

A Comparative Study on Efficacy of Topical L-Lysine versus Cadexomer Iodine Ointment in Chronic Wound Healing

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Abstract

Background: Humans are constantly subjected to injuries that result in cell death and tissue destruction. Healing is part of the response to this injury and represents an attempt to maintain normal structure and function. It overlaps the inflammatory process. Healing is the restoration of integrity to an injured tissue. Wound healing is accomplished by three mechanisms: Contraction, repair, and regeneration.

Aims and Objectives: Aim of the study is to determine the efficacy of topical L-lysine in the management of chronic wound healing in terms of rate of granulation tissue formation, time for epithelialization, and duration of taking treatment and comparison with the efficacy of Cadexomer iodine ointment.

Materials and Methods: This study was a hospital-based (inpatient department [IPD] and outpatient department [OPD]) longitudinal follow-up study. All patients who were admitted in IPD and who came to OPD for a chronic non-healing wound in the Department of General Surgery at Calcutta National Medical College and Hospital between February 2020 and February 2021 were included in the study; the age of 18 years or above, diagnosed as a case of chronic wound and those who gave written consent were included in the study.

Results: Out of 54 patients who underwent treatment with topical L-Lysine, the mean rate of granulation tissue formation was 80.48% of ulcer surface area, and the mean duration of taking treatment from the hospital was 32.81 days. Out of 54 patients who were treated with topical Cadexomer iodine, the mean rate of granulation tissue formation was 53.30% of ulcer surface area and the mean duration of taking treatment was 58.67 days.

Conclusion: Topical L-Lysine can be considered as a better option in the management of chronic wound compared to topical Cadexomer iodine.

Key words: Cadexomer iodine, Chronic non-healing ulceration, L-lysine hydrochloride

INTRODUCTION

Humans are constantly subjected to injuries that result in cell death and tissue destruction. Healing is part of the response to this injury and represents an attempt to

maintain normal structure and function. It overlaps the inflammatory process.

In mammals, that mentioned process is represented by the granulation tissue formation. However, granulation tissue matures only into dense connective tissue and forms a scar. The replacement of lost tissue by scar tissue is termed repair. The major components of the repair reaction are – The extracellular matrix and cells.

The extracellular matrix has five major components; collagens, basement membranes, elastic fibers, structural glycoproteins, and proteoglycans.

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Collagens bind to cell surfaces and modulate morphogenesis, chemotaxis, platelet adhesion and aggregation, cell attachment, and cell phenotype.^[1]

Factors involved in wound healing are macrophage-derived growth factor, platelet-derived growth factor, epidermal growth factor, fibroblast growth factor, and transforming growth factor-beta.

Healing is the restoration of integrity to an injured tissue. Wound healing is accomplished by three mechanisms: Contraction, repair, and regeneration.

A chronic wound may be defined as one that fails to heal in the expected time; for a wound of that time which is <3 weeks. The entire category of skin ulcers is now included in the term chronic wound. Although skin ulcers such as diabetic, venous, and arterial ulcers might be initiated by trauma, the condition of the tissue in which these acute wounds occur results in a predictably slow or difficult course of healing. The management of chronic wounds includes the correction of underlying disease processes also.^[2]

Non-surgical modalities to enhance healing and care of soft-tissue wounds are growth factors, human skin equivalents, newer topical agents (Collagen, Hyaluronic Acid, Beta Glucan, Silver Arglaes, L-Lysine Hydrochloride, and Cadexomer Iodine), Pharmaceuticals (Oxandrolone), and Devices (VAC, Radiant Heat Bandage, and Topical Hyperbaric Oxygen Therapy).^[3-10]

L-Lysine Hydrochloride has shown improvement in both the rate and quality of wound healing. Another feature of this molecule is its ability to support healing process in long-standing wounds. On histopathology, lysine-treated wounds showed a thickening of the dermoepidermal layer, with increased cell proliferation from the basal keratinocytes.

Topically lysine-treated chronic wound beds showed a controlled degree of inflammation and angiogenesis. Besides, the cellular and serum growth factors' entry to the wound bed was ensured, thereby augmenting the healing process *in situ*.

