Negative Pressure Therapy in the Surgical Treatment of Diabetic Foot

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The study aims to assess the significance of negative pressure therapy in the treatment of diabetic foot.The objectives intend to evaluate the healing time required after applying the method and the functional consequences for the patient. A prospective study was conducted on a sample of 37 patients with diabetic foot were monitored their clinical course between September 2014 - April 2017, following negative pressure therapy. There were used vacuum assisted closure devices (VAC ™ -Hartman) in order to apply negative pressure to the wound, while complying with specified settings (negative pressure, time of use of a kit) in accordance with patients' outcome.There were monitored changes in wound size (planimetric and volumetric measurement), their bacterial load and duration of treatment. Healing was obtained in all cases, to an average hospital stay of 27.3 days and 8 days of therapy application.The negative result of microbial cultures was obtained after an average of 6.45 days by simultaneous application of negative pressure and antibiotic treatment according to the antibiogram. Skin grafts were necessary to close the defect in 4 cases. After basic treatment of the wound, auxiliary methods such as negative pressure contribute to the healing.In patients with diabetic foot who were required surgical intervention, the use of negative pressure therapy yielded a significant benefit in the preservation of the affected limb, after minimal excision.The results we obtained throughout our experience recommend use of NPTW technique as indication for abdominal wall surgery in closing abdominal wall defects, compartment syndrome and surgical site infection after prosthetic mesh.

Keywords:negative pressure, diabetic foot, wound volume

The first experience in the use of negative pressure therapy occurred in 1987 when it was used in the treatment of soft tissue injuries and septic wounds. The procedure was improved in Germanyby Muller, who applied it to 300 patients with infected wounds, and in 1998 Kovacs et al. described using the technique in the treatment of chronic leg ulcers

Numerous articles were published in the early 1990s and the spectrum of indications was expanded for chronic wounds (leg ulcers, decubitus ulcers). In early 2000s a significant extension of indications of applicability of the technique was noted. Fleischmann described the method of exposure to subatmospheric pressure of the wound to obtain debridement and wound healing in 1993 in patients with open fractures.

By applying negative pressure therapy in the surgical field in the last 20 years, it was promoted a new approach to treat infections of the surgical wound. Due to its benefits, this therapy is currently being introduced widely, becoming the method of choice in some pathologies, with favorable results in the treatment of the *diabetic foot* wounds, minimalizing surgical gestures, keeping the affected limb.

The overall incidence of amputation is between 2.8 to 43.9 / 100,000 in the general population and from 0.46 to 13.7 / 1000 patients with diagnosed diabetes [1,2].The proportion of the amputation due to diabetes out of the total non-traumatic amputations are between 40 and 80%, which means a frequency of 10-30 times higher than in the general population [1].

The objectives of wound healing are represented by minimizing blood loss, replacement of defects with new tissue (granulation tissue followed by scar tissue) and to restore an intact epithelial barrier as quickly as possible.

Thus, auxiliary therapy such as ensuring local hyperbaric oxygen atmosphere, the administration of growth factors, skin-substitutes, grafts of cultivated keratinocytes, electrical stimulation and local drainage, with or without flushing by sealing the woundin negative pressure, may constitute the conditions forlocal healing[2]. Increasing blood flow in the circulation and compromised or damaged tissue oxygenation enhance the ability of resistance to infection.

Successful healing of wounds, spontaneous or after surgery, is correlated with the bacterial load of the affected tissue which must be less than 10u bacteria per gram of tissue.

The study aims to demonstrate the usefulness of the method and its clinical use, which is increasing the benefits it brings to both patients and medical establishment.The objectives of the study are to assess the healing time after applicating the method, the extent of the surgical procedure and the functional consequences for the patient.

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Experimental part

Material and method

The prospective study was conducted on a sample of 37 patients hospitalized in the Hospital Surgery Clinic I- II St. Spiridon, Iasi. The period of the study was between September 2014 - April 2017. Data used were those related to the patients' demographic, history of the underlying disease, complications and markers of inflammation. All wounds were monitored by measuring the sizes (cm^2 and cm^3) and photographed during evolution.

