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Original Research Article

A Hospital-Based Study Assessing Debridement for Ulcer Healing by Secondary Intention by Papain Debridement versus Using Povidone Iodine Solution: A Comparative Study

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Abstract

Aim: The aim of the present study was to compare enzymatic debridement for ulcer healing by secondary intention by papain debridement versus using povidone iodine solution.

Methods: The Present study was single-center, prospective, comparative study, conducted in Department of General Surgery. Study duration was 11 months. 200 patients randomly divided into two groups each after matching for confounding factors Group 1 - 100 patients treated with papain-urea Group 2 - 100 patients treated with Povidone iodine.

Results: The overall mean age of patients in both groups was 48.22±12.68 in Group A and Group B 47.33±13.37. The maximum number of patients was in the age group of 56-64 years in both Group A and Group B (36 and 44 patients respectively). In Group A, there are 70 male and 30 female patients. In Group B there are 66 male, 34 female patients. The total number of diabetics in the study included 200 patients (12%) in group A, while 18% in group B. The total number of hypertensives in the study included 8% in group A and 6% in group B while patients having both DM and HTN 8% in group A, 6% in group B. The most common site affected among group A subjects was left foot (24%) followed by right foot (20%), the least site affected was right thigh (2%) and right hand (2%). The most common site affected among the group B subjects was left leg (22%) and right foot (22%) followed by left foot (20%) The least site affected was left hand, right and left forearm (2%). The commonest organism on Culture sensitivity taken on day 1 for all patients was Staphylococcus aureus – 24 patients, Enterococci – 12 patients, no growth in 7 patients.

Conclusion: There was shorter duration of hospital stay, earlier wound disinfection and a greater number of patients who underwent earlier skin grafting in papain urea group. The results were statistically significant and in favour of papain urea. Thus we concluded that use of papain urea is highly recommended as compared to povidone iodine in management of non-healing ulcers.

Keywords: Chemical Debridement, Papain Urea Group, Povidone Iodine, Non-Healing Ulcers.

Introduction

A chronic wound is one that is physiologically compromised as a result of the wound-healing cycle being disturbed by factors such poor angiogenesis, innervation, or cellular migration, among others. [1] Various factors, such as comorbidities [for example diabetes, autoimmune illness, peripheral artery disease (PAD)], an elevated body mass index, anatomic location, and drugs, affect the precise timeframe for full epithelialization. [2,3] Chronic wounds in palliative care encompass fungating malignant wounds, diabetic ulcers, venous and arterial leg ulcers, and pressure ulcers. [4] Almost always, the wounds that palliative care patients frequently experience are a direct outcome of their advanced disease status. Palliation enhances a patient's quality of life and makes them feel more comfortable, but it does not treat their illness. In palliative care, a multidisciplinary team approach to treatment tries to enhance patients' and their families' quality of life rather than treat the underlying cause. [5,6]

Among various debridement methods, enzymatic wound debridement uses proteolytic enzymes to hydrolyze the denatured proteins in wound eschar tissue. This highly selective debriding method has been widely used to remove necrotic/ devitalized tissues, [7-11] particularly in patient populations not amenable to surgical debridement. [12,13] Over the years, enzymatic debridement has been shown to be a clinically effective, safe, and inexpensive method of removing necrotic tissue. There is sufficient evidence in clinical practice and in the clinical literature that enzymatic debridement is a well-established practice with skin and wound care professionals. [11,14,15] Successful topical treatment of chronic wounds requires not only adequate debridement, but also control of bioburden and moisture balance. Wound dressings are commonly used for controlling wound bioburden and managing wound exudate. Frequently, enzymatic debriding agents are applied in combination with other topical therapeutic drugs, such as antimicrobial and moisture control dressings.

Bolton and Fattu [14] discussed in their review of the literature that enzymatic debriding agents are typically used in conjunction with moist wound dressings and serve as adjuncts to the autolytic debridement process. Clearly, such combinations may allow several treatment objectives to be addressed simultaneously, including exudate and bioburden management, debridement, and tissue regeneration. To allow maximum debriding efficacy, a good delivery system, a sustained period of enzyme activity, and an optimal wound environment are required. In conjunction with other wound dressings, such as antimicrobial or moisturizing, the compatibility between the debriding enzyme and dressings may account for the potential loss of efficacy of the debriding enzyme. Enzymes are proteins, and any factors that could cause a conformational change to a protein could potentially affect enzyme activity. In addition, molecules that can bind to the active site of an enzyme may block substrate binding to the enzyme and inhibit enzyme activity.

