

Original Research Article

A prospective study on effectiveness of use of papain urea based preparation in dressings compared with regular conventional dressings in diabetic foot ulcers

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ABSTRACT

Background: Diabetic foot ulcer is a very common condition encountered in surgical practise. Wound management pose a good challenge for a treating surgeon due to its physical, mental and social implications. The devitalised necrotic tissue present in ulcer does not favour the wound healing as it increases the chance of infection and delays appearance of granulation tissue. Hence debriding of devitalised tissue plays a key role in wound care. In present study, we used papain urea based preparation in dressings which is an autolytic agent. This study was conducted to evaluate the effectiveness of use of papain urea based preparations compared with regular conventional dressing in diabetic foot ulcer management.

Methods: This was a prospective study conducted in K. R. Hospital, Mysore, Karnataka, India. 60 eligible subjects with diabetic foot ulcers were selected and subjects were randomly allocated into two groups Group A and Group B with 30 subjects in each group. Subjects in Group A underwent dressing with papain urea based preparation and in Group B underwent regular conventional dressing. Results were assessed with respect to percentage decrease in necrotic tissue, incidence of infection, appearance of granulation and hospital stay.

Results: Among Group A subjects percentage reduction of necrotic tissue was more, granulation appeared early and the hospital stay was less compared to Group B subjects which were statistically significant. However, there was no significant difference with respect to incidence of infection in both groups.

Conclusions: Papain urea based preparation is effective in diabetic foot ulcer care.

Keywords: Autolytic, Debridement, Papain urea

INTRODUCTION

Diabetic foot is the commonest complication among diabetics which is defined as any infection, ulceration and/or necrosis of deep tissues associated with neurological abnormalities and various degree of peripheral vascular disease of lower limbs. The major contributors for the formation of diabetic ulcers includes neuropathy, foot deformity and ischemia.¹ Diabetic ulcers inflict an enormous financial burden on society since

amputations are associated with substantial direct (hospitalisation and medication) as well as indirect (loss of working days) costs.² For management of wounds there have been lot of methods available ranging from simple dressing to more advanced vacuum assisted dressings. Research studies have demonstrated that presence of devitalised tissue in ulcers enhances bacterial growth, reduces resistance to infection, delays formation of granulation tissue and impedes reepithelialisation.³⁻⁸ Hence debridement of devitalised tissue is cornerstone in

ulcer care.⁸⁻¹⁰ Debridement can be surgical, mechanical or autolytic. In present study, we use a autolytic agent papain urea for autolytic debridement. Papain is a nonspecific proteolytic enzyme derived from the fruit of papaya tree (*Carica papaya*). It breaks the fibrinous material in the necrotic tissue.¹¹⁻¹² It requires the presence of sulfhydryl groups found in necrotic tissue.¹³ The addition of urea helps in exposing the activators of papain by altering three-dimensional structure of proteins and breaking Hydrogen bonds.¹⁴ This study was conducted to assess the effectiveness of use of papain urea based preparation in dressings for diabetic foot ulcers in comparison with regular conventional dressings.

METHODS

This study was conducted in K R Hospital, Mysuru, Karnataka, India. The study was conducted between January 2016 to December 2016. 60 eligible subjects were selected and randomly allocated into two groups Group A and Group B of 30 subjects each. Informed valid consent was taken.

Inclusion criteria

- Subjects with Diabetic foot ulcers with devitalised tissue
- Subjects with controlled Diabetes mellitus
- Subjects without any other contributory comorbidities.

Exclusion criteria

- Subjects aged >70 years
- Subjects with uncontrolled diabetes mellitus
- Subjects with other contributory comorbidities.

Subjects in Group A underwent dressing with Papain Urea based preparation that is after cleansing the wound Papain urea based preparation was applied over necrotic area and covered with gauze.

Subjects in Group B underwent regular conventional dressing. In both groups dressing was done every alternate day. Ulcer and devitalized tissue assessed and measurements taken with sterile gauze and scale. Culture swab used to collect specimen for culture and sensitivity whenever there was infection. Appropriate antibiotics were administered according to culture sensitivity reports.

The results were analysed between two groups with respect to percentage reduction in necrotic tissue, infection rate, appearance of granulation tissue and hospital stay.

Statistical methods used

- Descriptive statistics

- Independent sample t-test.
- Cramers V-test
- Repeated measure ANOVA.

RESULTS

In present study, the mean age in Group A was 49.16 ± 6.14 years and in Group B was 49.73 ± 5.41 years (Table 1). In Group A there were 16 males and 14 females and in Group B there were 15 males and 15 females (Table 1). The average size of the ulcer in Group A was $192.3 \pm 24.8 \text{ cm}^2$ and in Group B was $152.2 \pm 27.5 \text{ cm}^2$ (Table 1). Both groups were comparable with respect to age, sex and size of the ulcers.

