



A COMPARATIVE STUDY OF THE EFFECTIVENESS OF EPIDERMAL GROWTH FACTOR IN THE MANAGEMENT OF CHRONIC LEG WOUNDS

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Abstract

Background: Chronic wounds, particularly non-healing ulcers, are among the most common surgical conditions encountered in clinical practice. These wounds are characterized by their failure to progress through the normal stages of healing despite regular wound dressings and appropriate local treatment, often resulting in prolonged morbidity and increased healthcare costs. The present study aims to investigate the healing effects of recombinant human epidermal growth factor (rhEGF) on chronic non-healing ulcers and to evaluate the effectiveness, safety, and patient acceptability of epidermal growth factor (EGF)-based wound dressing as a therapeutic modality¹.

Methods: A randomized, prospective, comparative study was conducted in the Department of General Surgery at RIMS, Raichur, involving 120 patients for 5 months from June 1st 2024 to October 30th 2024 with chronic non-healing ulcers. The participants were randomly allocated into two groups of 60 patients each. Group A received epidermal growth factor (EGF) dressing, while Group B received normal saline dressing as the control treatment.

Results: A total of 120 patients who consented to participate in the study were randomly allocated into two comparable groups of 60 patients each. The trial group received topical 0.01% epidermal growth factor (EGF) gel dressings, while the control group received standard antiseptic wound dressings. Baseline demographic characteristics, including sex distribution, were comparable between the two groups. On comparison of treatment outcomes, the trial group demonstrated a significantly greater reduction in ulcer area than the control group ($p < 0.001$), indicating the superior efficacy of topical EGF in promoting wound healing.

Conclusion: Epidermal growth factor (EGF) is an effective therapeutic option for the management of chronic non-healing ulcers owing to its cost-effectiveness, wide availability, ease of administration, and potential to reduce the duration of hospital stay.

Key Words: Epidermal growth factor, gel dressing, Chronic non healing ulcer

Introduction

Chronic wounds, particularly non-healing ulcers, are among the most common surgical conditions encountered in clinical practice. These wounds are characterized by their failure to heal despite regular wound dressings and appropriate local treatment. Common examples include diabetic foot ulcers, venous leg ulcers, and pressure ulcers. Their persistent nature poses a significant therapeutic challenge, making the management of chronic wounds a continuing concern for surgeons².

The traditional belief that wounds should be kept dry has gradually been replaced by evidence supporting the benefits of a moist wound-healing environment³. Moist wound dressings promote the formation of healthy granulation tissue and facilitate faster wound healing. Over the past two decades, a wide range of advanced wound dressings and topical therapeutic agents have been introduced for the management of chronic wounds. Various non-conventional topical treatments, including normal saline, aloe vera, collagen, gentian violet, benzoyl peroxide, impregnated gauze, topical insulin, mercurochrome, oxygen therapy, sugar, and vinegar, have been investigated for their potential role in wound healing³. Among these, topical epidermal growth factor (EGF) has demonstrated promising results in the treatment of chronic wounds, including pressure ulcers, venous ulcers, decubitus ulcers, and leprosy ulcers. Therefore, the present study was undertaken to evaluate the effectiveness of topical EGF dressing compared with conventional sterile wound dressing in the management of chronic non-healing ulcers⁴.

Epidermal Growth Factor (EGF) is a 53-amino acid polypeptide that plays a critical role in regulating cell growth, proliferation, migration, and differentiation during wound repair. Chronic wounds often exhibit reduced levels of endogenous growth factors and impaired cellular responses, leading to delayed healing. Topically applied recombinant human epidermal growth factor (rhEGF) helps restore these deficiencies and promotes wound healing through several mechanisms⁵.

Mechanism of Action

1.Binding to Epidermal Growth Factor Receptor (EGFR)

- oEGF binds to specific epidermal growth factor receptors (EGFR) present on the surface of keratinocytes, fibroblasts, endothelial cells, and other cells involved in wound healing.
- oThis binding activates the receptor's intrinsic tyrosine kinase activity, initiating intracellular signaling pathways such as the MAPK/ERK, PI3K/Akt, and JAK/STAT pathways⁶.

