 patients

(16.8%) – from type 1 DM. The average duration of DM was 23.7 ± 6.4 years.

Depending on the application of local treatment methods, patients were divided into two groups. The main group included 55 people (51.4%) who underwent VT for local treatment, and 52 patients (48.6%), who received standardized local treatment, depending on the course of the wound process, comprised the comparison group.

Patients in both groups received treatment in accordance with the international protocols for treatment of DFS, which included the prescription of antibacterial therapy, depending on the sensitivity of microflora derived from wounds, insulin therapy, angioprotectors, alpha lipoic acid preparations, medications that improve the rheological properties of the blood, disaggregation drugs. All patients underwent surgical interventions aimed at sanation of foci of infection in the form of surgical debridement of purulent foci. We conducted empirical antibiotic therapy with broad-spectrum antibiotics. After obtaining the results of bacteriological control, on average on the 3rd-4th day, antibacterial therapy was adjusted according to the results of antibiogram. The groups of patients did not differ in terms of age, glycemia, duration of DM, severity and character of PN lesions.

Along with clinical research, all patients were provided with a comprehensive laboratory and instrumental examination, which included: general blood and urine tests, blood glucose levels, biochemical blood tests, coagulogram, ECG, foot radiography, ultrasound color angioscanning (USCAS) of the lower extremities, bacteriological and cytological studies, as well as measurements of the area and pH-metry of the wounds on the 1st, 4th, 7th, 10th, 13th days after surgery. pH measurements were conducted by the portable pH meter Kelilong RN-061(A). To measure the wound area, we used the digital online service and the LesionMeter software during the hospitalization and on the 4th, 7th, 10th, 13th days. Morphological studies were performed using biopsy material by histological method from the bottom of the wound (53 biopsy samples). The criterion for exclusion from the study was the presence of signs of critical ischemia of the lower extremities, confirmed by USCAS. Correction of carbohydrate metabolism was conducted under the control of blood glucose, with the participation of endocrinologist. In addition, patients were examined by contiguous specialists, if necessary.

The incision of abscess and phlegmon of the foot was conducted in 23 patients (41.8%), amputation and exarticulation of the toes – in 25 patients (45.5%), resection or amputation of the foot – in 7 patients (12.7%) of the main group; necrectomies, including the multiple (staging) ones were performed in 32 cases. In the comparison group, the structure of surgical interventions did not differ significantly. The result of surgical interventions was the formation of wounds with an area from 5.9 cm^2 to 62.1 cm^2 .

The main goal of treating patients in both groups was to prepare the wound for closure or create conditions for healing of the wound by the secondary adhesion. The main stages of local treatment of diabetic ulcers in patients of the main group included mechanical debridement, irrigation with solutions of antiseptics, followed by applying a bandage with a medicinal agent. In the process of treatment we always adhered to the "moist wound healing" principle. In different phases of the wound process, various means of local treatment were used.

In order to accelerate wound cleansing and its healing, we applied VT, which was conducted after the provisional necrectomy and wound cleansing in patients of the main group using the HEACO NP32 (UK) device on the 2nd-3rd days after surgery, in the absence of bleeding from the wounds. We considered the following factors as necessary for VT: satisfactory arterial blood supply and granulating wound surface, sufficient exudate in the wound, diameter greater than 2 cm, medicinal compensation of the patient. We evaluated the efficacy of VT based on clinical manifestations of the wound process, cytological and morphological studies, and the rate of the wound size reduction. VT was preceded by removal of devitalized tissues from the wound, irrigation with aqueous 0.02% chlorhexidine solution and drying. The wound was filled with a sponge cut in its size, soaked with silver ions, Betadine and Ringer's solution in the ratio of 1:2. The wound was sealed over the sponge using a film with a pad, which was connected to the tube with the VT device. Aspiration was started with the constant negative pressure of 105 mm Hg. In 12 hours, we injected 20 ml of Betadine, cooled to 10° C and diluted, through the tube. We retained the exposure for 3 minutes and then reconnected to the device. Overnight instillations were conducted twice, and starting from the second day, the negative pressure was increased to 125 mm Hg. In 3 days, the device was switched off and the sponge was replaced. At the same time, we conducted antibiogram, cytological and pH-metry studies. The procedure was repeated for three times. The duration of VT was 10 days, with a bandage replaced once every 3 days. For this method of treatment, the Patent of Ukraine for utility model was obtained No. 126213 [8].