Laboratory investigations carried out before the beginning of the negative pressure therapy have included laboratory tests (CBC, markers of infection), X-rays, an antibiogram sampling from the wound or from secretions externalized prior to surgerical gestures.The above mentioned parameters were monitored throughout the whole treatment period in accordance with recordingthe data on the duration of negative pressure therapy, the number of surgical debridement between wound dressings and negative pressure values used. Patients were monitored until the wound has completely healed.

Prior to the application of the VAC ™ device for negative pressure, the appropriate surgical debridement of all wounds was applied, afterwards being cleaned and well irrigated by the jet lavage (H, O, , betadine and saline).

NPWT dressing has been designed according to the wounds, which are then sealed with a semi-permeable film from the kit.

Pressure level was set individually for each patient based on their needs, using continuous suction initially, and intermittent suction subsequently, ranged between 40 and 110 mm Hg.

Pressure settings were dependent on the local conditions of the wound and pathological conditions of the patientwere considered.

Dressing change was performed every 48-72 h by doctor.

Results and discussions

In relation to the admission of the patients in the hospital, their number was variable (2014-3 patients, 2015-9 patients, 2016-18 patients, 7 patients-2017). Demographic data revealed that 22 of 37 patients were male and 15 female, aged between 38 and 82 years, with an average of 65 years (mean age, 67 men; mean age, 63 women). Regarding their living area, 65% came from the countryside.

The patients who came to the emergency unit represented 67.5% (25 patients) and 32.5% (12 patients) were admitted for various chronic complaints.

The complications of the underlying disease (diabetes mellitus) found in patients in the study group were peripheral neuropathy, vasculopathy, neuropathy and diabetic retinopathy.

Comorbidities recorded were hypertension, severe anemia and peripheral vascular disease.

Depending on the extent of the surgical procedure underwent by the patients on admission, these were classified as: major and minor.

The major ones were the amputation of the leg (6%) and of the thigh (6%) and the minor wasrepresented by necrectomy (13%), amputations of fingers with metatarsal head resection (23%); incision, draining and debridement (29%); amputation of the anterior foot (23%).

Healing was obtained in all cases to a period of hospitalization that ranged from 5 to 49 days and an average of 27 days. The period in which negative pressure therapy was applied in the studied group was between 3 and 16 days.

The average time of use of the dressing was 8 days, at a rate of change of the dressing between 48 and 72 h, the average of which was 63 h.

Wound planimetric measurement at study entry ranged from 7.5 cm^2 to 69 cm^2 with an average of 25.52 cm^2 and wound volumetric measurement of the same pacients at study entry ranged from 7.4 cm^3 to 287 cm^3 with an average of 97.6 cm^3, their closing being achieved after application of the therapy. Antibiogram were collected prior to initiation of treatment and until the closing of the defects, their negativity average yield after 6.5 days (fig.1,2 – pacient wound at time of admission in Surgery Clinic I-II Sf.Spiridon Iasi ; figure 3,4 - end of treatment at same pacient from fig. 1,2).

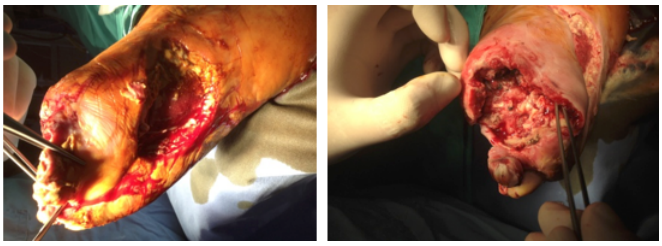

Fig. 1,2. Pacient wound at time of admission in Surgery Clinic I-II Sf.Spiridon Iasi

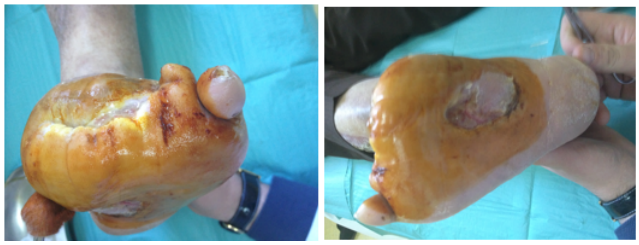

Fig. 3,4 - end of treatment at same pacient from figure 1,2

The negative pressure used ranged from a minimum of 40 mmHg and a maximum of 110 mmHg according to local wound conditions, taking into account the pathological characteristics of the patient, the average utilization of 72 mmHg.

