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New approach for treatment of diabetic ulcer

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Abstract

Diabetic foot ulcer is a principal diabetic complication. It has been shown that diabetic patients have decreased growth factor concentrations in their tissues, particularly epidermal growth factor. Growth factor shortage impairs wound healing, which leads to chronic non healing wounds and sometimes eventual amputation. Ischemic diabetic foot ulcer is the most difficult to treat and confers the highest amputation risk. but we found new approach for treatment of diabetic ulcer, Injecting epidermal growth factor deep into the wound bottom and contours encourages a more effective pharmacodynamic response in terms of granulation tissue growth and wound closure. Epidermal growth factor injected into the ulcer matrix may also result in association with extracellular matrix proteins, thus enhancing cell proliferation and migration. Heberprot-P is an innovative Cuban product containing recombinant human epidermal growth factor for peri- and intra-lesional infiltration; evidence reveals it accelerates healing of deep and complex ulcers, both ischemic and neuropathic, and reduces diabetes-related amputations.

Introduction

Diabetic foot ulcer (DFU) is a localized injury to the skin and/or underlying tissue of the foot of patients with diabetes mellitus; the occurrence of foot problems increases the risk of amputation and death of these patients. A number of studies have shown that diabetic patients have a decreased amount of growth factor concentrations, mainly epidermal growth factor (EGF). Naturally found in the body, EGF stimulate and promote cell growth and regeneration by binding to its receptors -epidermal growth factor receptors (EGFR). Epidermal growth factor acts as a healing agent in that it speeds wound recovery by triggering the synthesis of collagen, elastin and hyaluronic acid . It follows then for diabetic people with a reduced amount of EGF have more of a likelihood to have impaired wound healing to such extremes as to develop severe complications that may require amputation of the lower limb. Half of DFUs occur in the plantar surface and the other half in other areas of the foot. Neuropathy, peripheral artery disease (PAD), deformities of the foot related to motor neuropathy and minor foot trauma, infection and osteomyelitis are major threats

relating to DFU. was Eradication of the infection is difficult and recurrences are common, leading to purulent ulcers, functional distortion of the foot and the need for amputation. The lifetime risk of diabetic patients developing a DFU is 25% > 50% of non-traumatic lower-extremity amputations are related to DFU infections and 85% of all lower-extremity amputations in diabetic patients are preceded by a DFU. Up to 70% of diabetic patients with a DFU-related amputation die within five years of their amputation .To treat diabetic foot ulcers we use Heberorot-P it is and extract of epidermal growth factor pharmaceutical product was conceived at the center for genetic Engineering and biotechnology Because it has significant influence on a patient's overall quality of life in that it not only accelerates the healing process, reduces the number of surgeries needed for the removal of damaged tissue and reduces the risk of development of such complications as infections and gangrene but it also reduces risk of amputation and reduces hospitalization costs[1]. The aim of these report is to discuss the mechanism of action , adverse effect and contraindication of Heberprot-P.

Materials and methods:

A pilot study was performed in 20 patients older than 18 years with diabetes mellitus and full thickness lower extremity ulcer with more than 4 weeks of evolution. Informed consent to participate in the study was given by the patients. Exclusion criteria were foot ulcer area 1 cm 2, cardiomyopathy (recent acute myocardial infarction, unstable angina or uncontrolled heart failure), renal failure. The exclusion criteria were evaluated during an initial period (2 weeks) when patients received only the standardised good wound care and no more than a 30% decrease in the ulcer size was required so they started using Heberprot-P containing 75 mg (one vial) of EGF, three times a week on alternate days up to complete wound healing, together with a standardised good wound care regimen. Ulcers were cleansed daily using saline or chlorhexidine in case of contamination or infection. Sharp debridement was indicated whenever necessary to remove necrotic tissue[2].

Results:

All patients had type 2 diabetes and five (25%) patients received insulin. The average ulcer size was 16 3 21 3 cm2. In nine (45%) patients, wounds were localized to

monotherapy, two of them incubating calcaneous. Other sites were toes in eight (40 0%), the outer edge of the foot in two (10 0%) and the inner edge in one (5 0%) patients. The main risk factors were the previous history of ulcers in 13 (65 0%) patients, history of amputation in 10 (50 0%) and foot deformation in 10 (50 0%) of patients .Full compliance with treatment was reported in 17 (85%) patients. Voluntary outages were reported in three cases (15%). A complete granulation response was achieved in all patients, at a mean time of 2,3, 6, 3, 8 days . Complete wound closure was obtained in 17 (85%) patients , The mean time to complete closure was 44 3 8 9 days Amputation was not necessary any way and relapse was reported in one patient 6 months after complete closure[2].

Discussion:

The primary objective of treatment for DFU is to obtain complete wound closure as expeditiously as possible, in this sense , this study that the continuity of the treatment with intralesional Heberprot-P up to complete wound closure is feasible and safe to promote healing of chronic DFU during the 8 week treatment period , a complete granulation response appeared in 73% of the patients. Completewoundhealingwasreachedin54% of the patients after 20 weeks since the beginning of the treatment the analysis of present study showed that the continuity of treatment was associated to improvement in the rate of both granulation response and complete wound closure. Generally, when complete granulation occurs following administration of the formulation, a partial epithelization is also present that continue until complete closure, although treatment had ceased. It seem that the stimulation of granulation response by Heberprot-P treatment is an important step to enhance healing[2].

Mechanism of action:

For chronic and complex wounds such as diabetic:

The first step Rescue stunned cells, generally fibroblasts , Induction of proliferation of fibroblasts, fibroblasts and vascular Mio- Precursors (angiogenesis), Cell migration. and the last step Activation of genes for extracellular matrix synthesis[3].

Adverse events:

The most common clinical adverse events reported with the use of Herberprot-P are pain and burning sensation at administration site the most frequent . pain reported was mild to moderate in intensity and was not associated with treatment suspension. a dose effect relation associated with appearance of shivering and chills was consistently obtained in all trials at both doses used 25mg and 75 mg and in the pooled analysis intensity was mild to moderate and symptom appearance was not association with treatment suspension[3].

Contraindications:

Herberprot-P is not recommended:

To the patients who used to be hypersensitive to the medicine or any of its ingredients. The medicine Herberprot-P is forbidden to the patients with oncologic pathologies near the location of the injection of the medicine.

It is not recommended to the patients with decompensate cardiomyopathy , diabetic coma or diabetic ketoacidosis[3].

Conclusion:

Heberprot-P is a unique therapy for the most complicated and recalcitrant chronic wounds usually associated with high amputation risk. Local injection in complex diabetic wounds has demonstrated a favorable risk–benefit ratio by speeding healing, reducing recurrences and attenuating amputation risk.

References:

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