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Research Article

DRESSING WITH TOPICAL APPLICATION OF EPIDERMAL GROWTH FACTOR GEL IN THE MANAGEMENT OF CHRONIC WOUNDS: A PROSPECTIVE STUDY

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ABSTRACT
Wound healing is a physiological phenomenon that involves a complex series of integrated cellular and biochemical responses. Treatment with growth factors is beginning to gain worldwide importance since is an effective method to promote wound healing. There have been many basic research studies on wound healing using several growth factors including basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF). In this study we have used a topical formulation containing human recombinant epidermal growth factor in treating various types of cutaneous wounds in 25 patients. Outcome of this study showed that wounds can be treated effectively dressing with epidermal growth factor gel. Which promotes the wound healing process, reduces wound pain and thus improves the patients quality of life.

Keywords: *Wound Healing, Epidermal Growth Factor, Topical Formulation*

INTRODUCTION
Despite the progress achieved in the past few decades, wound healing remains a difficult issue to which modern medicine does not always have an efficient response. Methods like hemotherapy, which consists of applying dressings soaked in blood to the wound itself, have been applied in order to accelerate the healing of certain difficult wounds. Physicians who used this treatment were unaware that they were in fact treating wounds with growth factors (Iwayama-Hibino *et al.,* 2009; Triquet *et al.,* 1994). In 1962, Cohen *et al.,* reported on a protein called epidermal growth factor (EGF), found among nerve growth factors (NGFs) extracted from mouse submandibular gland. EGF stimulates the proliferation of various cells, including fibroblasts and epithelium derived cells such as keratinocytes (Gospodarowicz, 1974). In this study we are highlighting the utility of topical application of epidermal growth factor in treating chronic wounds.

MATERIALS AND METHODS
This clinical study was conducted as a prospective study in one of the tertiary referral hospitals at coastal Karnataka. The proforma was designed to include relevant demographic information, history of illness and examination findings.

a) Inclusion criteria:

-Patients with cutaneous ulcer due to traumatic defects, burns, ulcer of venous etiology, decubitus ulcer, diabetic foot.

b) Exclusion criteria:

-Patients on treatment with immunosuppressors, corticoids, patients with severe peripheral arteriopathy.

-Patients suffering from severe malnutrition, malignant cachexia, autoimmune diseases.

At the initial examination, patients' age, sex, general health state and comorbidities, age and size of the wounds as well as previous local and systemic treatments were recorded using a standardised questionnaire.

Study was accomplished by allocating the patients with chronic wounds in to two groups with 25 patients each: study group (group1) and a control group (group 2). Patients were randomized to two groups by block randomization using a computer program. Allocation was concealed from patients and observers.

In group1 wounds were applied with topical gel containing recombinant human epidermal growth factor and covered with a sterile dressing bandage.
Control (group2) wounds were dressed with paraffin gauze and covered with standard dry dressings.
Dressing change was done daily in both the groups. Treatment efficiency was evaluated with respect to the duration in both the groups. The first evaluation was done on day five. Subsequent evaluations were done at two day intervals until 1 month or complete healing. At the beginning and end of the study, we evaluated the condition of the wound by recording the parameters like proportion of slough, granulation and epithelial tissue. Meanwhile eventual adverse effects were also recorded throughout the follow-up period.

RESULTS AND DISCUSSION

Results

Altogether, 50 patients were included in our study; which included 27 males and 23 females. The gender distributions in the 2 groups were almost similar and there were no statistically significant differences between the study and control groups with respect to gender and age (Table 1). The average age for study group was 62 years and group 2 was 60 years.

Table 1: Age and sex distribution of the study and control group

	Study group (Group1)	**Study group (Group2)**
Mean Age	62	60
Male: Female	13:12	14:11

Traumatic defects, burns, ulcer of venous etiology are the most frequent pathologies in our study (Table 2).

Table 2: Clinical type of ulcer included in our study

Cause proportion	**No of subjects**	
	Group 1	**Group 2**
Venous leg ulcer	5	5
Decubitus ulcer	6	6
Diabetic ulcer	5	5
Burn	4	4
traumatic wound	3	3
Others	2	2

The majority of the patients had chronic wounds, which were six months old on an average.The general health was assessed as very good in 20 patients and age-appropriate in 20 patients. 10 patients had a reduced physical state due to comorbidities.