Bridge Technology (multiple cavities aspiration drain) was used in two patients in the study group. In all cases continuous suction was used initially, the device then being set to the intermittent suction (fig. 5,6 - Bridge - multiple cavities aspiration drain). For a number of 3 patients,aspiration drain was associated with local instillations containing antibiotic (according to the antibiogram) and the results were favorable, being confirmed by the antibiogram. In one case two shifts of the kit were performed and in two cases it took three shifts.

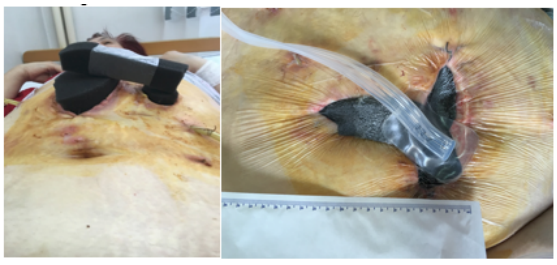

Fig. 5, 6 - Bridge - multiple cavities aspiration drain

Loss of sensitivity specific to neuropathy, at the lower limb, combined with a weak monitoring can cause any injuries to go unnoticed, to infect, reaching, in serious cases, to situations where amputation (finger or toe) remain the only solution.

Chronic degenerative complications, such as diabetic microangiopathy and neuropathy, are closely connected

to the disease evolution and duration [3]. Diabetic peripheral neuropathy may develop despite intensive hyperglycaemic control. Other risk factors are probably involved in its evolution. There is also convincing evidence that a slight improvement of lipid profile, arterial pressure and body mass index are linked with a significant decrease in the risk of diabetic neuropathy occurrence. In diabetes, the association between increased blood viscosity, increased aggregation capacity and low erythrocyte deformability causes blood circulation to slow down and aggravates hypoxia [4].

Number amputations associated with diabetes increased successively in 2006-2010, so that in 2010 there have been 5,827 such cases, 41.32% more than in 2006 [5].

Results in Surgery II Clinic Hospital St. Spiridon- Iasi, after the introduction of this method in the treatment of diabetic foot, indicated a significant reduction of the major surgical gestures to 12% (amputation of the calf and thigh) from the results obtained by the conventional treatment methods applied to the 34% of patients. From 311 diabetic patients admitted to the clinic in the last 2 years before using this technique, 102 patients were practiced a major surgical gesture.

A number of studies have demonstrated the benefits of negative pressure therapy in the treatment of infected wounds, showing superior efficacy compared to conventional dressings [6].

In the study, we obtained an average of 8 days of use of the technique to the closing time of the defect or grafting, with an average hospital stay of 27 days, as sustained by McCallon [6] in the case of diabetic foot, where the duration of healing obtained halved compared to treatment with a simple dressing of lesions.

The mechanisms of action of the negative pressure wound therapy may be quantified for generating micro and macrodeformation to the wound [7].

Analysis of the above mentioned elements has shown that the tissue in the vicinity of the sponge structure is subject to compressive forces. In general, regular microenvironment, but very variable created during this therapy is causing micro deformation. Microdeformations represent the result of the morphological integrated mechanics, the shape of the cells being an important determinant of their function [8.9]. Furthermore, it is known that cells can adapt to physical stress and thus the cell functions can be initiated by physical anddynamic changes.

Angiogenesis is initiated by the cell bed microdeformation that cause local hypoxia and thus leads to an increase in the vascular endothelial growth factor (vascular endothelial growth factor - VEGF). The temporary reduction of blood flow to the edges of the wound stimulates angiogenesis through hypoxia-inducible factor (HIF) -1alfa -> VEGF with an increase in density of microcirculation [10-12].

In many types of vascular-endothelial injuries, a drop in the fibrinolytic capacity of the endothelium was recorded, either by plasminogen activator synthesis decrease or by an increase in the amount of PAI-1 (Plasminogen activator inhibitor type 1) released after the injury, an idea confirmed in our study by the direct correlation between vWF (von Willebrand Factor) and PAI-1, both in females and males [13].

Small and dense LDLc (LDLcholesterol) particles seem to be the marker of a series of anomalies including HDLc (HDL-cholesterol) concentration decrease, apoB concentration increase, insulin sensitivity decrease, and procoagulant changes (PAI-1 increase) [13].

