

Epidermal Growth Factor Versus Conventional Wound Dressings In Treatment Of Diabetic Ulcers- A Comparative Study

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Abstract : With the advent of various advances in medical technology in twenty first century, many techniques have been tried to heal chronic leg ulcers. Although there exists no ideal wound dressing in the management of chronic wounds especially diabetic ulcers, several methods of wound dressing is being used and still evaluated. Hence we conducted the following study to evaluate the efficacy of Epidermal Growth Factor over conventional dressings in the healing of diabetic ulcers.

The study was a prospective case control comparative Study titled "Epidermal growth factor versus conventional wound dressings in treatment of diabetic ulcers- A comparative study" done in the department of General Surgery, K S Hegde Medical Academy, during the time period August 2014 to August 2016, on cases of diabetic ulcers who visited the OPD and IPD of K.S. Hegde Hospital, Mangalore. Study was conducted on 40 consenting patients who met the predefined criteria, divided into 2 groups of 20 patients with the Epidermal growth factor dressing and 20 patients with conventional dressing.

The data was collected in a proforma and the details transferred to a master chart and the results were analyzed.

Statistical Analysis was done using SPSS software version 23.0. In our study we used paired t test to check the level of statistical significance. A 'p' value less than 0.05 ($p < 0.05$) is considered significant.

In our study a total of 40 cases, of which 20 with conventional dressings and 20 with EGF dressings were studied. There was no significant difference in the demographic factors or the duration and size of the ulcer between the two groups of study. In our study males predominated in the study population. Acute wounds of less than 1 month duration were mostly studied. There was increased rate of granulation tissue formation and the size of the ulcer decreased drastically with EGF therapy

In our study we concluded that Epidermal Growth Factor definitely has an edge over the conventional dressings in the healing of diabetic ulcers in terms of granulation tissue formation, and healing of the ulcer especially in diabetic wounds of less than one month duration.

Keywords: Epidermal Growth Factor, Conventional dressings, Diabetic ulcers ,Wound healing

I. Introduction

Diabetes is considered as the health crisis of the 21st century. Approximately 15% of all patients with diabetes develop diabetic ulcers. Due to the associated diabetic neuropathy these ulcers are left unattended and are often followed by amputations in the later stages. Due to the increased glucose levels in the tissues, these diabetic ulcers are mostly infected. In recent years the technology of dressing has developed significantly, and several new products which reflect greater knowledge of tissue repair physiology have been produced and successfully used for the management of various types of chronic ulcers. However there is limited information to guide treatment of diabetic ulcers.¹

Growth factors play a very important part in the process of wound healing. Epidermal Growth Factor was discovered by an American Biochemist Stanley Cohen in 1986, for which he won Nobel Prize in physiology and medicine.² Epidermal growth factor is a type of growth factor which is synthesized by the cells of the hematopoietic system namely the megakaryocytes, macrophages monocytes and keratinocytes as shown by Loot, Kenter et al. 2002. It act by regulating the proliferation, migration and differentiation of cells by a mechanism of binding to receptor kinases on target cells.³

Epidermal growth factor induce cellular proliferation through the EGF receptor, which has a tyrosine kinase cytoplasmic domain, a single trans membrane domain, & an extra cellular domain involved in EGF binding & receptor dimerization. The proliferative effects of EGF are signaled through several pathways. EGF promotes mitogenesis of fibroblasts, endothelial cells and keratinocytes.

The functions of epidermal growth factor are⁴⁻⁷

- Helps in keratinocyte migration,
- Helps in fibroblast function
- Helps in formation of granulation tissue.
- participates in dermal wound healing by
 - stimulation, proliferation, and migration of keratinocyte
 - stimulation and proliferation of endothelial cells, and stimulation and proliferation of fibroblast
 - Facilitating dermal regeneration.
- EGF is one of the key signaling molecules in stimulating epithelial cell motility, making it a required factor for re-epithelialization
- EGF is a major stimulator of fibroblast migration and wound contraction

Studies have proved that EGF is more useful in acute than in chronic wounds as this factor is readily degraded in the chronic wound milieu. There are limited studies in Indian subcontinent and no major studies in south Indian population conducted so far. This study is intended to show the efficacy of epidermal growth factor over conventional dressings in the healing of diabetic ulcers.

II.Aims And Objectives Of The Study

The aim of the present study was to study the efficacy of epidermal growth factor over conventional dressings in the healing of diabetic ulcers.

III. Materials And Methods

The study was a prospective case control comparative Study conducted in the Department of General Surgery, K. S Hegde Hospital during the time period August 2014 to August 2016.

The study was done on 40 patients

- 20 patients with epidermal growth factor dressings
- 20 patients with conventional wound dressings

The dressing method was decided by the patient after explaining everything about both the dressings.