2.Stimulation of Keratinocyte Proliferation and Migration

- oEGF promotes the proliferation and migration of keratinocytes from the wound edges.
- oThis accelerates re-epithelialization, resulting in rapid closure of the wound surface^{6,7}.

3.Fibroblast Activation

- oEGF stimulates fibroblast proliferation and migration into the wound bed.
- oActivated fibroblasts synthesize collagen, elastin, fibronectin, and other extracellular matrix (ECM) proteins, providing structural support for tissue repair^{6,7}.

4.Promotion of Angiogenesis

- oEGF indirectly enhances the formation of new blood vessels by stimulating endothelial cell proliferation and increasing the production of angiogenic factors such as vascular endothelial growth factor (VEGF).
- oImproved blood supply increases oxygen and nutrient delivery to the healing tissue.

5.Enhancement of Granulation Tissue Formation

- oBy stimulating fibroblasts and endothelial cells, EGF promotes the development of healthy granulation tissue, which serves as the foundation for wound healing.

6. Collagen Synthesis and Extracellular Matrix Remodeling

oEGF increases collagen deposition and regulates matrix metalloproteinases (MMPs) and their inhibitors, facilitating balanced extracellular matrix remodeling and improving wound strength⁸.

7.Reduction of Inflammation

oChronic wounds are characterized by persistent inflammation. EGF helps shorten the inflammatory phase by promoting progression to the proliferative phase, thereby facilitating tissue repair⁹.

8.Acceleration of Overall Wound Healing

oThrough its combined effects on epithelialization, granulation tissue formation, angiogenesis, and extracellular matrix synthesis, EGF shortens healing time and increases the likelihood of complete wound closure^{9,10}.

Clinical Uses of Epidermal Growth Factor (EGF)

Topical or injectable recombinant human EGF has been used in the management of several difficult-to-heal wounds, including:

- ☐ Diabetic foot ulcers
- ☐ Venous leg ulcers
- ☐ Pressure (decubitus) ulcers
- ☐ Chronic non-healing traumatic ulcers
- ☐ Burn wounds
- ☐ Post-surgical wounds with delayed healing
- ☐ Leprosy ulcers
- ☐ Radiation-induced skin ulcers (selected cases)
- ☐ Skin graft donor and recipient sites
- ☐ Oral mucosal ulcers and corneal epithelial defects (specialized formulations)

Aim And Objectives Of The Study

- 1.To determine effectiveness of recombinant human epidermal growth factor (rhEGF) on chronic non-healing ulcers
2. To evaluate safety, and patient acceptability of epidermal growth factor (EGF)-based wound dressing as a therapeutic modality

Materials And Methods

Source of data :

Patients presenting to General Surgery OPD of RAICHUR INSTITUTE OF MEDICAL SCIENCES, RAICHUR and diagnosed with lower limb chronic non healing ulcer. The study was conducted for a period of 5 months from June 1st 2024 to October 30th 2024.

Method of collection of data:

This study was a cross sectional study, on a total of 120 patients presenting with lower limb chronic non healing ulcer to Department of General Surgery, RIMS, from June 1st 2024 to October 30th 2024 Investigator personally collected information from patients in a well pre-structured proforma which contains information on demographic details and other relevant information.

Period of study: June 1st 2024 to October 30th 2024

Study design: Comparative Cross-sectional study

Inclusion Criteria :

- ☐ Patients willing to participate in the study.
- ☐ Patients between the ages of 20 and 50, both sexes, were hospitalized with chronic non-healing diabetic ulcers, varicose veins, and any other non-malignant etiology.

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- ☐ Patients presenting chronic non healing ulcers with or without signs and symptoms of peripheral arterial disease involving lower limb like intermittent claudication, rest pain, ulceration, and gangrene..

Exclusion Criteria:

- ☐ Patients with peripheral arterial disease of upper limbs.
- ☐ Pregnant women.
- ☐ Patients with age less than 18 years.
- ☐ Patients who have already undergone surgical procedures like stenting, lumbar sympathectomy and arterial bypass grafting.
- ☐ Patients with deep vein thrombosis, severe arterial insufficiency, severe neuropathy, renal insufficiency, malignant ulcers, or parasitic ulcers were excluded from the study.

