Original Research Article

The Role of Epidermal Growth Factor Cream in Healing of Diabetic Foot Ulcer- Comparative Analytical Study in South India

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ABSTRACT

In spite of growing advances in medical technology and understanding of ulcer healing, no ideal method for treating the much dreaded Diabetic foot ulcer are defined. Numerous wound care methods, innovative natural healing processes, induced enhanced healing using innate and synthetic materials and simultaneous correction of comorbidity are postulated. This study is intended to evaluate one of the high technology modern advancements in wound care the use of epidermal growth factor for expected wound healing and to evaluate its role with a control group.

This prospective analytical case control comparative study is carried out in the Department of General Surgery Kanyakumari Government Medical College for the period of one year from 2017 January to 2017 December. The patients with diabetic foot coming for treatment are grouped into two groups under randomized control trial method with 25 patients in each group. The control group is treated with conventional methods and the experimental group with standardized Recombinant epidermal growth factor. (Regen-D 150) applications.

The data collected were tabulated and using SPSS software version 23.00 statistical analysis done. In our study we could observe statistically significant improvement in wound healing in the group receiving Recombinant epidermal growth factor cream. The pain score and the reduction in the size of ulcers are significant. The literature reviews also confirm this finding. Hence we conclude and propose it is worth using the Recombinant epidermal growth factor cream in diabetic foot ulcer to obtain early and complete wound healing.

Key word: Diabetic foot ulcer, Epidermal growth factor, wound healing, granulation tissue

INTRODUCTION

Diabetes Mellitus, the metabolic disorder has percolated to the community across the world and become a global pandemic disease in the current century. The rise in the life expectancy, usage of junk food, sedentary life style and metabolic syndrome has paved the way for steady progression of the disease in the country. India has scored largest burden of Diabetic individual next to china. [¹] With scientific advancement and based on research many innovative treatment modalities are suggested. However due to lack of clear guidelines on treatment protocol and no uniform availability or affordability of treatment procedure, 15% of persons having diabetes proceed to Diabetic foot Ulcer and resulting in amputation. [²]

In 1962 Stanley Cohen, a renowned Biochemist in the Vanderbilt University Tennessee discovered and published the
epidermal growth factor and its significant role in the process of wound healing. [3] In 1986 he got the Nobel Prize for his research on his success on isolation of this peptide from a mouse and showing it had an impact on the eruption of incisor tooth and eyelid opening.

In 2002 Loot and Kenner et al had demonstrated the ability of haemopoietic cells to synthesize this epidermal growth factor. Epidermal growth factor acts by proliferation, mitogen and maturation of cells, by the mechanism of binding receptor kinase on target cells. [4]

EGF is a single chain polypeptide comprising 53 amino acid and having the molecular weight of 6200 Daltons. ECF stimulate cell proliferation, differentiation and maturation all important process in wound healing. [5]

Diabetic Ulcer are developing by the progression of neuropathy (sensory, automatic, motor) vasculopathy ( micro and macro) and enhanced atmosphere for growth of microorganism by providing good culture media and imbibing the chemotactic properties of leukocyte and macrophages. [6] Early diagnosis of metabolic disorder of glucose, proper health education, lifestyle modification and special focus on foot care can prevent the development of ulcer and complication. Appropriate usage of antibiotics, proper and adequate wound debridement, usage of tailor made dressing materials, off-loading the pressure and use of appropriate foot wear can prevent the ulcer resulting in amputation. 80% amputations happening today or due to Diabetic foot ulcer. [7]

Impact of various roles of EGF in ulcer pathogenesis and wound healing, recombinant human epidermal growth factor (rhEGF) progressed as a viable therapeutic option and as a most attractive growth factor for enhancing chronic wound healing. [8] EGF acts by stimulation, proliferation, and migration of keratinocyte; fibroblast stimulation and formation of granulation tissue; stimulation and proliferation of endothelial cells facilitating dermal regeneration and stimulator of fibroblast migration and wound contraction. [9]

**Aims and objectives of the study**
The present study aims to study the efficacy of recombinant epidermal growth factor and its advantages over the conventional wound care methods.

**MATERIALS AND METHODS**

**Study design:** It is a prospective randomized (1:1) double blind, case controlled analytical comparative study to evaluate the efficiency of human epidermal growth factor cream (Regen-D 150G) used in the wound care of diabetic foot ulcer.

**Duration:** one year 2017 January to 2017 December
The study was done with 50 patients and they were randomized into two group
1. Control group - 25 patients
2. Experimental group – 25 patients

**Inclusion Criteria**
- Patient with diagnosis of Diabetic Foot Ulcer with Wagner grade 1 – 2
- Age 25-75 both sex
- Blood sugar is on control with medication
- Ulcer size 2-10 cm.

**Exclusion Criteria**
- Patient with active systematic infection or comorbidities
- Ulcer size more than 10 cm
- Immuno compromised individuals
- Patient having diabetic foot ulcer of Wagner grade more than 3
- Patient not willing to give consent
- Pregnancy
- Malignancy
- Chronic alcoholic and smokers

**Procedure:** The demographic data of all participants collected. Diabetic status assessed. Adequate surgical debridement of the ulcer was done. The ulcer is washed using normal saline and complete hemostasis secured. Swab culture done. Measurement of wound was done on day 1, 15, 30. After randomization and obtaining
consent, for the control group dressing was done with Povidone ointment and for the experimental group with adequate application of Recombinant Human epidermal growth factors available in standardized preparation Regan-D 150 g.

**Ethical consideration**

This proposed study ethical clearance obtained from the college ethical board. Both written and oral information in local language given to the participants of the study and then signature obtained. Demography data and study data were collected. Participants were given the option to withdraw from the study at any time.