L-lysine monohydrochloride (L-lysine) has been shown to promote therapeutic angiogenesis in wound healing. Datta *et al.* demonstrated angiogenic capability of lysine in wound healing for the 1st time. The angiogenic and the property of tissue regeneration of this molecule has been utilized in this study.^[11,12]

Cadexomer iodine ointment is yellow-brown-colored ointment containing Cadexomer iodine (50% w/w)

equivalent to 0.9% w/w available iodine. When in contact with wound exudates, Cadexomer iodine absorbs fluid and removes exudates, pus, and debris from the wound surface.

Aims and Objectives

The general objective is to study the efficacy of topical L-lysine and Cadexomer iodine ointment in the management of chronic wound healing.

A specific objective is to study the efficacy in terms of the rate of granulation tissue formation, time for epithelialization, and duration of taking treatment.

MATERIALS AND METHODS

This study was a hospital-based (inpatient department [IPD] and outpatient department [OPD]) longitudinal follow-up study. All patients who were admitted in IPD and who came to OPD for chronic non-healing wound in the Department of General Surgery at Calcutta National Medical College and Hospital were included in the study and they were made to understand about the study in details including the rationale, aims and objective of the study, study-related procedures, potential discomfort, and benefits of participation.

Ethical Clearance

Proper Ethics Committee review and due clearance were obtained before the conduct of this study from the institution dated 13.02.2020.

Study Area and Population

All patients who were admitted in IPD and who came to OPD for a chronic non-healing wound in the Department of General Surgery at Calcutta National Medical College and Hospital between February 2020 and February 2021 were included in the study

Inclusion and Exclusion Criteria

Patients aged 18 years or above, diagnosed as a case of a chronic wound and those who gave written consent, were included in the study. Non-cooperative and non-consenting patients, patients with malignant conditions, and patients with conditions where definitive treatment was surgical intervention were excluded from the study.

After taking proper consent, 108 patients who had a chronic wound confirmed on physical examination and fulfilled the inclusion and exclusion criteria were enrolled in the study. These 108 patients were randomized into two Groups A and B, 54 in each using a simple random table. In which Group A patients applied locally L-Lysine and Group B patients applied locally cadexomer iodine, and these patients were followed up for 12 weeks for,

healing rate, rate of granulation tissue formation, and rate of epithelialization. Data were extracted from patients and patient characteristics of the two groups were well matched. Data were charted in relation to age, sex, etiology, and rate of granulation tissue formation as percentage of ulcer surface area. Statistical analysis was done to compare these two groups using an appropriate statistical method accordingly.

Plan for Analysis of the Data

Analysis of the data was done by standard statistical methods using statistical software. The results were analyzed by unpaired Student's t-test which showed a significant difference in rate of granulation tissue formation and duration of receiving treatment from hospital ($P < 0.05$).

RESULTS

The 108 patients admitted for the study were divided into two groups. Group A with treatment A (topical L-lysine with mechanical debridement) and Group B with treatment B (Cadexomer Iodine). The patient's characteristics of the two groups were well matched as given in Table 1.

The mean age of Group A was (48.65 ± 11.72) and the mean age of Group B is (47.74 ± 12.72) [Table 2].

Sex-wise distribution: M: F ratio in Group A was 32:22 and in Group B is 31:23 [Figure 1].

The mean of rate of granulation tissue formation calculated using the formula Length x Breadth. In Group A is 80.48 ± 17.35 , and in Group B is 53.30 ± 21.13 [Table 3].

The mean duration of taking treatment for Group A is 32.82 ± 13.67 and for Group B is 58.67 ± 17.10 [Table 4].

- Increased rate of granulation tissue formation was seen in treatment with topical L-Lysine group (Group A) compared to treatment with topical Cadexomer iodine group (Group B)
- Shorter duration of treatment was observed in the case of Group A compared to Group B
- Follow-up observations revealed that Group A (treatment with topical L-Lysine) suffered from lesser complications such as wound contractures, pain, and residual raw areas compared to Group B (treatment with topical Cadexomer Iodine).

