

## THE PHARMA INNOVATION - JOURNAL

### Martorell's Syndrom: Diagnosis and Treatment

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Martorell's syndrome is a rare form of trophic leg ulcers, which is diagnosed in patients with a long medical history of hypertension. The peculiarity of these ulcers is their frequent localization in the lower third of the anterior-lateral surface of the tibia and pain syndrome on a relatively small area and depth of injury. This study describes the diagnostic criteria and proposes a comprehensive approach to the treatment of the problem, including the prescription of antihypertensive remedy, intravenously 100 ml infusions of 4, 2% Arginine hydrochloride solution and 400 mg of deproteinized hemoderivative of calf blood with combined ointment local treatment (betamethasone (100 mg), gentamycin sulfate (100 mg), as well as Melladerm PLUS gel. The proposed comprehensive treatment of Martorell's ulcers eliminated the pain of all patients within 14 days of therapy and facilitated a complete epithelization of leg ulcers in 84.2% of patients within 60 days.

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*Keyword:* Martorell's Syndrome, Hypertensive Ischaemic Ulcer.

#### 1. Introduction

Despite the long history, the relevance of trophic leg ulcers has not lost its significance in modern medicine. The most common causes of trophic ulcers is a neglected form of chronic venous insufficiency and violation of arterial vasculature in patients with occlusive arterial disease of the lower limbs. Approximately 0.5% of adult population in Western countries suffer of active trophic leg ulcer and nearly 0, 6-1, 4% have an ulcer history <sup>[1]</sup>. Each year between 300,000 and 4.5 million people in the United States with ulcers of the lower limbs seek a qualified health care <sup>[2]</sup>. In total, the frequency of trophic leg ulcers among patients aged 45 and over is 3.5 per 1,000 inhabitants per year and has remained almost unchanged over the past 20 years <sup>[3]</sup>.

In 1945 a spanish anhioloh F. Martorell described a case of trophic leg ulcer that developed as a result of hypertension with normal pulsation in the arteries of the lower limbs, which later became known as a Martorella's syndrome. At the same time the reports of this disease under

different names, such as hypertensive ischemic ulcers, ulcer hypertensive legs, ischemic ulcers in the legs of patients with hypertension, emerged in other countries. However the number of such publications in the literature was not numerous <sup>[5, 6, 7]</sup>.

The poor awareness of the features of the disease course and the main clinical manifestations of this pathology among surgeons, cardiologists, dermatologists results in diagnostic mistakes in determining the nature of trophic leg ulcers making it impossible to select the proper treatment strategy. Taking into account the above mention, the aim of the study was to cover basic diagnostic and therapeutic approaches in treatment of patients with the Martorell's syndrome.

#### 2. Materials and Methods

19 patients with Martorell's syndrome have been under medical treatment for 2 years at clinical faculty of the Department of Surgery of Ivano-Frankivsk National Medical Academy of Post-

graduate Education. 89.5% of them were women. The age of patients ranged from 42 to 75. All of them had a long medical history (10 to 30 years) of malignant hypertension.

The following criteria for the diagnosis of Martorell's syndrome were identified:

- Presence of a trophic ulcer that is localized in the anterior-lateral surface of the lower third of the tibia;
- Long medical history of hypertension;
- Absence of chronic venous insufficiency, neurotrophic disorders and occlusion diseases of lower limbs arteries;
- Results of pathology report.

Medical history of ulcer of 15 patients ranged from 6 to 12 months, and 4 patients had a 24-month illness period. The origin of ulceration of 14 patients was a micro trauma. In rest cases ulcers formed with no significant reason. The essential for the diagnosis is a character of ulcers: the size of tested ulcer ranged from 2x6 cm to 5x8 cm with jagged edges. The bottom is covered with a dense layer of necrotic tissue with fibrinous layers. One can observe a local perifocal edema and tissue pigmentation around ulcers. All patients felt a severe pain in the area of ulcer irrespectively the position of a limb. According to published data, ulcers of most patients are formed symmetrically on both legs [7], but in our study ulcers localized on both legs only in 2 (10.5%) patients.

