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Diabetes & its Complications

An Amazing Cure

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ABSTRACT

We reported previously that topical treatment of Diabetic Foot Ulcers (DFU) with authentic human epidermal growth factor (rEGF) in addition to debridement surgery was over 50% more efficient than the latter operation employed alone. In this communication, using the facile topical protocol, we further demonstrate that rEGF is not only capable of healing DFU, but was also shown to be effective in bringing a traumatic wound, which was caused by the amputation of the three larger toes of an ulcerated foot, to complete healing.

Keywords

Amputation, Authentic human epidermal growth factor, Complete healing, Diabetic foot ulcers, Topical treatment.

Abbreviations

DFU: Diabetic foot ulcers; EGF: Human epidermal growth factor; rEGF: Authentic recombinant human epidermal growth factor.

Introduction

Diabetic Foot Ulcers (DFU), one of the major health-threatening side effects afflicting patients with diabetes mellitus, are chronic ulcerations of the lower limbs. As a result of diabetic peripheral neuropathy and vascular damage, thereby leading to poor circulation and deficient supply of skin growth factors to wounds occurring in lower extremities, DFU are difficult to heal. Various methods including wound debridement [1], hyperbaric oxygen therapy [1], electrical stimulation [2], maggot therapy [3-4] and skin grafting [2], have been employed for treating DFU. These treatments result commonly in some degree of healing but rarely in the complete closure of chronic wounds associated with diabetes.

In 2003, our group pioneered the application of a treatment protocol combining wound debridement and a skin growth factor, human epidermal growth factor (EGF), for effective (95%) healing of DFU [5]. The EGF employed was expressed and purified from a genetically engineered *Escherichia coli* excretion system [6-10]. The resulting recombinant EGF (rEGF) was not only shown to be biologically potent, but also highly stable. More importantly, it is authentic in structure, thus sharing the same amino acid sequence with that of its natural counterpart produced in our bodies [7].

Subsequently, topical treatments using rEGF as the active ingredient for various kinds of wounds including: DFU [5,11], serious scalds [11-12], an acute immunological disorder – Steven Johnson Syndrome [13-14], and hard-to-heal bedsores commonly afflicting elderly and handicapped individuals [11,14], have all resulted in successful outcomes. The findings further lend support to the view that rEGF is an active ingredient for treating a wide range of wounds. They also shed light on the controversial results attained in previous studies regarding the application of EGF to wound healing. In many of them, the identity/primary structure of EGF employed was not explicitly disclosed, thus leading to conflicting observations [15-16].

To further explore the application of rEGF to the healing of recalcitrant wounds, we applied the same treatment protocol, involving the use of 0.04% (w/w) rEGF [5,17], to treat a traumatic injury resulting from the amputation of the first three toes of an ulcerated foot. In this communication, we report our success in treating such a severe wound.

Results and Discussion

In many cases of DFU, despite the implementation of wound care management procedures, e.g. debridement surgery [1], the ulceration concerned may continue to deteriorate to result in an incurable wound, which requires amputation in attempting to halt the progression of complications.

An 80-year-old diabetic German patient underwent amputation in which the first three toes of his right foot were trimmed for over 6 months (Figure 1). Despite being treated using conventional

procedures for a long duration, there was no sign that the surgical wound would heal and the pathological conditions might get worse to result in destructive side effects such as infections. The patient was recommended to try one of our commercial products, Platinum cream (Platinum), in which 0.04% (w/w) rEGF is employed as the active ingredient (www.gene-viante.com). Although Platinum had never been applied to treat wounds which were as severe as that shown on the affected foot (Figure 1), and there were controversial findings reported by others regarding the efficacy of EGF on wound healing [15-16], based on the superb performance previously achieved by rEGF in treating various types of wounds [5,11-14,17], we were hopeful that it would work equally well to promote healing of the residual limb.

The open wound was treated using the protocol established previously for topical management of various hard-to-heal wounds [17]. In short, a wound was first thoroughly cleansed (with diluted Dettol) and it was then allowed to air dry. Subsequently, a film of Platinum containing 0.04% (w/w) rEGF (www.gene-viante.com) was layered on the wound, which was then covered up with a gauze pad. The whole process was repeated twice daily and the progress of healing was monitored closely.

The treatment regimen worked well on the traumatic wound (Figure 1). Despite handling a pretty large area involving the truncation of the first three toes from the right foot (Figure 1), rEGF appeared to exert an active role in the healing process. The wound was shown to heal readily and effectively, as reflected by the lack of signs of infection, inflammation or excessive exudate production (Figure 1), which are commonly found in infected or unsuccessfully treated wounds [18-19]. With continuous application of the topical protocol [17], the healing of the surgical wound progressed satisfactory to result finally in complete closure in about 7 weeks (Figure 1). Our successful achievement in the present study may prove to represent a practical approach for effective healing of recalcitrant wounds such as lower extremity injuries resulting from surgical amputations.

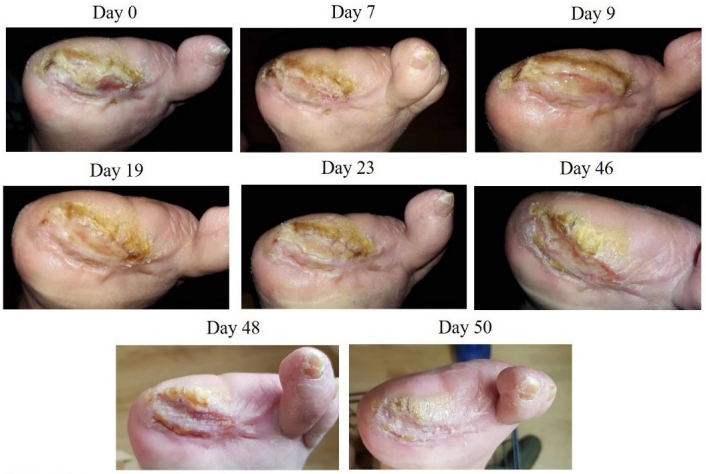

Figure 1: Treatment of an unhealed amputation injury. The pictures depict the progress of healing of the wound caused by the surgical removal of the first three toes of the right foot of an 80-year-old diabetic male patient. Despite being treated with conventional treatment methods, there was no sign of healing of the wound for over 6 months. The wound was then topically treated with Platinum containing 0.04% (w/w) rEGF. The duration of the treatment is shown on top of the picture. Day 0 stands for prior to commencing treatment.

The application of rEGF produced in our laboratory to the treatment of various types of wounds has led corroboratively to a positive healing effect [5,11-14,17], which contradicts to previous results reporting conflicting observations [15-16]. The inconsistent outcomes were found to result from the use of different EGF isoforms. In many studies the peptide sequence of EGF was not disclosed, thus creating a false impression that the same EGF molecule was employed [15]. As a matter of fact, despite the presence of the information concerned, the sequence was revealed to be unauthentic, thus presenting a different primary structure from that of native EGF [15, 20]. Since our application of rEGF, which is authentic in structure [5,7,10-11,14], to the treatment of various wounds results consistently in a positive outcome, the findings lend strong support to our interpretation that authentic EGF, e.g. rEGF, possesses the required conformation to interact with its cellular receptor to perform its biological functions [11,14-15].

Conclusion

DFU are chronic wounds which have been shown to be difficult to heal. Employing rEGF in combination with a simple topical treatment protocol, we have achieved high rates of success in healing DFU. In the current communication, we further demonstrate that rEGF performs effectively in treating a recalcitrant wound resulting from the amputation of the first 3 toes of an ulcerated foot.

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