Comparative Study of Papaya Dressing versus Conventional Dressing in Ulcer Healing

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ABSTRACT

BACKGROUND

Wet to dry normal saline mechanical debridement is the most common, cost effective debridement method, which is used widely,[1] including in our hospital setup in wound care management. Papaya is an enzymatic debriding agent which has been in use for many years.[2] We wanted to compare the effectiveness of papaya and normal saline in healing of ulcers and evaluate the role of papaya dressing in wound debridement, granulation tissue formation, reduction in ulcer size, and ulcer healing.

METHODS

This is a comparative interventional study of 100 patients done at Sri Venkateshwara Medical College, Tirupathi, from December 2017 to December 2018. Patients were selected and randomized into two groups - Group I (treated with papaya) and Group II (treated with normal saline). Patients were clinically assessed at the time of inclusion and daily dressing was done. Patients were assessed weekly for 4 weeks and response noted regarding slough reduction, granulation tissue formation, reduction in ulcer size, and overall response to treatment. Additional treatment and follow, up to 3 months were recorded.

RESULTS

The disappearance of slough / necrotic tissue was significant in the papaya group in the third and fourth week when compared to the normal saline group. 23 patients in the normal saline group, and 27 patients in the papaya group did not require any additional treatment. 22 patients underwent SSG in the normal saline group and 19 patients in the papaya group. Five patients underwent secondary suturing in the normal saline group and four patients in the papaya group. 23 patients in the normal saline group and 27 patients in the papaya group did not require any additional treatment.

CONCLUSIONS

Papaya is a better and effective debriding agent in comparison to wet to dry normal saline dressing and it also promotes faster granulation tissue formation. Overall response to treatment with papaya is good.

KEYWORDS

Papaya Dressing, Normal Saline Dressing, Ulcer Healing

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BACKGROUND

Wound management is a fundamental part of the general surgical practice since ancient times. In recent years, the prevalence of diabetic foot ulcers is growing at epidemic proportions throughout the world and has become a significant contributor to chronic non-healing wounds.[3] Many challenges are faced while dealing with chronic non - healing ulcers. Although wound management is the main activity in surgical wards, there is always a scope for improvement in the surgical practice. Therapeutic strategies have evolved over the years with wide varieties of dressing options available for wound cover, wound bed preparation, activation of wound healing, and repair.[4]

Technological advancements have also resulted in bioengineered skin substitutes for skin coverage and topical applications of recombinant platelet-derived growth factors in wound management.[5] The wound repair sequence is controlled in each stage by inhibitors and activators that are naturally produced by our immune system. Cellular migration, proliferation, matrix deposition, and remodelling causes progress in wound healing[6] Devitalized tissue and exudates act as a mechanical barrier to the movement of cells and provide an ideal environment for bacterial proliferation.[7] The presence of devitalized tissue results in excess production of pro-inflammatory cytokines and prolongated inflammatory response.[8] Hence in wound healing, wound bed preparation plays a critical role in achieving a conducive environment. I have discussed significant emphasis on enzymatic wound debridement with papaya. In this particular study, I have compared two debridement methods wet to dry normal saline dressing and enzymatic debridement with papaya.

We wanted to study and compare the duration of growth of granulation tissue, the mean duration of hospital stay, and the clinical outcome, in both the study groups.

METHODS

This study is a randomized, comparative interventional study carried out in Sri Venkateshwara Medical College Hospital from December 2017 to December 2018. The Institution's ethical committee approved the study. The study group comprised of a hundred patients with ulcers due to diabetes mellitus wound infections.

Patients were selected, randomized, and divided into 2 groups.

- Group – 1: 50 patients attended with papaya dressing.
- Group – 2: 50 patients attended with wet to dry normal saline dressing.

Method of Data Collection

- Clinical assessment done during the time of inclusion
- A complete history and detailed examination is done at taking in.
- Ulcer and necrotic tissue accurately measured.
- Assessment of ulcer using sterile gauze and graph paper.
- Area of ulcer calculated in cm^2.

Inclusion Criteria

- Patients aged more than 18 years with diabetic ulcers. and infected ulcers.
- Wagner's ulcer grade-II.

Wagner's Ulcer Grade

- Grade – I: Superficial ulcers.
- Grade – II: Deep ulcers up to subcutaneous tissue exposing soft tissue or bone.
- Grade – III: Abscess formation underneath /osteomyelitis.
- Grade – IV: Gangrene of part of tissue/limb/foot.

Exclusion Criteria

- Ulcers with acute active infections.
- Wagner's ulcer grade more than III.
- X-Ray features with underlying osteomyelitis.
- Diabetic foot associated with significant vascular disease.
- Uncontrolled diabetes mellitus.
- Patients with hepatic, renal and haematological disorders which impair wound healing.
- Patients using immunosuppressive drugs, long term steroid therapy, radiotherapy, or chemotherapy.