Inclusion Criteria

- Patients aged 20-80 years of age.
- Patients with diabetes whose blood sugar level are controlled by oral hypoglycaemic drugs or insulin.
- Ulcer size 3-10 cm

Exclusion Criteria

- Patients with any active systemic infections.
- Ulcer size more than 10cm.
- Immuno compromised individuals.
- Any chronic pathology or systemic therapy which would obstruct the healing process.
- Patients with \geq Grade III Wagner classification of diabetic ulcer

Procedure

Any dressings from the wound was removed and discarded. Wound irrigation was done with normal saline. Surgical debridement was done and adequate hemostasis achieved, following which

- 20 patients received topical Epidermal growth factor dressing.
- 20 patients received conventional wound dressing

The size of the ulcer measured in day 1, day15 and one month

IV.Results And Observations

Gender distribution

Males predominated in our study. However between the two groups there was no statistical difference in the gender

		Group		Total
		Cases	Controls	
SEX	F	2 10.0%	2 10.0%	4 10.0%
	M	18 90.0%	18 90.0%	36 90.0%
Total		20 100.0%	20 100.0%	40 100.0%

Table 1 – Gender Distribution within group

Graph 1: Gender distribution within group

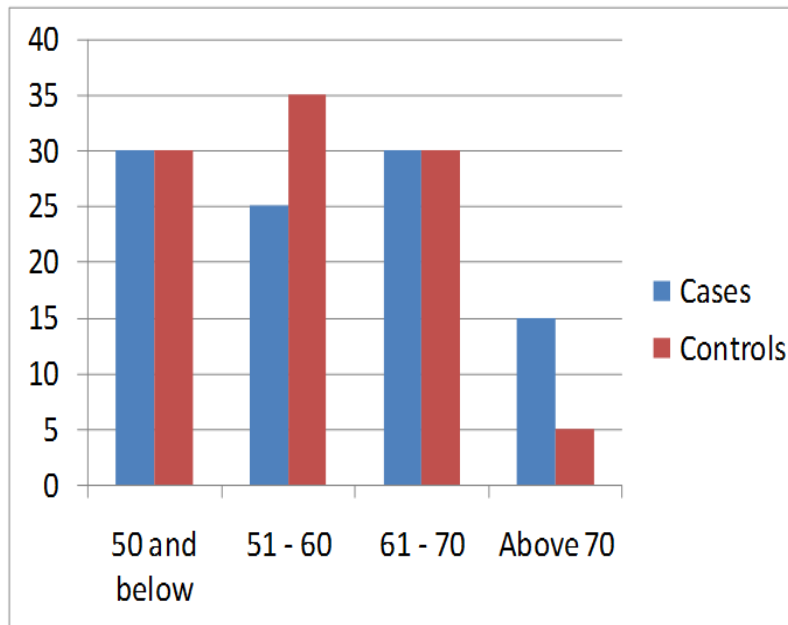
Age Distribution

In our study the mean age in the case group was 57.60 years and in control group was 58.37 years. Between the two groups there was no statistical difference in the age

		Group		Total
		Cases	Controls	
AGE	50 and below	6 30.0%	6 30.0%	12 30.0%
	51 - 60	5 25.0%	7 35.0%	12 30.0%
	61 - 70	6 30.0%	6 30.0%	12 30.0%
	Above 70	3 15.0%	1 5.0%	4 10.0%
Total		20 100.0%	20 100.0%	40 100.0%

Fishers exact test p=.721, NS

Table 2: Age Distribution within group



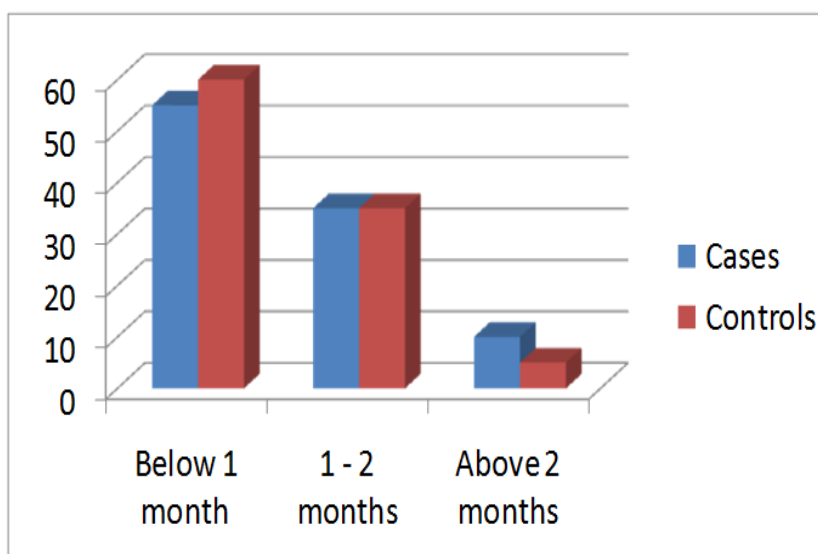
Graph 2: Age distribution percentage within group

Duration of the ulcer

In our study, there was no statistical difference in the duration of ulcer between the two groups. Most of the ulcers were of less than one month duration in both the groups

		Group		Total
		Cases	Controls	
DURATION OF ULCER	Below 1month	11 55.0%	12 60.0%	23 57.5%
	1 - 2months	7 35.0%	7 35.0%	14 35.0%
	Above 2 months	2 10.0%	1 5.0%	3 7.5%
Total		20 100.0%	20 100.0%	40 100.0%