Table 3: Wound condition at the end of study

Wound Features	**Group 1 (Wound area in %)**
Epithelialization	25%
Granulation tissue	90%
Slough	10%

At the end of 1 month of treatment, slough fell from 60 to 10% in group1. At the same time, the area covered with granulation and epithelial tissue markedly increased drastically in group 1compared to group 2. The wound size (length x width) fell significantly i.e. from 4.5x3 cm to 3 x 2.5 cm in group 1. Four wounds were completely re-epithelialised at the end of the study. The number of patients reporting wound pain decreased markedly in the course of the five dressing changes compared to control group. A

significant acceleration of epithelialization across the wound surface was noted following daily EGF treatments. Apart from mild discomfort and itching around the wound site in 2 cases, no other significant adverse effects were recorded in study group.

Mean & SD were calculated for age and extent of decrease in wound size for 2 groups separately. "Statistical analysis was performed using the SPSS computer package version 20.0. The mean± SD was used for quantitative variables. Independent samples t-test was applied, to assess the differences in means of quantitative variables between patients and controls. P- value and Confidence intervals were calculated. P<0.05 was considered as statistically significant.

Discussion

When the skin is injured, the body initiates a cascade of processes that eventually lead to a re-epithelialisation of the wound area (Martini, 1997). As a fundamental response to tissue injury, wound healing is a normal complex process including four general phases of hemostasis, inflammation, cell proliferation, extracellular matrix production, and remodeling, which usually in each phase occurs consequently in a regulated manner (Gosain and DiPietro, 2004; Mathieu *et al.,* 2006). If the precisely coordinated interplay of inflammatory cytokines, mitogenic growth factors, extracellular components and enzymes such as proteases is disturbed, stagnation of the repair process can occur, resulting in a chronic wound (Scheithauer and Riechelmann, 2003). Chronic wounds are of various origins and have different aetiologies. Vascular causes such as venous insufficiency, arterial occlusive disease, diabetic angiopathy and neuropathy are the most common systemic disorders. At the local level, infections, and the presence of a foreign body in the wound can delay wound healing. In addition, prevailing systemic diseases include malnutrition, malignant cachexia can also hamper wound healing (Izadi and Ganchi, 2005). Taking a systematic and disease-specific diagnosis of these local and systemic factors is a prerequisite for successful wound treatment (Grey *et al.,* 2006). Because of the complex pathophysiology of a chronic wound, therapy should not be directed only toward isolated local factors. Rather, a more holistical approach to treatment should be taken (Schultz *et al.,* 2003). Parameters like size and location of the wound, the degree of exudation, presence of slough, necrosis, and possible signs of infection as well as the healing phase of a wound at any given time of the wound state influence the choice of the appropriate wound dressing (Gillitzer, 2002).

Epidermal growth factor (EGF) — which is produced by platelets, macrophages and monocytes — interacts with EGF receptors on epidermal cells and fibroblasts (Nanney, 1990) EGF.

primarily acts to stimulate epithelial cell growth across the wound, and also acts on fibroblasts and smooth muscle cells. A number of studies have demonstrated the effects of EGF on wounds through the shortening of healing time, increasing the tensile strength of the skin and reducing unfavourable tissue effects (Brown *et al.,* 1986; Epstein *et al.,* 2000). Topical application of EGF stimulates epithelialization of partial-thickness wounds and produces a positive impact on the underlying dermis during the early phases of wound repair (Lillian, 1990).

It has been reported that repeated treatment with EGF increases the epithelial cell proliferation in a dose dependent manner and accelerates the wound healing process, whereas a single EGF treatment has no noticeable effect on the wound-healing rate (Brown *et al.,* 1986; Kim *et al.,* 1997). The study conducted by Doerler *et al.,* demonstrated that the novel EGF-containing wound dressing was generally well tolerated and safe. Combined with the significant wound surface reduction, it can be regarded as an adequate novel treatment option which is corroborating with our study result (Doerler *et al.,* 2014). The results of the study conducted by Khanbanha showed a significant promotion in the wound healing process in the group given gel containing EGF treatment, compared to treatment with the same gel without EGF which is also corroborating our study findings (Khanbanha *et al.,* 2014).