DISCUSSION

Wound dressing has achieved by modern wound dressing agents that help in granulation tissue formation and

Table 1: Comparison of Patient Characteristics

	GROUP A	GROUP B
No. of patients	54	54
Range of age	24-75	23-75
M: F	32:22	31:23
Range of ulcer surface area in square cm	6-400	6-360

Table 2: Age-wise Distribution

Age (years)	18-30	31-40	41-50	51-60	61-70	71-80
Group A	4	9	17	13	10	1
Group B	7	8	15	14	8	2

Table 3: Rate of granulation tissue formation as percentage of ulcer surface area

	>90%	81-90%	71-80%	61-70%	51-60%	≤50%
Group A	21	9	7	7	4	6
Group B	4	5	4	4	3	34

% granulation tissue formation

Table 4: Mean Duration Of Taking Treatment

	10-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
Group A	8	27	6	6	4	2	1	0
Group B	0	6	3	5	6	21	10	3

No. of days of treatment

Table 5: Etiology-wise Distribution

	Diabetic ulcer	Bed sore	Infected wound	Traumatic wound
Group A	18	10	13	13
Group B	21	12	11	10

rapid wound healing. The level of providing adequate environment promoting wound healing are physical protection, the raw surface, absorbing exudates, and controlling infections by several drugs.

At present, scenario of wound dressing system is compared not only with the basis of granulation tissue formation but also the duration of treatment of the patient which is considered as a measurement of morbidity of a patient.

The study was performed as a prospective, randomized, controlled, and comparative study to compare the efficacy of using topical L- Lysine and topical application of Cadexomer iodine in the management of chronic wound.

The average age group in this study was 48.19 years and the range of age which was studied was in between 23 and 75 years. Out of a total of 108 patients, 61 patients were in between the age group of 23 and 50 years of age

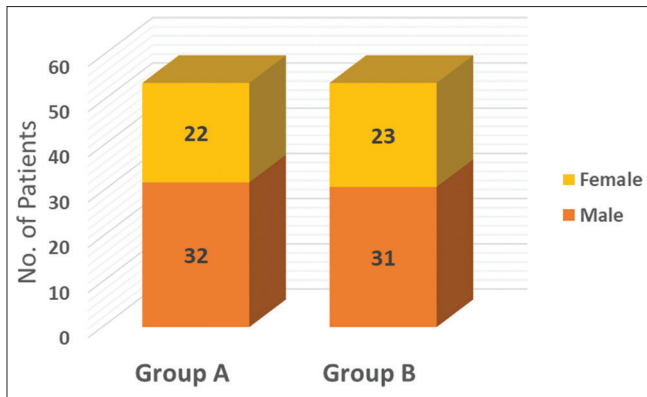


Figure 1: Sex-wise distribution

group and this age group is the economically productive period of life [Tables 1 and 2].

In the Indian society, males lead more outdoor life and are prone to road traffic accidents and this fact has been reflected well in this study. The overall sex ratio between males and females was 21:15 [Figure 1].

The different etiologies are included in this study and this reflects that diabetic ulcers are the major cause of chronic wound in each group [Table 5].

The mean rate of granulation tissue formation calculated using the formula Length x Breadth, in both groups was 80.45% (SD = 17.35) for Group A and 53.30% (SD = 21.13) for Group B. Hence, it can be seen that in case of patients with chronic non-healing wound who took treatment with topical L-Lysine had a higher formation of granulation tissue compared to the patients who took treatment with topical Cadexomer iodine [Table 3].

The total duration of treatment from the hospital also compared. The mean number of days treatment was 32.82 days (SD = 13.67) for Group A and 58.67 days (SD = 17.10) for Group B. Hence, the morbidity is less in the case of the patients who took treatment with topical L-Lysine than the patients took treatment with topical Cadexomer iodine [Table 4].

The results were analyzed by unpaired Student's t-test which showed a significant difference in the rate of granulation tissue formation and duration of receiving treatment from the hospital ($P < 0.05$).

Limitations of the Study

Although the sample size of 108 patients is sufficient for statistical analysis, a randomized controlled comparative study with a much larger population may help to further detail findings.

The cost burden is also not analyzed (e.g. transportation cost to come to hospital) in this study as this can be influenced by various factors other than dressing cost.

After granulation tissue formation, some patients needed skin grafting for wound coverage, and after skin grafting, the percentage of wounds which took skin graft better was not analyzed in this study.

CONCLUSION

In this study, it can be concluded that the rate of healing process was better in the case of treatment with topical L-Lysine Group (Group A) compared to treatment with topical Cadexomer iodine group (Group B). It was also observed that the overall duration of treatment is less in the case of Group A than Group B. Thus, topical L-Lysine can be considered as a better option in the dressing of chronic non-healing wounds; this may be due to its properties of angiogenesis and tissue regeneration. Further studies with larger population groups may help in understanding this topical agent in the management of chronic wound healing.

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