Table 1: Percentage reduction of necrotic tissue.

Factors	Group A	Group B
Age	49.16 ± 6.14 years	49.73 ± 5.41 years
Male	16	14
Female	15	15
Average size of ulcer	$192.3 \pm 24.8 \text{ cm}^2$	$152.2 \pm 27.5 \text{ cm}^2$

In present study among Group A subjects there was 72.27 ± 4.68 % reduction in necrotic tissue whereas in Group B there was 24.62 ± 3.74 % reduction of necrotic tissue. There was statistically significant difference in percentage reduction of necrotic tissue (P-value=0.03) (Table 2).

Table 2: Comparison of factors.

Factors	Group A (n=30)	Group B (n=30)	P-value
% reduction of necrotic tissue	72.27 ± 4.68 %	24.62 ± 3.74 %	0.03
Incidence of infection	10 (33.33%)	12 (40%)	0.705
Appearance of granulation	8.73 ± 2.37 day	16.03 ± 4.68 day	0.001
Hospital stay	15.40 ± 4.02 days	23.26 ± 5.48 days	0.001

10 subjects among Group A and 12 subjects among Group B had infection during the study. There was no statistically significant difference with respect to incidence of infection among two groups (P-value 0.705) (Table 2). Most common organism isolated was *Staphylococcus aureus* followed by *Pseudomonas aerogenosa*. Infections were treated according to culture sensitivity reports.

The mean day of appearance of granulation tissue among Group A was 8.7 ± 2.37 day whereas in Group B it was 16.03 ± 4.68 days. In group A appearance of granulation was early compared to group B which was statistically significant (P-value 0.001) (Table 2).



Figure 1: Dressing with papain urea based preparation.

The mean hospital stay in Group A was 15.40 ± 4.02 days and in Group B was 23.26 ± 5.48 days. The hospital stay was significantly less in Group A compared to Group B (P-value 0.001) (Table 2).



Figure 2: Dressing with Papain urea based preparation.



Figure 3: Dressing with Papain urea based preparation.

DISCUSSION

Diabetic foot ulcer is a very common condition treated by surgeons. The effective management of such ulcers is very essential because poorly managed cases may land up in limb amputations which is a physical, mental and social burden for the patients. Research studies have demonstrated that presence of devitalised tissue in ulcers enhances bacterial growth, reduces resistance to infection, delays formation of granulation tissue and impedes reepithelialisation.³⁻⁸ Hence debridement of devitalised tissue is a key step in wound care.

Debridement can be surgical, mechanical or autolytic. Surgical debridement is an invasive procedure where we use surgical instruments and remove the necrotic tissue. It is the fastest way of debridement. However, it is invasive and in some patients it may require anaesthesia. Mechanical debridement done using wet or dry gauze, which does not discriminate between viable and non-viable tissue. Autolytic debridement is a form of Chemical debridement wherein we use an autolytic agent which autolyses the devitalised tissue and it is non-invasive. Various autolytic agents are available like collagenase, papain urea, papain urea chlorophyllin copper complex etc. In present study, we have used Papain urea based preparation in wound care comparing it with regular conventional dressings.

In present study results were assessed with respect to percentage decrease in devitalised tissue, appearance of granulation tissue, incidence of infection and hospital stay. In group A there was $72.27 \pm 4.68\%$ reduction in necrotic tissue whereas in Group B there was $24.62 \pm 3.74\%$ reduction of necrotic tissue. The P-value is 0.03 which was statistically significant. 10 out of 30 subjects among Group A and 12 out of 30 subjects among Group B had infection during the study. There was no statistically significant difference with respect to incidence of infection among two groups (P-value 0.705). Most common organism isolated was *Staphylococcus aureus* followed by *Pseudomonas aerogenosa*. Infections were treated according to culture sensitivity reports. Among Group A granulation appeared on 8.7 ± 2.37 day whereas in Group B it took 16.03 ± 4.68 days. In group A appearance of granulation was early compared to group B which was statistically significant (P-value=0.001). The mean hospital stay in Group A was 15.40 ± 4.02 days and in Group B was 23.26 ± 5.48 days. The hospital stay was significantly less in Group A compared to Group B (P-value =0.001)

In a study conducted by Hebda et al found that papain urea was more effective compared to collagenase in wounds.¹⁵ In two other studies conducted by Hobson et al and Levenson et al demonstrated that combination of enzyme (Papain) with a mucolytic agent (urea) is more effective than using enzyme alone.^{16,17}

Overall in present study we observed that Group A subjects who underwent dressings with papain urea based preparation had early and better healing and less hospital stay compared to subjects in Group B who had regular conventional dressings. Hence, we conclude that the use of papain urea based preparation in dressing is effective in management of diabetic foot ulcers.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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