The aim of the present study was to compare enzymatic debridement for ulcer healing by secondary intention by papain debridement versus using povidone iodine solution.

Materials and Methods

The Present study was single-center, prospective, comparative study, conducted in Department of General Surgery, Narayan Medical College and Hospital, Sasaram, Bihar, India Study duration was 11 months

Inclusion criteria: Patients aged between 18 to 64 years with (non-healing) ulcer, wound present over a bony prominence in a mobility compromised individual, full thickness or partial thickness wounds involving bone or muscle, wounds with nonviable tissue attached to the wound base.

Exclusion criteria: Patients with age less than 18 and more than 64 years. Ulcers with severe active infection. Wounds with x-rays suggestive of osteomyelitis. Patients with systemic conditions impairing wound healing such as renal, hepatic and haematological causes. Patients on long term steroids, on chemotherapy and immunosuppressants Study was explained to patients and a Informed Written Consent was taken from all patients. 200 patients randomly divided into two groups each after matching for confounding factors Group 1 - 100 patients treated with papain-urea Group 2 - 100 patients treated with Povidone iodine. The included patients were subjected to: Detailed clinical history, General Physical examination and local ulcer examination. Investigations (Routine blood investigations- Complete blood count, renal function tests, blood sugars), Radiological- X ray wherever indicated, Swab Culture sensitivity(C/S) form ulcer on Day 1 in all patients, and subsequent C/S on variable days. Assessments were done Debridement of slough/nonviable tissue, reduction in ulcer size, granulation noted. Discharge, odour, induration noted for overall response to treatment. Dressings were done using same technique – cleaning with saline and application of ointment (collagenase/papain – urea) and putting a dressing. Patients were assessed for wound size, appearance of granulation tissue, appearance of epithelization, resolution of peri wound erythema, resolution of peri wound edema, organisms isolated/growth on culture sensitivity duration of hospitalization and day of wound disinfection (culture negative) on day 1,7,14,21,28. All data collected was stored in MS Excel spread sheet and statistical analysis was carried out with the help of SPSS (version 20) for windows package (SPSS Science, Chicago II, USA) and EpiInfo application. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-square test. Quantitative data was represented using Mean +/- SD and t-test was applied. p value < 0.05 was considered as statistically significant.

Results

Table 1: Demographic data

Age in years	Group A n (%)	Group B n (%)
18-25	4 (4)	12 (12)
26-35	12 (12)	6 (6)
36-45	16 (16)	22 (22)
46-55	32 (32)	16 (16)
56-64	36 (36)	44 (44)
Mean ± SD	48.22±12.68	47.33±13.37
Gender		
Male	70 (70)	66 (66)
Female	30 (30)	34 (34)
Co-morbidities		
Diabetes	12 (12)	18 (18)
Hypertension	8 (8)	6 (6)
Diabetes and Hypertension	8 (8)	6 (6)
No Co-morbidity	72 (72)	70 (70)

The overall mean age of patients in both groups was 48.22±12.68 in Group A and Group B 47.33±13.37. The maximum number of patients was in the age group of 56-64 years in both Group A and Group B (36 and 44 patients respectively). In Group A, there are 70 male and 30 female patients. In Group B there are 66 male, 34 female patients.

The total number of diabetics in the study included 200 patients (12%) in group A, while 18% in group B. The total number of hypertensives in the study included 8% in group A and 6% in group B while patients having both DM and HTN 8% in group A, 6% in group B.

Table 2: Site affected

Site of ulcer	Group A		Group B	
	Right	**Left**	**Right**	**Left**
Foot	20 (20)	24 (24)	22 (22)	20 (20)
Leg	16 (16)	20 (20)	16 (16)	22 (22)
Thigh	7 (7)	2 (2)	2 (2)	6 (6)
Hand	2 (2)	7 (7)	6 (6)	2 (2)
Forearm	0	2(2)	2 (2)	2 (2)

The most common site affected among group A subjects was left foot (24%) followed by right foot (20%), the least site affected was right thigh (2%) and right hand (2%). The most common site affected among the group B subjects was left leg (22%) and right foot (22%) followed by left foot (20%) The least site affected was left hand, right and left forearm (2%).