Results and discussion

Manifestations of neuropathy were characteristic of all patients with DFS. The magistral blood flow in the femoral-popliteal-femoral segment was retained in all patients, which was confirmed by the data of USCAS.

As a result of microbiological studies of the wounds secretion taken during the surgery, we found that mono-infection was isolated in 31 patients (56.4%) in the main group: in 21 patients (67.7%) *St. aureus* was cultured, in 5 patients (16.1%) – *Enterobacter*, in 3 patients (9.7%) – *Accinetobacter*, and in 2 patients (6.5%) – *Proteus* was isolated. In the microbial associations of the main group, we detected that the combination of *Enterobacter* and *E. fecalis* prevailed, which was cultured in 22 patients (40.0%), and fungal flora (*Candida albicans*) was observed in 2 people (3.6%). In the comparison group, monoculture was found in 35 patients (67.3%), and microbial associations similar to those cultured in the main group – in 17 patients (32.7%), whereas the fungal flora was not isolated. In 25 patients (71.4%) *St. aureus* was cultured, in 4 patients (11.4%) – *Enterobacter*, in 5 patients (14.3%) – *Accinetobacter*, and 1 patient (2.9%) – *Proteus* was isolated.

In the analysis of morphological configuration before the treatment, that is, after surgical debridement of the wound, the pattern of the wound process in patients of both groups was similar. In the morphological study of tissues before treatment, the wound surface was represented by necrotic, PN with fibrin masses, without a clear margin, numerous colonies of cocci bacteria and leukocytic infiltration were observed. The dermis, and the elements of connective tissue were in the state of destruction with the formation of numerous abscesses. In addition,

microcirculation disorders were detected in the tissues: dilatation of the vessels, the phenomena of stasis therein, microthrombosis, the destruction of the wall. Destructive processes with dissociation of myofibrils were intensified due to the pronounced interstitial edema. The cytological examination of wounds supplemented the morphological configuration. We observed, for the most part, a necrotic type of cytogram, which was represented by degenerately altered neutrophilic granulocytes, monocytes at different stages of degeneration, cytolysis and decay, necrotic masses and coarse-fibered intercellular substance.

In most patients, immediately after surgery, the pH-metry of discharge from the wounds tends to acidosis, which had uncompensated character (5.0-5.5) in 34 patients (61.8%) in the main group, indicating the severity of the course of the destructive process. The clinical manifestations of the inflammation phase were corresponding: acute edema, hyperemia, progressive infiltration of the edges of the wound, pain at palpation against the background of sharp deterioration in general health and expressive changes in blood tests (leukocytosis up to $16.0 \times 10^9/l$), ESR acceleration (25-60 mm/hour). In patients with a higher pH index of secretions from the wound, the inflammatory reaction was weaker. The analysis of results of cytological studies with acidosis (pH – 5.5-6.0) found a large number of neutrophils in all samples, most of which were in the stage of regeneration with fragmentation of nuclei, vague cytoplasm. In this case, degenerative phagocytosis predominated. Subcompensated acidosis (pH – 6.0-6.5) was detected in 21 patient (38.2%) of the main group; the cytological pattern was consistent with the inflammatory type (IT), where the entire field of view was occupied by neutrophilic leukocytes with a decrease in the number of degenerative forms and with completed phagocytosis, there was an increase in the number of macrophages (MCP). In the cytoplasm, bacteria, remnants of molten white blood cells, and digestive vacuoles with clear contours were found. In all samples, insignificant number of fibroblasts (FBLs), polyblasts (PBLs) were observed. The inflammatory and regenerative type of cytogram in patients of the main group was not detected on the first day after surgery.

On the 4th day after surgery, in 6 patients (10.9%) of the main group and 11 patients (21.2%) of the comparison group, the wound process exacerbated; we observed secondary wound necrosis, increased body temperature above 38.0°C, worsening pain in the wound area, decrease in the pH of the wound medium (5.5-6.0) with degenerative-inflammatory (DI) and IT types of cytograms, in which the FBLs appeared, MCP with incomplete phagocytosis, decreased the number of FBL. In the capillaries, there were signs of stasis, agglutination of erythrocytes, edema and swelling of endothelial cells, and their desquamation. Microthrombosis was frequently observed. The lumina of many vessels were significantly narrowed, the walls were thickened due to plasma infiltration, fibrinoid necrosis or sclerosis. There was marked proliferation of endothelial cells and pericytes, infiltration of the vascular walls by numerous polynuclears with the formation of proliferative-infiltrative, destructive panvasculitis and thrombovasculitis. Such hemodynamic and structural changes caused focal necrosis of granulation tissue.

