Int. J Med. Pharm. Res. (P-ISSN: 2958-3675 | E-ISSN: 2958-3683)
Available on: https://ijmpr.in/

International Journal
of Medical and Pharmaceutical Research

ORIGINAL ARTICLE **OPEN ACCESS**

EFFECT OF TOPICAL RECOMBINANT HUMAN EPIDERMAL GROWTH FACTOR ON WOUND HEALING IN DIABETIC FOOT ULCERS- A RANDOMIZED CONTROLLED TRIAL

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OPEN ACCESS

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Received: 07-04-2025
Accepted: 10-05-2025
Available online: 20-05-2025

A B S T R A C T

Background: Diabetes mellitus, characterized by chronic hyperglycemia due to insulin secretion defects or resistance, leads to microvascular and macrovascular complications. Diabetic foot ulcers (DFUs), a severe manifestation of these complications, contribute significantly to morbidity and the risk of amputations among diabetic patients. Effective wound management in DFUs is critical, and growth factors like recombinant human epidermal growth factor (hEGF) have shown promise in promoting wound healing through cellular proliferation and angiogenesis.

Aim: This study aimed to assess the efficacy of topical recombinant hEGF in enhancing wound healing in diabetic foot ulcers compared to conventional saline dressing.

Materials and Methods: In this randomized controlled trial, 80 patients with diabetic foot ulcers were recruited and allocated into two groups: Group A received normal saline dressing with topical recombinant hEGF, while Group B received normal saline dressing alone. Participants were matched for demographic variables including age, gender, and duration of diabetes. Wound size, rate of granulation, and duration of hospital stay were measured at baseline, 7, 14, and 21 days. Data were analyzed using independent t-tests and chi-square tests, with statistical significance set at $p < 0.05$.

Results: The study found that Group A, treated with recombinant hEGF, had a significantly greater reduction in wound size and area compared to Group B. Final wound size and duration of hospital stay were significantly lower in Group A. Staphylococcus aureus was the most commonly isolated organism, followed by Escherichia coli. There were no significant differences in adverse effects between the groups.

Conclusion: Topical recombinant hEGF, when used with normal saline dressing, significantly improves wound healing in diabetic foot ulcers, evidenced by reduced wound size and shorter hospital stays. These findings suggest that incorporating recombinant hEGF into standard DFU care protocols could enhance treatment outcomes and potentially lower healthcare costs.

Keywords: Diabetic foot ulcer, recombinant human epidermal growth factor, wound healing, diabetes mellitus, normal saline dressing, wound size reduction.

INTRODUCTION

Diabetes mellitus is a metabolic disorder marked by hyperglycemia due to impaired insulin secretion or resistance, often

leading to complications like diabetic foot ulcers (DFUs). DFUs result from ischemia, neuropathy, infection, and are a major cause of amputations. Wound healing in diabetic patients is often prolonged and complex. Effective DFU management requires a multidisciplinary approach using therapies like glycemic control, debridement, and advanced dressings. Growth factors, particularly Epidermal Growth Factor (EGF), play a key role in wound repair by promoting cell proliferation, angiogenesis, and granulation tissue formation. EGF acts through specific receptors to stimulate epithelial and fibroblast activity. Reduced growth factor levels are linked to chronic, non-healing DFUs. This study evaluates the efficacy of topical recombinant human EGF (hEGF) compared to saline dressings in promoting faster healing. The aim is to determine whether hEGF shortens healing time and hospital stay.

Wagner created an early and still widely used classification system at hyperbaric wound healing centers. This classification was only based on clinical evaluation (the depth of the ulcer and the presence of necrosis) and did not take into account diversity in the vascular state of the foot. The ulcers are classified as follows:

- Grade 1: Superficial ulcer – Skin and subcutaneous tissue only
- Grade 2: Deep ulcer to tendon, muscle, joint capsule, or bone
- Grade 3: Deep ulcer with abscess, osteomyelitis, or tendinitis
- Grade 4: Partial foot gangrene
- Grade 5: Whole foot gangrene

AIMS & OBJECTIVES

Aim:

To study the efficacy of topical application of recombinant hEGF over conventional dressing in diabetic foot ulcers.

Objective:

Primary objective

- To observe the reduction in wound size, duration required for wound healing and duration of hospital stay.

Secondary objective

- To find out the possible adverse effects of local application of recombinant hEGF in diabetic ulcers.

MATERIAL & METHOD

Study Setting:

Patients presenting to the department of General Surgery, KARPAGA VINAYAKA INSTITUTE OF MEDICAL SCIENCE AND RESERCH CENTRE who were treated for diabetic foot ulcers conservatively

Study design: Randomized controlled study

Study participants: all the patients presenting with diabetic foot ulcer.

Study duration July 2024-january 2025

a) **Inclusion criteria**- The inclusion criteria for the patients were as follows:

- Diabetic patients with foot ulcers
- Age of the patient: 30-80 years

b) **Exclusion criteria** - The exclusion criteria were as follows:

- Diabetic ulcer with gangrenous lesion and or involving underlying bone
- Uncontrolled diabetes patients
- Patient with hypersensitivity reactions to hEGF gel (redness, itching,Urticarial lesion, blebs)
- Chronic non healing ulcers due to other etiologies

Sampling

Sampling population: Patients between 30-80 years of age with diabetic foot ulcer

Sampling technique: Simple random technique

Study duration:18 months

Calculation of sample size:

- Sample size calculated using the mean standard deviation from the previous study with respect to percentage reduction in wound size difference at 6^{th} week which is above 20.28+_17.39 and 31.7+_17.06 of hEGF dressing (Group A) and normal saline dressing (Group B) respectively.