Conclusion

The results demonstrate the positive contribution of topical application of epidermal growth factor in stimulating wound healing. This method could be used as a first line of treatment for patients with impaired healing. But the cost factor associated with this method is considered as one of the important drawbacks in implementing this in economically weaker section of the patients. This strikingly simple

approach could have a significant impact on wound care. However, further research studies are needed to support and to assess the real benefits of our findings in wide population, for this technique to be used as a standard protocol.

REFERENCES

Brown GL, Curtsinger L and Brightwell JR *et al.*, (1986). Enhancement of epidermal regeneration by biosynthetic epidermal growth factor. *The Journal of Experimental Medicine* **163**(5) 1319–24.

Brown GL, Curtsinger L, Brightwell JR, Ackerman DM, Tobin GR, Polk HC Jr, George-Nascimento C, Valenzuela P and Schultz GS (1986). Enhancement of epidermal regeneration by biosynthetic epidermal growth factor. *The Journal of Experimental Medicine* **163** 1319-1324.

Doerler M *et al.*, (2014). A novel epidermal growth factor--containing wound dressing for the treatment of hard-to-heal venous leg ulcers. *Advance in Skin and Wound Care* **27**(10) 456-60.

Epstein JB, Gorsky M, Guglietta A, Le N and Sonis ST (2000). The correlation between epidermal growth factor levels in saliva and the severity of oral mucositis during oropharyngeal radiation therapy. *Cancer* **89**(11) 2258–65.

Gillitzer R (2002). Modern wound management. *Der Hautarzt* **53** 130-47.

Gosain A and DiPietro LA (2004). Aging and wound healing. *World Journal of Surgery* **28**(3) 321–326.

Gospodarowicz D (1974). Localisation of a Fibroblast Growth Factor and Its Effect Alone and with Hydrocortisone on 3T3 Cell Growth. *Nature* **249** 123-127.

Grey JE, Enoch S and Harding KG (2006). Wound assessment. *British Medical Journal* **332** 285- 88.

Iwayama-Hibino M, Sugiura K, Muro Y and Tomita Y (2009). Successful topical hemotherapy with a new occlusive dressing for an intractable ulcer on the toe. *The Journal of Dermatology* **36** 245–8.

Izadi K and Ganchi P (2005). Chronic wounds. *Clinics in Plastic Surgery* **32** 209-22.

Khanbanha N, Atyabi F, Taheri A, Talaie F, Mahbod M and Dinarvand R (2014). Healing Efficacy of an EGF Impregnated Triple Gel Based Wound Dressing: In Vitro and In Vivo Studies. *BioMed Research International* **2014** 10.

Kim JS, McKinnis VS, Adams K and White SR (1997). Proliferation and repair of guinea pig tracheal epithelium after neuropeptide depletion and injury in vivo. *American Journal of Physiology* **273** L1235-1241.

Lillian B Nanney (1990). Epidermal and Dermal Effects of Epidermal Growth Factor During Wound Repair. *Journal of Investigative Dermatology* **94** 624–629.

Martini P (1997). Wound healing – aiming for perfect skin regeneration. *Science* **276** 75-81.

Mathieu D, Linke JC and Wattel F (2006). Non-healing wounds. In: *Handbook on Hyperbaric Medicine* 401–28,

Nanney LB (1990). Epidermal and dermal effects of epidermal growth factor during wound repair. *Journal of Investigative Dermatology* **94**(5) 624–9.

Scheithauer M and Riechelmann H (2003). Review part I: Basic mechanisms of cutaneous woundhealing. *Laryngo-Rhino-Otologie* **82** 31-35.

Schultz GS, Sibbald RG, Fallanga V, Ayello EA, Dowsett C, Harding K, Romanelli M,Stacey MC, Teot L and Vanscheidt W (2003). Wound bed preparation: a systematic approach to wound management. *Wound Repair and Regeneration* **11** 1-28.

Triquet B, Ruffieux P, Mainetti C, Salomon D and Saurat JH (1994). Topical hemotherapy for leg ulcers. *Dermatology* **189** 418–20.