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Intralesional epidermal growth factor treatment on diabetic foot ulcers: one centre experience*

*Diyabetik ayakta intralezyonel epidermal growth faktör kullanımı: bir merkezin deneyimi**

Aydın Çifci[1], Birhan Oktaş[1], Şenay Arıkan Durmaz[3], Aşkın Güngüneş[3], İrfan Karahan[4], Taner Sarak[5]
[1]Kırıkkale University, Faculty of Medicine, Department of Internal Medicine, Kırıkkale, Turkey
[2]Kırıkkale University, Faculty of Medicine, Department of Orthopedics and Traumatology, Kırıkkale, Turkey
[3]Kırıkkale University, Faculty of Medicine, Department of Endocrinology, Kırıkkale, Turkey
[4]Yenimahalle Traning and Research Hospital, Department of Internal Medicine, Ankara, Turkey
[5]Kırıkkale University, Faculty of Medicine, Department of Cardiology, Kırıkkale, Turkey

ABSTRACT

Introduction: The intralesional injection of recombinant human epidermal growth factor (EGF-IL) is a new approach for reducing amputations. In this study we aimed to show efficacy of EGF-IL with cases.

Material and Method: EGF-IL 75 µg application to 8 diabetic foot ulcers (6 males, 2 females; mean age: 60.3±9.3 years) was evaluated. Patients had history of prior standard treatments.

Results: All eight patients' wound healed completely.

Conclusion: In our experience on patients wounds wish priorly have healing problems, improved with intralesional EGF. This treatment is expensive and caused of some allergic reactions. Relation with malignancies are not known for long-term.

Keywords: Diabetes, foot ulcer, EGF, wound healing

ÖZ

Giriş: Rekombinant insan epidermal büyüme faktörü (EGF-IL) intralezyonel enjeksiyonu amputasyonları azaltmak için yeni bir yaklaşımdır. Bu çalışmada EGF-IL'nin olgularla etkinliğini göstermeyi amaçladık.

Gereç ve Yöntem: Sekiz diyabetik ayak ülserine (6 erkek, 2 kadın; ortalama yaş: 60.3 ± 9.3 yıl) EGF-IL 75 µg uygulandı. Hastalar daha önce standart tedaviler geçmişi vardı.

Bulgular: Sekiz hastanın tamamında, intralezyonel EGF tedavisinden sonra diyabetik ayak ülserleri iyileşti.

Sonuç: Tecrübelerimize göre, hastalarımızın yaraları önceden intralezyonal EGF ile iyileşen iyileşme problemlerine sahip olmak istemektedir. Bu tedavi pahalıdır ve bazı alerjik reaksiyonlara neden olur. Malignitelerle olan ilişki uzun süredir bilinmemektedir.

Anahtar Kelimeler: Diyabet, ayak ülseri, EGF, yara iyileşmesi

Corresponding Author: Aydın Çifci, Kırıkkale University, Faculty of Medicine, Department of Internal Medicine, 71450, Yahşihan, Kırıkkale, Turkey

E-mail: dr.aydin.71@hotmail.com

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Sorumlu Yazar: Aydın Çifci, Kırıkkale Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Yahşihan, 71450, Kırıkkale, Türkiye

E-posta: dr.aydin.71@hotmail.com

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INTRODUCTION

Prevalence of diabetes mellitus increases in Turkey and worldwide (1). Diabetic foot ulcer (DFU) is a serious complication related mortality. These lesions are huge social and economical problems for health care systems. The main etiologies of ulcers are neuropathy, ischemia and infections (2).

Treatment of DFU is complex and difficult. Blood glucose regulation, debridment and surgical revascularization are used in management. Hyperbaric oxygen treatment (HBOT) is a method whose effect is shown. HBOT increases healing and decreases amputation (3,4).

In negative pressure wound therapy (NPWT), the wound is covered with a sterile gauze or sponge. Negative pressure is performed continuously or intermittently. The action mechanism is not clearly understood yet. But affect can be easily observed rapidly (5). Numerous randomized controlled trials show benefits of healing faster and decreasin amputation by NPWT (6,7).

