

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, mitigation 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. EGF 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, life style 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 wears 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

	Male		Female		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Control	19	6	6	24	25	100
Experimental	20	80	5	20	25	100
Total	39	78	11	22	50	100

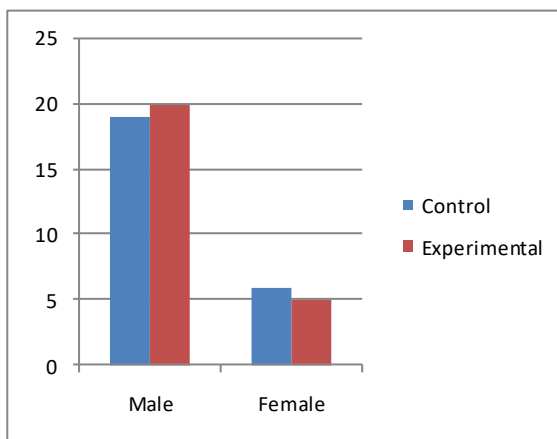


Fig:1: Gender Distribution in both the groups .

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

	Control		Experimental		Total	
Age below 40	2	8	3	12	5	10
40-50	4	16	3	12	7	14
50-60	9	36	10	40	19	38
60-70	6	24	5	20	11	22
Above 70	4	16	4	16	8	16
Total	25	100	25	100	50	100

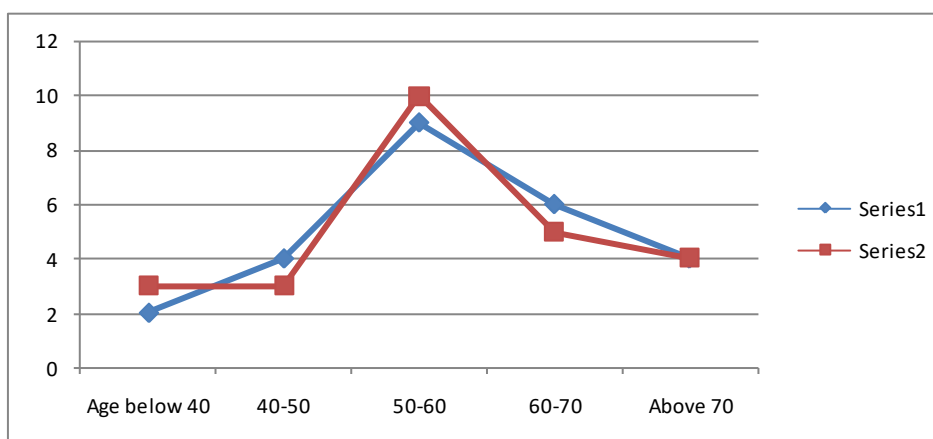


Fig: 2 Distribution of age in both the groups.

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.

	Mean	Std. deviation	95% confidence interval of difference		Bonferroni "P" Value	
			Lower	Upper		
Experimental						
Day 1-15 th	2.90970	1.95287	1.99573	3.82367	.000	HS
Day 1-30 th	4.7692	2.05014	3.5985	5.09388	.000	HS
Day 15 th - 30 th	1.8594	1.58945	1.11556	2.60334	.000	HS
Control Group						
Day 1-15 th	1.43050	1.47412	0.74059	2.12041	.000	HS
Day 1-30 th	2.4690	2.2078	1.4357	3.5023	.000	HS
Day 15 th - 30 th	1.01421	1.01421	.056384	1.51316	.000	HS

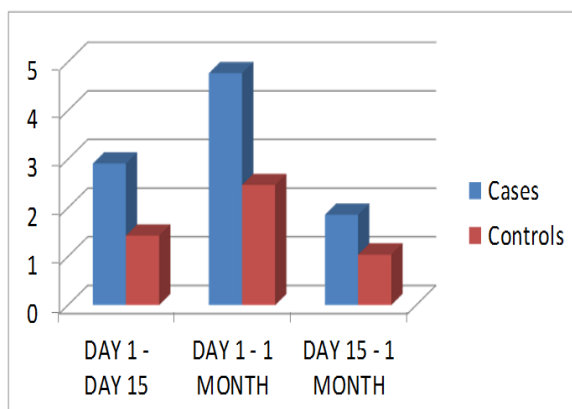


Fig 3: Comparison between changes in ulcer size in two groups

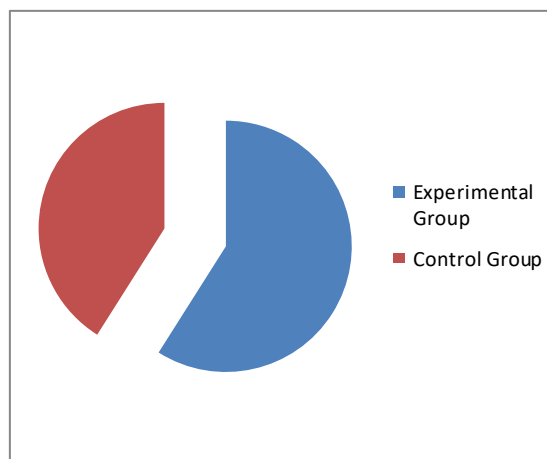


Fig :4: Percentage of wound healed in both the groups

4. Comparison between healed ulcers in two groups

The number of ulcers healed in experimental group is statistically significant P value 0.014

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

	Completely healed Ulcer	D-Value
Experimental Group	23(92%)	0.014
Control Group	16(60%)	

5. Reduction in wound size comparison

The reduction in wound size is significantly high in the experimental group with Recombinant Epidermal growth factor cream application .It is also noted the significant reduction in the size was most apparent and prominent in the first 15 days than the second 15 days.

Table 5: Showing the paired difference in wound size reduction

	Group	Paired Differences				t value	p value	
		Mean	Std. Deviation	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1	Experimental	2.90970	1.95287	1.99573	3.82367	2.698	.010	sig
DAY 1 - DAY 15	Control	1.43050	1.47412	.74059	2.12041			
Pair 2	Experimental	4.7692	2.5014	3.5985	5.9398	3.053	.004	HS
DAY 1 - 1 MONTH	Control	2.4690	2.2078	1.4357	3.5023			
Pair 3	Experimental	1.85945	1.58945	1.11556	2.60334	2.051	.046	sig
DAY 15 - 1 MONTH	Control	1.03850	1.01421	.56384	1.51316			

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%, $p < 0.03$).^[13]

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.

In accordance with the study results published by Hoon et al, Yera- Alos IB et al, Fernández-Montequín, Tuyet HL et al, Man Wo Tsang et al, Ramakrishna et al, Huo Qiu et al, Dogan, Demirer et al, Yang s et al, Afshari M et al, Richard et al, Doerler et al, and Khanbanha et al.^[14-18] our study showed a positive effect on wound healing and granulation issue formation.

Fernández-Montequín et al had postulated the intralesional 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.

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