Table 3: General characteristics

Characteristics	Group A	Group B	P Value
Appearance of Granulation tissue (days)	3.540± 0.86	3.550± 0.88	<0.001
Appearance of Epithelialization (days)	7.72± 1.88	12.38 ± 2.48	<0.001
Day of Resolution of Periwound Erythema (days)	4.535 ± 1.15	7.73 ± 1.22	<0.001
Day of Resolution of Periwound Edema (days)	6.64 ± 1.54	10.55 ± 1.68	<0.001
Day of Wound Disinfection (days)	7.52 ± 1.86	10.18± 2.14	<0.001
Duration of Hospitalisation (days)	10.68 ± 2.68	12.18 ± 2.64	<0.001

In Group A (PAPAINUREA), the mean duration for Day of appearance of Granulation tissue was 3.540± 0.86 days. In Group B (PI), the mean duration for day of appearance of Granulation tissue was 3.550± 0.88 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of appearance of Epithelialization was 7.72± 1.88 days. In Group B (PI), the mean duration for day of appearance of Epithelialization was 12.38 ± 2.48 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of Periwound Erythema Resolution was 4.535 ± 1.15days. In Group B (PI), the mean duration for day of Periwound Erythema Resolution was 7.73 ± 1.22 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of Periwound Edema Resolution was 6.64 ± 1.54 days. In Group B (PI), the mean duration for day of Periwound Edema Resolution was 10.55 ± 1.68 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of Wound Disinfection (Culture negative) was 7.52 ± 1.86 days. In Group B (PI), the mean duration for day of Wound Disinfection

(Culture negative) was 10.18± 2.14 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration of hospitalisation was 10.68 ± 2.68 days. In Group B (PI), the mean duration of hospitalisation was 12.18 ± 2.64 days, difference was statistically significant ($p < 0.001$).

Table 4: Organism on C/S

Organism	N%
Staph aureus	24 (24)
Enterococci	12 (12)
Pseudomonas	6 (6)
Klebsiella	10 (10)
E.coli	10 (10)
Citrobacter	8 (8)
Streptococcus	11 (11)
Proteus	7 (7)
Acinetobacter	5 (5)
No growth	7 (7)

The commonest organism on Culture sensitivity taken on day 1 for all patients was Staphylococcus aureus – 24 patients, Enterococci – 12 patients, no growth in 7 patients.

Table 5: Split skin Grafting

Split skin Grafting	Group A	Group B
<28 days	60	80
>28days	40	20

In Group B (PI) 60% of cases underwent SSG before 28 days 40% of subjects underwent SSG after 28 days. In Group A (PI), 80% of cases underwent SSG. SSG before 28days 20% of subjects underwent SSG after 28days. Difference between group A and group B was statistically significant ($p = 0.02$).

Discussion

Wound management is an integral part of surgical practice, in depth understanding about the pathophysiology and the treatment options available will help the surgeon to achieve a better patient compliance. [16] The devitalized tissue present in chronic ulcers increases the chances of microbial infection and decreases wound healing. Various local and systemic factors such as pressure, infection, necrotic tissue, age, nutritional status, and co-morbid diseases can impede healing of ulcers. [17] Devitalized tissue and exudates act as mechanical barrier to migration of cells and provide an environment ideal for bacterial proliferation, [18] thus there is excess production of pro-inflammatory cytokines and prolongation of inflammatory response. [19] Ulcer care includes debridement of the necrosed tissue and a thorough cleaning and dressing of the wound. However, these methods of debridement differ as per the patient's condition. [20] Papain-Urea is the combination of a proteolytic enzyme (papain) and a chemical agent, which denatures nonviable protein (urea). [21]