Intralesional Epidermal Growth Factor (EGF-IL) is a new treatment approach for diabetic foot ulcers. EGF is released from platelets, macrophages, monocytes, and fibroblasts. It has serious role for healing. This approach isn't routine yet and hasn't high evidence with studies (8).

MATERIAL AND METHOD

Eight patients with diabetic foot ulcers followed in Kırıkkale University between 2014-2016 retrospectively. Two patients were female, six patients were male. Patients mean age was 60,3±9,3. The patients were treated with different types of therapies beforedoses. Patients characteristics was showed in table 1. EGF-IL treatment was performed between 5-12 doses. Patients demographics, ulcer place and Wagner stage are given in Table 1.

RESULTS

Table 2. EGF treatments and results

Patient	Numbers of EGF doses	Results after treatment
1	12	Complete healing and wound closed
2	9	Secondary healing and wound closed
3	5	Secondary healing and wound closed
4	12	Complete healing and wound closed
5	12	Secondary healing and wound closed
6	9	Epithelisation and secondary healing
7	9	Secondary healing and wound closed
8	5	Secondary healing and wound closed

DISCUSSION

EGF is a very important factor as epithelial cells and fibroblasts healer. Chronic diabetic ulcers have impaired EGF functions. In the ulcer margin, endothelial cells can't express adequate EGF. EGF receptors are reduced in ulcer endothelial cell. These states results as chronicity, poor franulation and epithelisation. EGF levels can be measured as a marker for evaluating treatment success (9,10). Lower extremity amputation has higher prevalance in diabetic patients. Country rates are different and shows characteristics properties. Chronic foot ulcer needs multidisiplinary approach for preventing amputations (11).

In a study 25 µgr EGF-IL was applied 3 times per week for 8 weeks to 29 patients who were at high risk of amputation due to Wagner 3 or 4 grade le-

Table 1. Patient characteristics

Patient	Age	Sex	Diabetes age	Lesion place	Wagner Grade	Prior treatment
1	74	Male	20	Right 5. Phalanx	4	Amputation from left 4.metatars level
2	65	Male	15	Left foot 5. Metatars	3	Debridment+NBWT
3	60	Male	22	Right foot 1. Phalanx	4	Amputation+debridment
4	66	Male	16	Left foot 1. Phalanx	3	Amputation+debridment
5	56	Male	33	Left heel, 2,3. Phalanx	3	Amputation+debridment
6	57	Female	35	Left 1. Phalanx and heel	3	Debridment
7	40	Female	25	3,4. Metatars	3	Debridment
8	64	Male	20	Foot sole	3	Debridment

sions. Prior to EGF application, all ulcers were followed for 15 or 25 days with sharp debridements and conventional therapy but remained refractory. Granulation tissue growth was observed after the eighth application in 86% of patients. After the 24th application, amputation was avoided in 17 patients (58%). Reepithelization was observed in 77% of patients, at an average of 66 days. At 1-year follow-up, relapse was seen only in 1 patient. The authors concluded that amputation rates could reduce by EGF-IL application in DFUs(8). In a multicentered double-blind placebo-controlled Phase III clinical study, intralesional application of 75 µg and 25 µg EGF doses and placebo were compared. Both doses were proven to be more efective than placebo. EGF-IL as 75 µg was obtained more effective than 25 µgr EGF-IL significantly on wound healing (12).

In another study the efects of 75 ug EGF-IL was studied on diabetic ulcers. Thirty-two patients with either Wagner grade 3 or 4 ulcers was treated with EGF-IL three times a week for 8 weeks. Nine pateients' Wagner grade 3 ulcers healed with full cicatrization and granulation, one underwent amputation. In Wagner grade 4 group, 20 patients' wound healed totally and 2 patients required amputation. Treatment duration was 46.5±8.9 days (13).

In our study, EGF-IL treatment was showed achievement the other studies. NPWT and surgical interventions were applied to patients and combine with EGF. Treatment was expensive but effective in patients which prior treatment was unsuccesful.

In our experience on patients wounds which priorly have healing problems, improved with intralesional EGF. This treatment is expensive and caused of some allergic reactions. Relation with malignancies are not known for long-term. In our opinion intralesional EGF treatment should be used wounds which were not healed with the other treatments.

DECLARATION OF CONFLICTING INTERESTS

The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

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