Figure 3: Duration of the ulcer



Graph 3: Duration of the ulcer (Group Cross tabulation % within Group)

Comparison of change in size of the ulcer within the group

There is significant change in the size of ulcer both in the control group and the case group between Day 1 to 15 days, Day 15 to 1 month and between day 1 to 1 month

Group		Paired Differences				Bonferroni p value	
		Mean	Std. Deviation	95% Confidence Interval of the Difference			
				Lower	Upper		
Cases	DAY 1 - DAY 15	2.90970	1.95287	1.99573	3.82367	.000	HS
	DAY 1 - 1 MONTH	4.7692	2.5014	3.5985	5.9398	.000	HS
	DAY 15 - 1 MONTH	1.85945	1.58945	1.11556	2.60334	.000	HS
Controls	DAY 1 - DAY 15	1.43050	1.47412	.74059	2.12041	.000	HS
	DAY 1 - 1 MONTH	2.4690	2.2078	1.4357	3.5023	.000	HS
	DAY 15 - 1 MONTH	1.03850	1.01421	.56384	1.51316	.000	HS

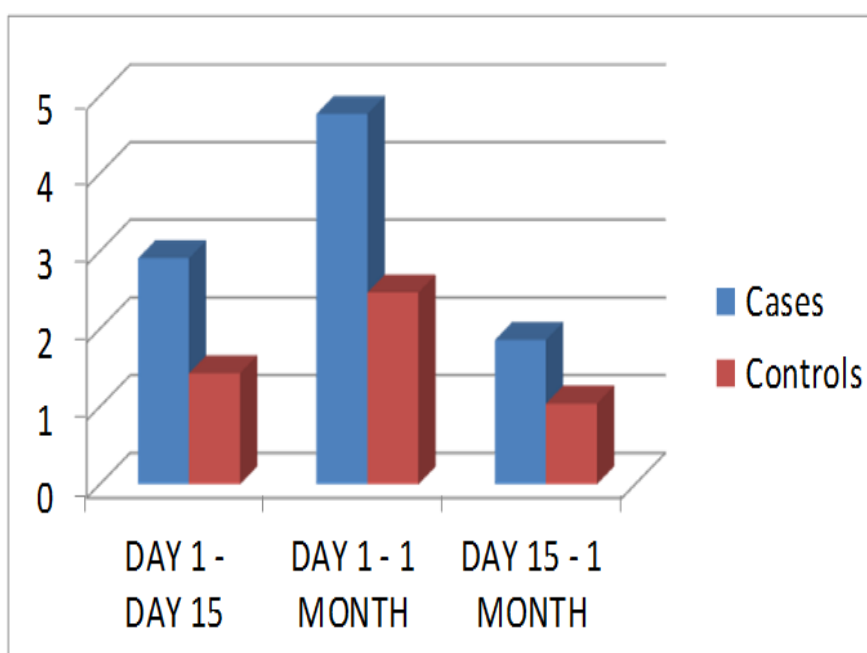
Table 4: Comparison of change in size of the ulcer within the group

Comparison of change between the groups over the duration

Between the two groups there was statistical difference in the change in the ulcer size following treatment with EGF. It was noticed that the decrease in ulcer size was more evident in the first 15 days when compared to the next 15 days.

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

Table 5: Comparison of change in size of the ulcer between the groups



Graph 4: Comparison of change in size of the ulcer between the groups

V. Discussion

Based on the analysis of the results and comparing with other similar studies, following inferences can be drawn:

- We found that in our study the size of the ulcer significantly decreased with EGF
- It was noticed that the decrease in ulcer size was more evident in the first 15 days when compared to the next 15 days.
- During this time the ulcer size has reduced more than 50% as compared to the conventional group in which the decrease in size was less than 25 % for most ulcers
- 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%
- In our study we also found that the patient satisfaction and co-operation 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
- The therapeutic achievements of EGF are by EGF receptor stimulation and cyto-protection and proliferation effects.

- Sanjeev singla et al showed 80% of patients showed complete response to EGF application, in our study group 50% reduction in size of the ulcer was noted at the end of one month. However their study period was two months⁸
- Our study showed a positive effect on wound healing and granulation issue formation this result is similar to the studies 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 al⁹⁻²¹
- Breeden et al in their study showed that topical EGF has moderately positive effect on wound healing and it can enhance burn wound healing by 1-4 days.²²
- Studies by S.P. Bennett et al and Crossland et al. found that EGF did not tend to demonstrably accelerate the healing process.^{23,24}

VI. Conclusion

In our study we have concluded that Epidermal Growth Factor definitely has an edge over conventional dressings in the healing of diabetic ulcers in terms of granulation tissue formation, and healing of the ulcer especially in diabetic wounds of duration less than a month

Limitations

The limitations of the study are

- As ours is a tertiary care centre, the cases don't represent the actual burden and type in the population at study
- The small sample size in comparison to the disease burden in the society
- The short duration of study as compared to the chronicity of the disease

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