The overall mean age of patients in both groups was 48.22±12.68 in Group A and Group B 47.33±13.37. The maximum number of patients was in the age group of 56-64 years in both Group A and Group B (36 and 44 patients respectively). In Group A, there are 70 male and 30 female patients. In Group B there are 66 male, 34 female patients. Gerstein AD et al [22] stated in his study that age-related differences in wound healing have been clearly documented. Although the elderly can heal most wounds, they have a slower healing process. Eaglstein WH [23] mentioned in his study that the inflammatory response is decreased with age, and undoubtedly this bears on some of the alterations in healing. The proliferative phase traditionally includes cell migration, proliferation, and maturation, all of which are changed with age. The total number of diabetics in the study included 200 patients (12%) in group A, while 18% in group B. The total number of hypertensives in the study included 8% in group A and 6% in group B while patients having both DM and HTN 8% in group A, 6% in group B. Beyene RT et al [24] mentioned in his study that preexisting diagnoses may significantly alter, delay, or inhibit normal wound healing. This was most commonly seen with chronic disorders, such as diabetes and renal failure but also occur secondary to aging and substance abuse. Less commonly, genetic or inflammatory disorders are the cause of delayed wound healing. In our study, when correlation of co-morbidities (DM) with wound healing and decrease in wound size was calculated, there was weak or no correlation and negative correlation respectively between in these factors.

The most common site affected among group A subjects was left foot (24%) followed by right foot (20%), the least site affected was right thigh (2%)

and right hand (2%). The most common site affected among the group B subjects was left leg (22%) and right foot (22%) followed by left foot (20%) The least site affected was left hand, right and left forearm (2%). The commonest organism on Culture sensitivity taken on day 1 for all patients was Staphylococcus aureus – 24 patients, Enterococci – 12 patients, no growth in 7 patients. In Group A (PAPAINUREA), the mean duration for Day of appearance of Granulation tissue was 3.540 ± 0.86 days. In Group B (PI), the mean duration for day of appearance of Granulation tissue was 3.550± 0.88 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of appearance of Epithelialization was 7.72± 1.88 days. In Group B (PI), the mean duration for day of appearance of Epithelialization was 12.38 ± 2.48 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of Periwound Erythema Resolution was 4.535 ± 1.15 days. In Group B (PI), the mean duration for day of Periwound Erythema Resolution was 7.73 ± 1.22 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of Periwound Edema Resolution was 6.64 ± 1.54 days. In Group B (PI), the mean duration for day of Periwound Edema Resolution was 10.55 ± 1.68 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration for day of Wound Disinfection (Culture negative) was 7.52 ± 1.86 days. Dalla P et al [25] mentioned in his study that in 12% patients 5 days were required for resolution of erythema.

In Group B (PI), the mean duration for day of Wound Disinfection (Culture negative) was 10.18± 2.14 days, difference was statistically significant ($p < 0.001$). In Group A (PAPAINUREA), the mean duration of hospitalisation was 10.68 ± 2.68 days. In Group B (PI), the mean duration of hospitalisation was 12.18 ± 2.64 days, difference was statistically significant ($p < 0.001$). In Group B (PI) 60% of cases underwent SSG before 28 days 40% of subjects underwent SSG after 28 days. In Group A (PI), 80% of cases underwent SSG. SSG before 28 days 20% of subjects underwent SSG after 28 days. Difference between group A and group B was statistically significant ($p = 0.02$). To maintain wounds in a favorable healing environment, various antimicrobial wound dressings are used to control infection and promote healing. When these dressings are used in conjunction with enzymatic debriding agents, compatibility between the enzyme and antimicrobial activity becomes a major concern. In addition, extensive growth of bacteria can also produce significant level of proteases, which may cause the degradation of various proteins and enzymes, including the exogenous proteins used for therapeutic purposes. In such wounds, the half-life of the debriding enzymes used could be significantly reduced. To generate an optimal environment for clean wound beds, the combined application of debriding enzymes with an antimicrobial agent could not only remove the devitalized tissues, but also control infection to minimize continuous tissue necrosis. The optimal combination should be such that the dressing materials do not display any inhibitory activity on the debriding enzymes, while the debriding enzymes do not alter the therapeutic activity of the antimicrobial agent.

Conclusion

There was shorter duration of hospital stay, earlier wound disinfection and a greater number of patients who underwent earlier skin grafting in papain urea group. The results were statistically significant and in favour of papain urea. Thus we concluded that use of papain urea is highly recommended as compared to povidone iodine in management of non-healing ulcers.

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