Repeated surgical interventions, adequate therapy improved the condition of patients: clinical symptoms re-

gressed, pH of the wound environment increased (6.0-7.0), degenerative forms of neutrophils decreased, activation of phagocytosis was observed.

Against the background of VT, swelling decreased, the formation of complete granulations intensified, the size and depth of the wound diminished, and border epithelization appeared. During the treatment, the dynamics of the size of the wound was regularly evaluated. In the absence of positive dynamics from VT, we interrupted it for alternative therapy with a return to it at another stage.

On the 4th day after surgery, bacteria were isolated from the wound only in 11 patients (20.0%) of the main group, while monoculture was detected in 6 (10.9%) of them in the form of *St. Aureus*, and in the association – in 5 patients (9.1%). In the comparison group, microflora was isolated in 38 patients (73.1%) with a microbial number of 10^5 . Monoculture was isolated in 26 patients (68.4%). In the comparison group, we observed the formation of new bacterial mixed associations in 12 patients (31.6%) due to the accession of new strains (*Klebsiella*, *E. coli*, *S. Epidermidis*).

On the 7th day after surgery, we revealed subcompensated acidosis with IT in 10 patients (18.2%) of the main group, and in 13 patients (23.6%) – compensated acidosis with IRT (inflammatory regenerative type) of the cytogram. In 32 patients (58.2%) of the main group, pH was within the range of 7.5-8.0. As the pH of the wound environment increased, there were DIT, IT and IRT of the cytogram that were characterized by a further decrease in the number of degenerative neutrophils forms with normalization of their structure and increased segmentation of the nuclei in relation to surgical debridement of PN lesions. An increase in the number of mononuclear cells, profibroblasts, and actively functioning microphages were revealed. The clinical presentation of these patients was characterized by pain relief in the wound, improvement of general state, significant reduction of purulent discharge from the wounds, activation of the processes of their cleansing.

Morphologically, tissue reactions of the inflammatory, proliferative and mixed type were observed. There was an increase in the volume of granulation tissue, the interstitial substance was without signs of edema, without fibrinoid deposits, rich in FBL. Inflammatory infiltrate of different intensity was presented by MCP, a large number of FBL, uneven aggregates of lymphocytes and polymorphic-nuclear leukocytes, with admixture of eosinophils. Young collagen fibers and proliferation of perivascular elements were detected. Histologically, epithelization and regeneration of the connective tissue of the dermis were observed.

On the 10th day after surgery, in patients of the comparison group, alkalization of the pH and the corresponding changes in the cytological pattern of wound imprints were observed. Thus, in 14 patients (26.9%), decompensated acidosis (pH 5.5-6.0) was retained, which was cytologically characterized by DIT of the cytogram. In 21 out of 52 examined patients of the main group, subcompensated acidosis (pH 6.0-6.5) was detected, in 17 patients – compensated acidosis (pH 6.5-7.5) with IT of the cytogram was observed. As the pH of the wound environment increased, there were DIT, IT, and IRT of the cytograms that were characterized by a decreased number of degenerative NFL forms, increased number of PBL, profibroblast (PFBL), and MCP. The regenerator type of the cytogram was not observed.

There was an increase in the relative volume of granulation tissue, but their reactions were incomplete, with a tendency to maturation into pathological types. Thus, the granulation tissue was tightened, with the phenomena of plasma infiltration, no collagen fibers were detected, alternating-inflammatory reactions prevailing, indicating resistance to treatment. The lumina of the capillaries remained rather wide, their walls were thickened. Inflammatory infiltrate of varying intensity was represented by MCP, a small number of lymphocytes and polymorphonuclear leukocytes, with admixture of eosinophils, a small amount of FBL.

On the 10th day, in patients of the main group, microbial associations were not detected, aerobic monoflora was isolated in 5 patients (9.1%). Moreover, in 3 (5.5%) of them *St. epidermidis* was cultured, and in 2 patients (3.6%) – *St. aureus* was isolated with a microbial number of 10^3 . In the comparison group, monoculture was found in 18 patients (34.6%), and microbial associations were found in 14 people (26.9%).

