



EPIDERMAL GROWTH FACTOR IN THE TREATMENT OF CHRONIC ULCER

Dr. V. Naganjani Chigurupati*

Assistant Professor of Pharmacology, Siddhartha Medical College, Vijayawada.
*Corresponding Author

Dr. Sankar Kurli

Professor of Pharmacology, Siddhartha Medical College, Vijayawada.

ABSTRACT

Growth factors are endogenous signaling molecules that regulate cellular responses for the wound healing process. The aim of the study is to compare the outcome of dressing a chronic ulcer with epidermal growth factor with that of conventional dressing with normal saline. The patients with chronic ulcer were divided into study and control groups of 20 each. In the study group, epidermal growth factor (EGF) gel was used as dressing; in control group, dressing was done with normal saline. Treatment was given for 8 weeks or until ulcer healed, whichever occurred first. After the eighth week of dressing in the study group, 90% of the patients showed complete ulcer healing. Whereas in control group only 30% of the patients showed complete ulcer healing. The results in healing were not significantly different in two study groups after 8-week duration.

KEYWORDS : chronic ulcers , EGF, normal saline

INTRODUCTION

Wound healing is a complex process influenced by a variety of factors. At each healing stage, a different set of specific cytokines and growth factors must interact with their receptors, other growth factors, and extracellular matrix (ECM) components at their target sites.¹ A chronic ulcer is an ulcer that does not heal in an orderly set of stages and in a predictable amount of time or wounds that do not heal within three months are often considered chronic.² Chronic ulcer symptoms usually include increasing pain, friable granulation tissue, foul odour, and wound breakdown instead of healing.³⁻¹¹ The fundamentals of caring for diabetic foot ulcers are off-loading, frequent debridement, and moist wound healing.¹⁰

MATERIAL AND METHODS

This prospective study was conducted after approval from institutional ethics committee at Government General Hospital, Vijayawada in included cases of chronic ulcer either admitted or attending Surgical OPD over 5 months period with effect from November 2018 to March 2019.

Inclusion Criteria

Patients older than 18 years with chronic ulcer (any ulcer that do not heal within three months) of grade 1–2 according to Wagner's classification were included in this study.

Exclusion Criteria

Patients suffering from osteomyelitis, carcinoma, vasculitis, connective tissue disease, immune system disorder, and those on treatment with corticosteroids, immunosuppressive agents, radiation therapy, and chemotherapy were excluded from the study.

Method

After explaining the procedure and purpose of study, informed consent was taken from all the patients. All the patients were subjected to complete hemogram, complete biochemistry, urine R/E, pus C/S, X-ray foot, and color Doppler study of lower limb to see for involvement of large vessels.

The wound area was determined by means of planimetry (greatest width × greatest length). Eligible patients were categorized into two groups: study group and control group of 20 each.

In the study group, epidermal growth factor (EGF) gel was applied as primary dressing and then covered with gauze, bandage, and tape. No other chemical was used. Dressing was changed daily. In the control group, isotonic NaCl solution moistened gauze was applied as primary dressing over the wound area and covered with bandage and tapes.

Treatment was given for eight consecutive weeks or until ulcer healed, which ever occurred first.

Evaluation of response was recorded on weeks 1, 4, and 8. At the end of the study period of 8 weeks, the patients were categorized subjectively as follows:

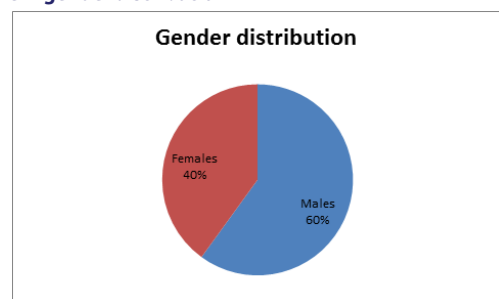
1. Complete responder—complete healing
2. Partial responder—50% or greater reduction in the product of two longest perpendicular diameters from baseline.
3. Noncomplete responder—<50% reduction.
4. Nonresponder—no reduction.

Follow-up

Evaluation was completed on weekly basis at each visit in the following manner.

1. Condition of the dressing and wound
2. Compliance with dressing use and change
3. Presence or absence of any adverse effects
4. Number of dressings changes since previous visit

Final evaluation was done at the eighth week or sooner if wound had healed.