The examination of patients included generally accepted clinical, laboratory and instrumental investigations. The usage of supersonic duplex angioscanning of lower limbs denied venous valve insufficiency or violation of arterial circulation of all patients. 6 (31.6%) of patients underwent a morphological examination of bioplate marginal zone of ulcers and the following changes were noticed: endoarteriolar proliferation of small peripheral vessels, subendothelial hyalinosis, appreciable lipid infiltration and a significant narrowing of the vascular lumen of precapillar part of hemocirculation. To correct a hypertension a

selection of drugs was individually proscribed to each patient by a cardiologist. The medical treatment included a combination of endovenous 100 ml infusions of 4.2% Arginine hydrochloride solution and 400 mg of deproteinized hemoderivative calf blood for 14 days followed by oral intake of 200 mg 3 times daily for a month period. For the purpose of anti-inflammatory and analgesic effect there was used intramuscularly 50 mg of dexketoprofen. The local treatment had combined effects on periulceral tissue and the ulcer itself. In an effort to reduce the inflammatory response the area around ulcer was cured with combined ointment (betamethasone (100 mg) and gentamycin sulfate (100 mg), and the surface of the ulcer was spread with Melladerm PLUS gel in order to clean and stimulate granulation and epithelialization.

The evaluation of the efficiency and safety of the therapy was performed on 1, 30 and 60 days of the treatment by the following parameters: severity of pain, ability to perform daily work, social and psychological discomfort, dynamics of trophic changes (size of ulcer, the tendency toward cleaning and granulation). The objectification of data was achieved by using a visual analogue scale. The change of trophic size was assessed with the help of photographic images by measuring the area of ulceration at the beginning and at the end of the treatment. In addition, it was made the evaluation of cleaning rate of the bottom of trophic ulcers, as well as the nature of granulation and epithelialization rate.

### 3. Results and Discussion

Combined with local cure the drug therapy is essential pathogenetically reasonable treatment regimen of patients with the Martorell's syndrome. The active fraction of deproteinized hemoderivative of calf blood detects an insulin action: increases the flow of glucose into cells, activates processes of aerobic and anaerobic oxidation of glucose, intensify the phosphate metabolism that results in the increase of resistance to hypoxia, improves oxygen utilization and tissue repair. The usage of arginine hydrochloride results in the activation of guanylate cyclase and increasing cyclic

guanosine monophosphate in the endothelium of blood vessels, reduces the activation and adhesion of leukocytes and platelets to the endothelium, inhibits the synthesis of endothelin-1, which is a powerful vasoconstrictive agent and stimulator of proliferation and migration of smooth muscle cells of the vascular wall. The L-arginine also inhibits the synthesis of asymmetric dimethylarginin which is a powerful stimulator of endogenous oxidative stress [8].

The proposed local cure takes a prominent place in the treatment regimen of patients with Martorell's ulcer. The usage of betamethasone in combination with gentamycin reduces inflammation of perifocal tissue through inhibition of release of inflammatory mediators and cytokines, decreased permeability of the walls of blood vessels and increase the number of education lipocortines that help combat with swelling. Due to the osmotic activity Melladerm PLUS gel provides acidic pH, controls the bacterial balance and maintains a moist level at the surface of the ulcer which has anti-inflammatory effects, reduces swelling, pain, cleans the wound and thus promotes a rapid healing.

The applied combined therapy for patients with Martorell's ulcers allowed to reduce the pain in 89.5% of patients and to clean ulceration in all patients within 14 days. However, the processes of epithelialization of Martorell's ulcers takes more time. In 30 days after the beginning of treatment the complete epithelization was observed only in 31.6% of patients. The ulcer area of 30% of patients decreased. After 60 days of treatment during the control test the complete ulcer healing was observed in 84.2% of patients, whereas 15.8% such area decreased by more than a half.

#### 4. Conclusion

The proposed diagnostic criteria for the Martorell's syndrome makes it easy to diagnose and choose the right treatment.

The therapy of hypertensive ischemic ulcers of legs requires an integrated approach involving cardiologists and surgeons to correct blood pressure with prescription of medication and

complete healing of trophic ulcers and prevent the recurrence. Using the proposed comprehensive approach in treating patients with the Martorell's syndrome, together with cardiology experts can eliminate pain and promote a complete healing of ischemic ulcers of legs, which significantly improves the quality of life for patients.

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