Methodology:

This was a cross-sectional observational study that included 120 cases diagnosed with chronic non healing ulcer with or without Peripheral Arterial Disease of the lower extremities. The methodology of the study consisted of taking a detailed clinical history in chronological order as soon as the patient was admitted.

A detailed clinical history of each patient with a chronic non-healing leg ulcer was obtained. The baseline ulcer dimensions were measured using a flexible measuring tape and recorded to the nearest 0.1 cm at the greatest length and width. Wound swab cultures were collected, and appropriate surgical debridement was performed before initiating treatment.

Participants were randomly allocated in a 1:1 ratio to either the intervention group (Group A) or the control group (Group B) using randomization software developed in Microsoft Visual Basic 6. Randomization was performed after patient enrollment by generating a computerized random sequence, and participants were assigned accordingly.

Group A (EGF Dressing): Topical epidermal growth factor (EGF) was applied to the ulcer, covered with 4–5 layers of sterile gauze and 5–6 sterile pads, and secured with a bandage. Dressings were changed daily. Group B (Conventional Dressing): The cleansed ulcer was dressed with two layers of antiseptic-soaked gauze followed by two layers of dry gauze, covered with 2–3 sterile Gamjee pads, and secured roller bandage. Dressings were changed daily.

Wounds in both groups were assessed daily, and healing progress was documented using standardized digital photographs (4× magnification, 20 cm distance). The treatment protocol was continued for two weeks, and wound healing outcomes were compared between the groups using a visual analogue scale (VAS). All observations were recorded in a structured proforma.

Visual Analogue Scale (VAS): Wound healing was evaluated using a 10-point VAS based on the percentage of new epithelial (skin) coverage. Scores ranged from 1 to 10, corresponding to 0–10%, 10–20%, 20–30%, and so on up to 90–100% wound coverage. A score of 10 indicated complete (90–100%) epithelialization, while a score of 1 represented minimal (0–10%) wound coverage

Statistical analysis

Statistical analysis was performed using GraphPad Prism software version 6.01. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while ordinal or score-based data were summarized as median with interquartile range (IQR). Categorical variables were presented as frequencies and percentages. Repeated-measures one-way analysis of variance (ANOVA), followed by post hoc multiple comparison testing, was used to compare continuous variables across different time points within the same group. Comparisons between two groups were performed using the independent t-test or Mann–Whitney U test, as appropriate. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant..

Results

1. 120 patients with chronic ulcers were equally randomized into two groups. The intervention group received 0.01% topical EGF gel dressings, while the control group received standard antiseptic wound dressings. Baseline demographic characteristics were comparable between the groups. The intervention group had a mean age of 40.7 ± 6.4 years (31–51 years), while the control group had a mean age of 46.9 ± 6.8 years (37–59 years). There was no statistically significant difference in age between the groups ($p > 0.05$).

Table 1: Sex wise distribution of patients.

GROUPS	MALE	FEMALE	TOTAL	P-VALUE
CONTROL	44	16	60	0.2
TEST	24	36	60	

2. Diabetic ulcers were the most common etiology, accounting for 22 (36.7%) patients, followed by traumatic ulcers (26.7%), post-burn ulcers (20.0%), and venous ulcers (16.7%). The distribution of ulcer etiology was comparable between the groups, with no statistically significant difference ($p = 0.90$).

Table 2: Cause wise distribution of ulcer.

GROUPS	DIABETIC	POST BURN	TRAUMATIC	VENOUS	TOTAL	P VALUE
CONTROL	24	12	12	12	40	0.9
TEST	20	12	20	8	60	
TOTAL	44	24	32	20	120	

3. In the control group treated with conventional antiseptic dressings, the mean ulcer area decreased from 20.0 ± 8.4 cm² at baseline (range: 12–35 cm²) to 13.1 ± 5.2 cm² after two weeks (range: 6–20 cm²).

Table 3: Mean distribution of ulcer area when treated with antiseptic (control) over two weeks.