**OBSERVATION**

1. **Gender Distribution**

   Male predomination (78%) observed. However there was no statistical significance between two genders between the experimental and control groups.

   **Table 1: Gender Distribution within group**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Percentage</td>
<td>Number</td>
<td>Percentage</td>
</tr>
<tr>
<td>Control</td>
<td>19</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Experimental</td>
<td>20</td>
<td>80</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>78</td>
<td>11</td>
</tr>
</tbody>
</table>

Fig: 1: Gender Distribution in both the groups .

2. **Age distribution**

   In our study mean age in the experimental group was 56 years and control group 57 years and not statistically significant.

   **Table 2: Age Distribution within group**

<table>
<thead>
<tr>
<th>Age below 40</th>
<th>Age 40 - 50</th>
<th>Age 50 - 60</th>
<th>Age 60 - 70</th>
<th>Above 70</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2</td>
<td>4</td>
<td>9</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>Experimental</td>
<td>8</td>
<td>16</td>
<td>10</td>
<td>24</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>20</td>
<td>19</td>
<td>30</td>
<td>100</td>
</tr>
</tbody>
</table>

Fig: 2 Distribution of age in both the groups .

3. **Comparison of change in size of the Ulcer due to healing**

   In our study as ulcer size are measured on day 1, 15th and 30th the results are observed and there is statistical significant between ulcer size reduction between control group and experimental group. On the 30th day the ulcer healing in terms of size ranged from 54-81.5% in the EGF group as compared to the conventional...
group in which the decrease in size ranged from 34-47%.

### Table 3: Comparison wound size reduction in both groups.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. deviation</th>
<th>95% confidence interval of difference</th>
<th>Bonferroni “P” Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental Day 1-15th</td>
<td>2.90970</td>
<td>1.95287</td>
<td>1.99573-3.82367</td>
<td>.000</td>
</tr>
<tr>
<td>Day 1-30th</td>
<td>4.7692</td>
<td>20.0514</td>
<td>3.5985-50.9388</td>
<td>.000</td>
</tr>
<tr>
<td>Day 15th-30th</td>
<td>1.8594</td>
<td>1.58945</td>
<td>1.11556-2.60334</td>
<td>.000</td>
</tr>
<tr>
<td>Control Group Day 1-15th</td>
<td>1.43050</td>
<td>1.47412</td>
<td>0.74059-2.12041</td>
<td>.000</td>
</tr>
<tr>
<td>Day 1-30th</td>
<td>2.4690</td>
<td>2.2078</td>
<td>1.4357-3.5023</td>
<td>.000</td>
</tr>
<tr>
<td>Day 15th-30th</td>
<td>1.01421</td>
<td>1.01421</td>
<td>0.05688-1.51316</td>
<td>.000</td>
</tr>
</tbody>
</table>

### Fig 3: Comparison between changes in ulcer size in two groups

**Table 4: Healed Ulcers in Experimental (n=25) and Control group (n=25)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Completely healed Ulcer</th>
<th>D-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental Group</td>
<td>23(92%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Control Group</td>
<td>16(60%)</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

In 1991 through a study conducted by Brown et al in people with chronic diabetic foot ulcer 90% of them were healed with application of Epidermal growth factor. [10] VK. Mohan et al in 2007 through a phase three clinical trial using Regen =D 150 ,stated Epidermal Growth factor result in healthy granulation and stimulate epithelialization, thus leading to final wound closure. [11] Tsang and colleagues in their study involving 61 diabetic patients with foot ulcer with Wagner score 1 or 2 and normal ABPI state treatment with 0.04% EGF accomplished much better healing. [12] Larijani et al. also found that after four weeks of treatment ,mean closure was significantly higher in patients treated with
epidermal growth factors comparing with the control group with the conventional treatment methods (71.2% vs 48.9%, p<0.03). 

In our study, we found that rhEGF improved the percentage of complete ulcer healing and in the size of the ulcer significantly. The decrease in ulcer size was more evident in the first 15 days when compared to the next 15 days. There was 50% reduction in the size of the ulcer as compared to the conventional group in which the decrease in size was less than 25%.

In our study we also noted that as compared to the first day, on the 30th day the ulcer healing in terms of size ranged from 54-81.5% in the EGF group as compared to the conventional group in which the decrease in size ranged from 34-47%. The patient satisfaction and cooperation was much better in the EGF group as compared to the conventional group in most ulcers. The possible reason attributed to this is the lesser need of surgical debridement due to lesser slough.

The amount of pain experienced was lesser in the study group as compared to the conventional group in most ulcers.


Fernández-Montequín et al had postulated the intralesion injections of epidermal growth factor had yielded more and quicker results as the wound milieu may destroy the growth factors. However in our study we have not used the injection but only the topical application of cream. [19]

**CONCLUSION**

Epidermal Growth Factor plays a major role in wound healing with better and faster resulted than conventional dressings in the healing of diabetic ulcers. The dreaded complication of amputation can be prevented by the appropriate use of epidermal growth factor in chronic diabetic foot ulcers.

**REFERENCES**


2. Hardwick J Sch Maljohan D et al Epidermal growth factor therapy and wound healing - Past future perspective the surgeon 2008 Jan 30.6(3) 172.7


4. Loots MA, Kenter SB et al Fibroblasts derived from Chronic Diabetic Ulcers differ in their response to stimulation with EGF, 1 GF – 1 bFGF and PDGF – AB compared to controls. European journal of Cell Biology 2002 Mar 31: 81 (3) 153-60


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