Depending on the underlying pathology, chronic wounds and swelling are often concomitant, and accumulated excess fluids being accepted as a contraventionalhealing factor by the compression effect exerting locally on cells and tissues. Applying negative pressure in these situations reduces extracellular fluid accumulation resulting in a better blood perfusion by reducing compression on the microvasculature [14]. Toxins, bacteria and exudate may be removed from the wound site along with the fluids [15].

The dressing is impermeable to proteins and microorganisms, reducing the risk of contamination of wounds, having limited permeability to water vapor and other gases, thus helping to maintain a moistand stable environment at the wound.

The lack of a wound bed which could allow the extension and cell adhesion, prevents the development of isometric tension within the cell, thus leading to its spheronising and finally to apoptosis, a situation that was not found in chronic wound bed [8].

Before applying negative pressure therapy,patients were subjected to debridement excision involving changing of the dressing twice a day, under surgical stress, maintaining systemic inflammatory response syndrome (SIRS) and also an increased risk of septic complications, while the negative pressure therapy system allowed a few days between procedures, thereby increasing patient comfort and decreasing hospital costs (time in the operating room, workload, materials)[16].

Microbiological surveillance of the wound after initiation of negative pressure therapy was shown to significantly improve the evolution, with an important reduction in the contamination of the wound. From a clinical point of view, necrosis was produced in a limited number of cases,obvious remission of SIRS and hipercatabolic syndrome was observed [17].

Negativity pathogen susceptibility was obtained in all patients studied, the mean being 6.45 days of use with results similar to those reported in the literature,where studies have certified decreased bacterial load of the wound for about 20% of patients in the four days of the establishment of negative pressure therapy and 60% of patients in 8 days after start of treatment. Studies of Morykwas and Argenta, Banwell et al. and Morykwas et al. have reported increased clearance of bacteria from the infected wound by using negative pressure therapy.

Measuring the surface or volume of evolving wounds is useful in documenting the results obtained or predicting them in the treatment of wounds.

This wound assessment can be done through several modes, the most commonly used are linear measurement, surface and wound volume estimation.

Linear measurement is a simple and reliable method, costs little to be implemented, and is portable. The method has its disadvantages, including the limited sensitivity of the method to changing wound dimensions and collecting information about its form.

Planimetry used for complex surfaces overestimates the defect by about 40% and in the case of circular wounds the defect is overestimated by about 25%.

Volumetry is used to evaluate all dimensional axes of a wound by giving the method superiority to planimetry in the case of irregular deep wounds.

A correct method, which offers accuracy in defect measurement, proposed by S.Resch, involves making gypsum molds that imprint defects. These later molds being submerged in water, in graduated cylinders, displace a

volume equal to their volume. The method presents as difficulty the time required for preparing the mold and also the inconvenience of the waiting time with the mold to the wound until it can be extracted.

The peculiarity in the evaluation method used by us in the study of the volume of a wound is the superposition on the defect to be dimensioned of a geometric form that corresponds more real to the defect itself. In the case of large complex wounds, various such geometric shapes were summed up, thus calculating the volume of the defect.

The measurement of the defects using the two ways of quantifying them (surface versus volume) and the correlation of these values with the negative pressure applied showed that there are statistically significant differences in wound volume (p value <0.0000118), but not with respect to the wound surface (p value <0.057).

Using the mathematical principle *the square-cube law* which describes the relationship between the volume and the area as a shape's size increases or decreases we were able to implement our data in the definition relation where pressure (p) is equal to the ratio of force (F) applied to the surface (S) unit.

Conclusions

In our study we observed that proper placement of the material interface with a suitable wound debridement is essential for the success of NPWT. The application of negative pressure reduces extracellular accumulation of fluid, leading to a better blood perfusion by lowering the compression to the microvasculature and bandage having limited permeability to water vapor and other gases helps maintain a moist and stable environment of the wound.

We recommend the use of intermittent suction technique whenever possible because in addition to the physical changes of the wound bed that lead to an increased bacterial clearance to this level, it alsofacilitates the association with local instillation of antibiotic. The use of negative pressure not adapted to local conditions can lead to ischemia of the wound bed related to the pressure applied.

Volumetry of the wound is a means of accurately quantifying their evolution, the correlations between the applied force and the surface of the wound are oriented to the negative pressure applied.

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