Duration(days)	Minimum	Maximum	Mean	SD	P-Value
0	12	34	20.01	8.4	<0.0001
2	11	33.9	19.3	7.8	
3	11	32.6	18.5	7.6	
5	9.5	30.01	17.4	7.5	
7	8.7	27.9	16.3	6.7	
9	8.1	25.8	15.5	6.2	
11	7.3	22.22	13.6	5.3	

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In the intervention group treated with topical epidermal growth factor (EGF), the mean ulcer area decreased from $32.1 \pm 16.6 \text{ cm}^2$ at baseline (range: 10–60 cm^2) to $8.8 \pm 3.7 \text{ cm}^2$ after two weeks (range: 4–18 cm^2), indicating a greater reduction in ulcer size compared with the control group.

Table 4: Comparison between two groups

Duration (Days)	Groups	Minimum	Maximum	Mean	SD	P-Valve
0	Test	10.02	60.01	33.00	16.7	0.02
	Control	12.20	35.02	20.03	8.5	
2	Test	9.70	44.9	26.2	11.00	0.06
	Control	11.30	33.78	19.2	7.8	
3	Test	9.30	40.02	22.3	8.90	0.3
	Control	11.20	33.80	18.5	7.60	
5	Test	8.50	40.09	19.2	7.20	0.5
	Control	9.50	32.52	17.5	5.30	
7	Test	7.00	29.50	15.2	6.80	0.6
	Control	8.80	30.02	16.4	4.80	
9	Test	6.30	24.6	13.6	6.10	0.3
	Control	8.20	27.5	14.9	4.2	
11	Test	5.20	24.10	10.5	6.1	0.06
	Control	7.40	25.07	13.8	4.2	
14	Test	4.30	20.50	8.8	5.4	0.01
	Control	6.02	20.10	13.20	3.50	

Discussion

120 patients with chronic non-healing ulcers were randomly allocated into two equal groups: a test group treated with 0.01% topical epidermal growth factor (EGF) dressing and a control group receiving conventional antiseptic/saline dressings. Patients were selected based on predefined inclusion and exclusion criteria and included diabetic, traumatic, infectious, and post-burn ulcers. Wound healing outcomes were assessed after treatment following institutional ethics approval¹¹.

Wound healing is a complex biological process involving cell migration, proliferation, extracellular matrix deposition, angiogenesis, and tissue remodeling. Several growth factors, including EGF, PDGF, FGF, TGF- β , G-CSF, and KGF, play key roles in these processes. EGF, first identified by Cohen in 1962, promotes fibroblast proliferation, collagen synthesis, epithelialization, and tissue regeneration, thereby accelerating wound healing^{12,13}.

Multiple clinical studies have demonstrated the efficacy of topical recombinant human EGF (rhEGF) in chronic wounds, particularly diabetic foot ulcers. Healing rates ranging from 73% to 87% have been reported, with significantly faster wound closure and greater ulcer size reduction compared with conventional dressings.

Topical EGF has also demonstrated a favorable safety profile. Most reported adverse effects were mild, such as transient skin irritation or over-granulation, while serious adverse events were uncommon and generally unrelated to EGF treatment. Evidence further suggests that faster wound healing with EGF may reduce the risk of wound infection and lower-limb amputation¹⁴.

Overall, current evidence supports topical EGF as an effective and safe adjunct in the management of chronic non-healing ulcers, resulting in faster healing, greater reduction in ulcer size, and improved clinical outcomes compared with conventional wound care¹⁵.

Conclusion

The present study included 120 patients with chronic non-healing ulcers, with a comparable distribution of male and female participants. Most patients were between 41 and 60 years of age, with the highest proportion belonging to the 41–50-year age group. Patients in the study group received topical 0.01% epidermal growth factor (EGF) dressing, which demonstrated superior healing outcomes compared with conventional antiseptic wound dressing, resulting in improved healing of chronic non-healing ulcers. Although the clinical efficacy of EGF dressing was encouraging, its widespread use may be limited by its relatively high cost. Despite the limitations of the present study, including limited resources and infrastructure, the findings support the potential role of topical EGF as an effective adjunct in the management of chronic non-healing ulcers. As chronic wounds have a multifactorial etiology, optimal management requires a multidisciplinary and holistic approach that addresses both local wound care and underlying systemic factors.

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