On the 13th day after surgery, in patients of the comparison group, the morphological configuration, the changes in cytogram and pH in general were consistent with the changes observed in patients of the main group on the 8th-10th days. During this period, post-operation studies were performed in 43 patients (78.2%) of the main group, since 12 patients (21.8%) were discharged for outpatient treatment. In 2 patients (3.6%) of the main group, subcompensated acidosis with inflammation was revealed, and in 10 patients (18.2%) – compensated acidosis with inflammatory regenerative types of the cytogram. In 31 patients (56.4%) of the main group, the pH of the wound environment varied within the range of 7.5-8.0. The wound was dominated by regenerative processes with IRT and RT of the cytogram, the main indicators of which were PBL and FBL. We did not observe necrotic and degenerative-inflammatory type of the cytogram in patients of the main group on the 14th-15th days of the postoperative period. In the majority of patients, there was a decrease in the number of neutrophils, MCP, a significant number of FBL, PBL, epithelial cells against the background of complete phagocytosis, which corresponds to the regenerative type of the cytogram.

The analysis of clinical observations and studies of pH of the wound content, as well as cytological data, suggests that the changes in these parameters correspond to the phases of the wound process: inflammation, regeneration, and scar formation. It is characteristic that at a certain level of pH, there is a corresponding cytological pattern. Thus, the maximum amount of neutrophils is detected at pH of the wound environment, which is 5.5-6.0, and reaches 60-80%, gradually decreasing with alkalization of the wound environment. At pH – 8.0-9.0, there are single degenerative forms of neutrophils. MCPs are present in wounds regardless of the pH nature of the wound environment, but their number reaches a maximum at pH 6.5-7.5, that is, in the phase of wound cleansing from dead cells and devitalized tissues. PBLs are the most active at pH 6.0-7.5 in all phases of healing, and, at a minimum of pH 5.0-5.5. FBL exhibit the highest activity at pH above 6.5. Their maximum amount is detected at pH 7.0-7.5 and decreases with granulation and wound epithelization. The activity of the epithelial cells appears at pH 7.0-8.5, they are not found in the sharply acidic reaction of the wound environment at pH 6.5-9.0. A wide range of fluctuations in the pH of the wound environment in patients with PN lesions of DFS leads to ap-

appropriate changes in the cells, which manifests itself by the long-term inflammation process, slow wound cleansing and ballast cell transformation, prolongation of the wound healing periods.

The rate of wound reduction in the main group was the largest on the 8th-10th days and was on average 3.9% per day, whereas in the comparison group – on the 14th-15th days, on average 1.3% per day.

In 2 patients (3.6%) of the main group, no marked epithelization and progression of granulation were observed. In these patients, VT was withdrawn on the 8th-10th days. Meanwhile, in 7 patients (12.2%) of the main group, wound healing was observed on the 14th-15th days after the surgery. In 34 patients (61.8%) of the main group, the size of the wounds decreased, pronounced marginal epithelization was observed, the bottom of the wound was covered with granulation tissue throughout the entire extent.

The term of inpatient treatment was 14.2 bed-days in the main group and 23.5±2.9 in the comparison group ($p < 0.05$). High amputation in patients of the main group was not conducted. 2 patients (3.8%) of the control group underwent transmetatarsal amputation of the foot due to the spread of the process, and 1 patient (1.9%) underwent high amputation of the limb.

Thus, the comparative analysis among the patients of the main group and the comparison group in different periods of comprehensive treatment shows acceleration of positive changes in clinical manifestations, cytological, morphological and pH-metric pattern against the background of VT on average by 5-7 days. The use of VT makes it possible to accelerate the transition to the second phase of the wound process, which affects not only the timing of treatment, but also the final result – the preservation of the lower limb in patients with DFS.

Conclusions

1. Induced vacuum-associated activation of the second phase of the wound process in DFS is crucial for wound healing, prevention of the infection generalization and loss of the lower limb.

2. The use of VT for complications of DFS significantly reduces the transition period of the wound process from the phase of inflammation to the regeneration phase, activates the reaction of inflammatory-proliferative and proliferative types, thus providing the conditions for healing of the wound.

3. Contact pH-metry and cytological examination of purulent wounds in patients with DFS is an objective method of control and prognosis the course of the wound process.

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Матеріал надійшов до редакції 08.08.2019.