OBSERVATIONS**Figure 1-gender distribution**

Out of 40 patients, 60% were male and 40% were female. In the study group, 18 (90%) patients presented with single ulcer, whereas 2 (10%) patients presented with two ulcers. In the control group, 19 (95%) patients presented with single ulcer, whereas 1 (5%) patients presented with two ulcers. Therefore, the study group had 22 ulcers and the control group had 21 ulcers. According to Wagner's classification in the study group, of the 22 ulcers, 10 were grade I and 12 were grade II ulcers. In the control group, 8 ulcers were grade I and 13 ulcers were grade II.

In aerobic cultures, the main organism isolated was Escherichia coli

42% and *Staphylococcus aureus* in 38% ulcers.

In anaerobic cultures, the main organisms isolated were *Peptostreptococcus* followed by *Bacteroides* and anaerobic streptococci.

Healing Response in the Study and Control Groups After 1 Week

After 1 week of dressing, in the study group, 12 were partial responders and 6 noncomplete responders, whereas 2 were nonresponders. In the control group, 3 patients were partial responders and 12 patients were noncomplete responders, and 5 were nonresponders.

Healing Response in the Study and Control Groups After 4 Weeks

After the fourth week of dressing, in the study group, complete responders were 15 and partial responders were 3. There was 1 noncomplete responder and 1 nonresponder.

In the control group, 5 patients were complete responders, 9 were partial responders. There were 2 noncomplete responders and 2 nonresponders.

Healing Response in the Study and Control Group After 8 Weeks

After the eighth week of dressing, in the study group, complete responders were 18 and partial responders were 1 with 1 noncomplete responder. In the control group, 6 patients were complete responders, 10 were partial responders. There were 2 noncomplete responders and 2 nonresponders.

DISCUSSION

The incidence of multiple ulcers was 10% in the study group and 5% in the control group patients. This is similar to the incidence as reported by Reiber et al.¹² In the present study, history of trauma before the development of ulcer was present in 15 (75%) patients of the 20 in the study group and in 16 (80%) patients of the control group of 20. According to Pecoraro et al.¹³, minor trauma has been reported as the most frequent cause leading to the development of ulcer. Ellenberg¹⁴ found that 90% of ulcers occurred under the pressure bearing areas with punched out edges. The same findings were observed in the present study, where of the 22 ulcers in the study group, 79% ulcers had punched out edges, whereas of the 21 ulcers in the control group, 77% had punched out edges while remaining 21% ulcers in the study group and 23% ulcers in the control group had sloping edges.

Healing Response in the Study and Control Groups Ulcers in the study group were clean and covered with healthy granulation and with minimal soakage, whereas control group ulcers were slower to heal. After the eighth week, there was only 1 nonresponder in the study group, rest of the patients responded well to EGF application. In the control group, patients' wounds had improved, soakage had decreased, and granulation tissue's proliferation was evident. Tsang, and Wong¹⁵ in their study on application of EGF on ulcers concluded that EGF significantly enhances ulcer wound healing.

Henemyre-Harris and Adkins¹⁰ in their study on addition of epidermal growth factor in an in vitro model reported improved healing of skin injuries following addition of EGF as compared with control. Wounds treated with EGF show increased number of fibroblasts. It is postulated that EGF promotes healing by stimulating migration and division of epithelial cells by increasing protein synthesis, such as fibronectin, which aids in cell attachment and migration. EGF has also been reported to increase tensile strength of wound incision promoting rapid closure. Although EGF does not induce synthesis of mRNA for extracellular matrix proteins such as collagen, EGF presumably increases the number of fibroblasts in wound through chemotaxis and mitosis, resulting in more collagen production.

RESULTS

The EGF dressing resulted in early healing of ulcers up to first 4

weeks as compared with conventional dressing (P value 0.012, 0.015, 0.025, and 0.049 in first, second, third, and fifth week). The results in healing were not significantly different in the two groups after 8-week duration, P value being 0.574 in the eighth week (results compared with chi square test statistically). The mean duration of stay in the study group was 19.3 days and 29.5 days in the control group (P0.011).

CONCLUSION

Despite many major advances in health care delivery to patients, high morbidity and mortality, loss of working hours, and expenditure associated with chronic ulcer which necessitate the need for a prompt and proper approach to ulcer management. The treatment of chronic ulcer is complex. Even when properly managed, wounds may not heal as expected; when they do heal, the closure is often temporary and difficult to maintain. The fundamentals of caring for chronic ulcers are off-loading, frequent debridement and moist wound healing. New advanced topical dressing with EGF leads to early healing with less complication rate as compared with conventional dressing. Therefore, it is concluded that EGF dressing is safe, convenient and cost effective in early healing of chronic ulcer and reduced hospital stay.

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