

Use of Human Epidermal Growth Factor in Non Healing Ulcer

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Abstract

Aim of the Study : To study the effect of human epidermal growth factor on non healing ulcers.

Method : A diabetic hypertensive patient with end stage renal disease presented with two ulcers on the upper limb. On one ulcer the molecule was applied where as the other one was treated without it. The results were documented on weekly basis.

Results : The ulcer on which the ointment was applied healed completely within 5 weeks where as the other one healed marginally.

Conclusion : Human epidermal growth factor promotes the wound healing at a faster rate than normal even in patients with co-morbidities, but probably can't substitute the skin grafting in ulcer management.

Introduction

End stage renal disease^{1,2} and diabetes remain as important causes of microangiopathy leading to non healing wound. The ulcerogenesis is multifactorial - due to neuropathy, vasculopathy, and various metabolic disturbances.³ However upper limb ulceration is very rare. Literature have described various approaches to this surgical problem namely aggressive debridement,⁴ hyperbaric oxygen therapy,⁵⁻⁸ prolonged antibiotic therapy.⁹ We have given a trial of topical application of Human epidermal growth factor to a patient and the effect has been described in the manuscript.

Case Report

A patient, 62 year male, diabetic hypertensive with end stage renal disease on regular insulin treatment and haemodialysis presented with a nonhealing ulcer

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of 5 weeks duration to ASRAM Medical College, Eluru. Patient was being treated by regular cleaning and dressing and antibiotics from a private doctor. However the ulcer showed no tendency towards healing. Patient was referred to the Department of Surgery by the nephrologist for further management of the non healing ulcer.

Investigations at presentation showed the following:

Haemoglobin = 5.8 gm%

Total leucocyte count = 19,800

ESR = 56 mm 1st hour

Platelet count = 2.1 lacs/cmm

RBS remained in control with aggressive insulin treatment i.e. 24-24-20 units of insulin plain (regular)

Total bilirubin = 2.3 mg/dL direct = 2.0 mg/dL indirect = 0.3 mg/dL

Blood urea = 129 mg%

Serum Creatinine = 4.2 mg%

Sodium = 141 mmol/L

Potassium = 5.3 mmol/L

Calcium = 8.2 mmol/L

Serum Cholesterol = 298 mg%

ECG showed left ventricular Hypertrophy

Chest X-ray cardiomegaly was found

Ulcer Characteristics

Patient presented with two ulcers on the left upper limb.

Ulcer - 1

Ulcer-1 had a dimension of 78 x 60 mm on the dorsum left hand. Depth was 7 mm on average with patches of slough on the floor. Multiple pockets of pus were present underneath the surrounding skin with profuse amount of seropurulent discharge from the floor. Oedema was present in the surrounding area. Although the radial artery pulsation was weak as compared to the opposite side, the rest of the upper limb pulsations and the condition of the vessel wall were normal. Sensory neuropathy was present in all 4 limbs. However the upper limb muscle power was found to be within normal limits. There was no involvement of the bones. Bacteriological examination of the wound swab revealed *Pseudomonas aeruginosa*, sensitive to myriad of antibiotics but as per the nephrologist's consultation piperacillin and tazobactam combination was administered, after adjusting with the creatinine clearance.

Ulcer - 2

The second ulcer, located on the back of the forearm, had a dimension 42 x 28 mm with an average depth of 4 millimeter. Floor was covered with pale pink granulation tissue with scanty amount of serosanguinous discharge.

After the local ethical committee approval, the patient was explained about the treatment process and a written consent was obtained before initiating the intervention.

The management policy consisted of antibiotic

treatment, control of oedema by hand elevation, massage and elastocrepe bandage application, and mechanical debridement of the slough.

The condition of the Ulcer 1 and 2 after one week is shown in Figs. 1 and 2 respectively. At this juncture we started applying Human Epidermal Growth Factor topically on Ulcer-1. Ulcer-2 was managed by sterile dressings **without the growth factor application**. Ulcer-1 picture after 1 week of treatment is shown in Fig. 3 where it can be observed that the granulation tissue has nicely developed and the margin has started healing, heralded by the bluish epithelium and sloping edge, with no trace of slough. At this stage, the main problem was to give a cover to the raw area of Ulcer-1. Accomplishing this was a real challenge since patients was having multiple risk factors namely age above 60 yrs, severe diabetes, anaemia, end stage renal disease, regular haemodialysis, dyselectrolytaemia and lastly hypertension, making

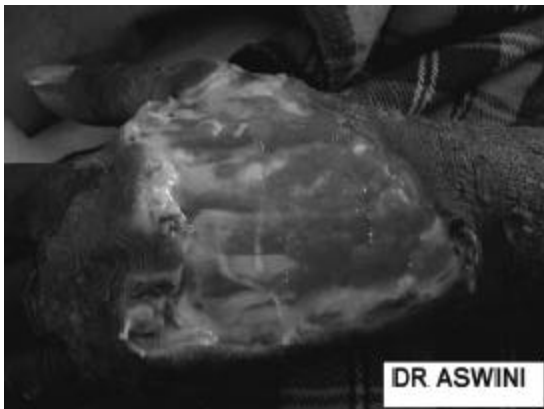


Fig. 1 : Ulcer-1 after 1 week of indoor admission

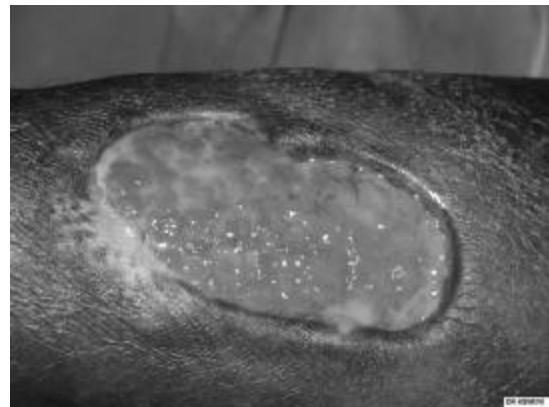


Fig. 2 : Ulcer-2 after 1 week of indoor admission



Fig. 3 : Ulcer-1 after 2 weeks of indoor admission (after 1 week of HEGF application)