The sample size is calculated as 72. Considering the 10% attrition rate, the sample size calculated as 80 (40 each group)

Sampling technique: Simple random technique

Outcome variables:
Independent variables-

- Age
- Mode of onset (traumatic/spontaneous0
- Site (dorsum/plantar)

Dependent variables

- Mean wound size reduction time
- Granulation
- Pus culture (colony count)
- Duration of hospital stay Budget for the Study – Rs. 40,000

hEGF gel 15g(1 tube for 1 patient approximately) Rs.1000

Present study included total of 80 patients fulfilling inclusion criteria are included.

RESULTS

Table 1: Mean age comparison between the groups

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Age	53.8	10.5	55.9	10.3	0.32

There is no significant difference in mean age between the groups.

Table 2: Gender distribution between the groups

		Group A		Group B		Chi-square
		Count	N %	Count	N %	(p-value)
nde r	F	16	40.0%	17	42.5%	1.21 (0051)
	M	24	60.0%	23	57.5%	

There is no significant difference in gender distribution between the two groups.

Table 3: Comparison of mean duration of diabetes mellitus between the groups

	Group A		Group B		Chi-square
	Mean	SD	Mean	SD	(p-value)
Duration OF DIABETES MELLI	8.3	5.1	9.2	4.6	0.32

There is no significant difference in mean duration of diabetes mellitus, however the duration in group A was shorter than group A.

Table 4: showing the presence of lesion between the groups

		Group A		Group B		Chi-square (p-value)
		Count	N %	Count	N %	
Modeofonset	Spontaneous	20	50.0%	18	45.0%	0.201 (0.654)
	Traumatic	20	50.0%	22	55.0%	
Limb	L	19	47.5%	20	50.0%	0.05 (0.823)
	R	21	52.5%	20	50.0%	
Site	Dorsum	20	50.0%	20	50.0%	-
	Plantar	20	50.0%	20	50.0%	

The mode of onset, limb involved and site were comparable between the groups.

Table 5: Comparison of pus culture report between the groups

		Group A		Group B		Chi-square (p-value)
		Count	N %	Count	N %	
ısC S	EC	8	20.0%	10	25.0%	7.71 (0.260)
	KP	5	12.5%	7	17.5%	
	IRS A	0	0.0%	1	2.5%	
	PA	6	15.0%	11	27.5%	
	PM	5	12.5%	3	7.5%	
	SA	13	32.5%	8	20.0%	

	SP	3	7.5%	0	0.0%	

There is significant isolation of staph aureus, followed by E. Coli (26%)

Table 6: Showing the reduction in wound size, area reduction and hospital stay

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
l wound size sqmm	2957.2	867.2	3323.3	634.0	0.15
wound size sqmm	2329.3	741.9	3028.6	571.3	0.01*
Area reduced	22.4	4.7	8.8	1.9	0.01*
n of hospital stay	14.6	4.9	16.5	4.5	0.01*

There is significant lower final wound size, are of reduction and duration of hospital stay among the group A patients compared to group B paitents.

DISCUSSION

Present study included total of 80 patients fulfilling inclusion criteria are included.
Group A: Normal saline dressing with Topical recombinant hEGF

Group B: Normal saline dressing
There is no significant difference in mean age between the groups.
There is no significant difference in gender distribution between the two groups.
There is no significant difference in mean duration of diabetes mellitus, however the duration in group A was shorter than group A.
The mode of onset, limb involved and site were comparable between the groups.
There is significant isolation of staph aureus, followed by E. Coli (26%)
There is significant lower final wound size, are of reduction and duration of hospital stay among the group A patients compared to group B paitents.

SUMMARY

- Present study included total of 80 patients fulfilling inclusion criteria are included.
- Group A: Normal saline dressing with Topical recombinant hEGF

- Group B: Normal saline dressing
- There is no significant difference in mean age between the groups.
- There is no significant difference in gender distribution between the two groups.
- There is no significant difference in mean duration of diabetes mellitus, however the duration in group A was shorter than group A.
- The mode of onset, limb involved and site were comparable between the groups.

- There is significant isolation of staph aureus, followed by E. Coli (26%)
- There is significant lower final wound size, are of reduction and duration of hospital stay among the group A patients compared to group B paitents.

CONCLUSION

The present study evaluated the effect of topical recombinant human epidermal growth factor (hEGF) on wound healing in diabetic foot ulcers, involving a total of 80 patients divided into two groups. Group A received normal saline dressing with topical recombinant hEGF, while Group B received normal saline dressing alone. The demographic characteristics, including mean age, gender distribution, duration of diabetes mellitus, mode of onset, limb involvement, and ulcer site, were comparable between the two groups.

Significant findings of the study include, Staphylococcus aureus was the most commonly isolated organism, followed by Escherichia coli (26%).Group A exhibited a significantly lower final wound size and a greater reduction in wound area compared to Group B.The duration of hospital stay was significantly shorter for patients in Group A compared to those in Group B.

These results indicate that topical recombinant hEGF, when used in conjunction with normal saline dressing, significantly enhances wound healing in diabetic foot ulcers. The reduction in wound size and area, along with a shorter hospital stay, suggests improved treatment efficacy and potentially lower healthcare costs for patients with diabetic foot ulcers. This study supports the incorporation of topical recombinant hEGF into standard wound care protocols for diabetic foot ulcers to improve patient outcomes.

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