Fig. 4 :Ulcer-1 after 3 weeks of indoor admission (after 2 weeks of HEGF application)



Fig. 6 :Ulcer-1 after 5 weeks of indoor admission (after 4 weeks of HEGF application)



Fig. 5 :Ulcer-1 after 4 weeks of indoor admission (after 3 weeks of HEGF application)



Fig. 7 :Ulcer-1 after 6 weeks of indoor admission (after 5 weeks of HEGF application)

him a very high risk case for surgery and anaesthesia as well. Providing a surgical skin cover may land up in graft failure due to the mentioned risk factors and if successful may result in fibrosis and contracture, disabling hand movements.

So we continued the topical application of recombinant epidermal growth factor on regular basis. Meanwhile the supportive treatments like management of ESRD, diabetes, regular physiotherapy and hand exercises were continued.

Observation and Results

The ulcer condition was assessed daily and pictorially documented on weekly basis as shown in Figs. 4, 5, 6, 7 (after 2, 3, 4 and 5 weeks respectively). Here it was observed that the Ulcer-1 healed completely, with full

range of movements in the hand, in 5 weeks time. However, the Ulcer-2, over the same period, showed only marginal healing, with a dimension of 35 mm x 22 mm, which is displayed in Fig. 8. Following this comparison study i.e. after 5 weeks (that is after complete healing of Ulcer-1 versus marginal healing of Ulcer-2), we started the topical application of the epidermal growth factor on Ulcer-2 as well (Patient demand for the ointment application was a contributing factor for this decision as well). After 2 weeks of treatment Ulcer-2 healed almost completely. The Ulcer-2 after 1st and 2nd weeks of treatment (that is Human Epidermal Growth Factor



Fig. 8 : Ulcer-2 after 6 weeks of indoor admission (taken at the same time of Fig. 7)



Fig. 9 : Ulcer-2 after 7 weeks of indoor admission (after 1 week of HEGF application)

application) is demonstrated in Figs. 9 and 10 respectively.

Conclusion

Human epidermal growth factor promotes the healing at a faster rate than normal even in patients with co-morbidities.

Advantages

- Faster wound healing.
- Absence of contracture as patient is on regular hand exercises and physiotherapy.
- No need for any surgical cover.

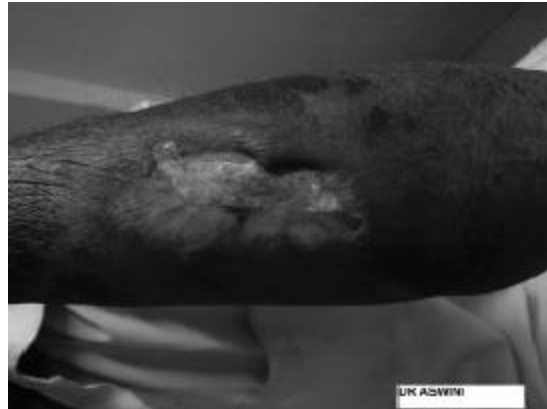


Fig. 10 : Ulcer-2 after 8 weeks of indoor admission (after 2 weeks of HEGF application)

Disadvantage

- The cost factor. The drug is very expensive.
- Maintenance of the cold chain

The conclusion is that

1. The human epidermal growth factor cannot substitute the skin grafting in ulcer management. However, in patients with multiple co-morbidities and in high risk surgical cases, selective use of this molecule remains an attractive alternative.
2. The human epidermal growth factor acts in acute and chronic inflammatory phase as well.

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LEARNING FROM OUR MISTAKES? TESTING NEW ICD TECHNOLOGY

More than 160,000 implantable cardioverter-defibrillators (ICDs) are implanted annually in the United States to prevent sudden death from cardiac causes in high-risk patients.

In 2004, the small-diameter, user-friendly Medtronic Sprint Fidelis ICD lead was approved by the FDA without premarket clinical testing. Three years later, after 268,000 implantations, the manufacturer voluntarily removed the lead from the market because it was prone to fracturing after implantation, causing inappropriate shocks and several reported deaths.

Soon, the three major ICD manufacturers will introduce a new ICD technology. This novel four-pole connector may have important clinical benefits, including a smaller, lower-profile pulse generator and a thinner lead, which should simplify the surgical procedure and enhance patients' comfort.

In our opinion, the decision by the FDA and industry to forgo pre-market clinical testing of the connector is not in the best interest of patients.

The single most important attribute of an ICD system is its ability to reliably detect and treat potentially lethal arrhythmias. However, innovations may harbour unknown hazards, and new ICDs should be thoroughly tested under the supervision of an investigational review board before they are adopted for widespread use. Only then can it be confidently stated that we have learned from our mistakes and will not repeat them.

Robert G Hauser, Adrian K Almquist; N Engl J Med; 2008; 359(24) : 2517-2519.