Investigations

- Complete blood count.
- FBS and PPBS.
- Renal function test.
- Liver function test.
- Wound culture and sensitivity.
- X-Ray of the involved part.
- Duplex scan, if vascular compromise is suspected.

Treatment Phase

- Patients are being randomized using a computer-generated random table after the stabilization of ulcers.
- All patients during the initial treatment phase underwent surgical debridement, and devitalized tissue removed.
- Daily cleaning and dressing did till ulcer became stable (i.e., no progression in size of ulcer).
- Good glycaemic control was achieved in diabetic patients and maintained throughout the treatment phase.
- Culture and sensitivity done during the treatment phase, and appropriate antibiotics started.
- Patients were assessed at 0 (randomization), 1, 2, 3, 4 weeks, and reviewed after three months.
- Reduction in slough, reduction in ulcer size, and progression in healthy granulation tissue formation noted weekly.
- Induration, discharge, and odour were noted weekly during this phase.
- Safety and tolerability of the study were closely monitored and assessed by questioning the patients regarding pain, itching, and hypersensitivity reaction during the treatment phase.
- The control group received wet to dry gauze dressing application with sterile gauze soaked with normal saline

(0.9 %) over the wound. Extra layers of an abdominal pad placed over the moist gauze, and twice-daily dressing change was done (68).

- In the study group, ulcers were cleaned with normal saline and washed thoroughly. Semi ripe papaya selected for all patients, washed and epicarp of the fruit peeled, and the fruit was grated finely and mashed into a paste and applied over the wound under sterile precaution (69). Dry gauze placed over the wound and the dressing was applied.
- All the patients treated until complete debridement.
- The reduction in slough and reduction in wound size in sq.cm. was assessed weekly from zero to four weeks. Granulation tissue formation in comparison to wound size was measured in percentage weekly till complete granulation. The endpoint was the presence of 100% healthy granulation tissue, which defined as pink tissue with a beaded and granular appearance.
- At the endpoint, whether any secondary procedure like SSG or secondary suturing, if done, was noted, and follows up was done for three months.

The study initially started in 130 patients, 65 patients in each group after randomization. 18 patients lost to follow up after the treatment phase. Three patients died during the follow-up phase (2 patients died of CVA & 1 patient died of MI). Five patients went against medical advice during the treatment stage. There were remaining 104 patients, 53 patients in the papaya group, and 51 patients in the normal saline group. First, 50 patients in each group in the random table taken into the study for comparison.

Statistical Analysis

- A probability value (p Value) < 0.05 the null hypothesis rejected, i.e., p-Value < 0.05 means there is a significant relationship between the two tests.
- The student's t-test (t-test) was used to find the difference between the means of the two groups.
- Chi-square ($\chi 2$) test was used to find the variation between percentages or proportions of categorical outcomes of the two groups.
- Other non-parametric test used to find the significance was Fisher's exact test.

RESULTS

- The mean age in the papaya group was 57.6 ± 9.4502 yrs.
- The mean age in the normal saline group was 54.2 ± 8.4201 yrs.
- There was no significant variation between the two groups.
- In papaya group: 54 % males and 46 % females
- In normal saline group: 56 % males and 44 % females.
- No significant variation between groups concerning gender noted.
- The study has 58 diabetes patients and 42 non - diabetes patients.
- In papaya group: 60 % diabetic patients and 40 % non - diabetes patients.
- In the normal saline group: 56 % diabetes patients and 44 % non - diabetes patients.
- No significant difference between groups concerning diabetes patients noted.
- Shows the study has 30 % have an ulcer in the right foot, and 29 % have an ulcer in the left foot.
- Totally 59 % have an ulcer in lower limbs.
- The other 41 % have an ulcer in other areas like thighs, back, arms, scrotum, and abdomen.
- The mean duration of ulcer in the papaya group was 7.56 ± 2.5964 days.
- The mean duration of ulcers in the normal saline group was 7.58± 1.8416 days.
- There was no significant variation between the two groups.
- The culture and sensitivity patterns in both groups were similar.
- The most frequently grown organism was E. coli, followed by Klebsiella.
- Mean ulcer sizes in both groups were alike.
- Both groups showed a reduction in ulcer size over the four weeks.

There was a significant difference in percentage reduction in slough / necrotic tissue with in the two groups.

- There was a significant difference in the reduction in slough / necrotic tissue between the two groups.
- In the second - week comparison, p-Value was 0.049, the third week it was 0.0003, and the fourth week it was 0.0082.
- Papaya group showed better slough reduction in 2nd, 3rd, and 4th weeks compared to normal saline.

Time Point	Normal Saline		Papaya		Difference	P-Value
	N	Mean	N	Mean		
Baseline	32	12.25	37	12.3514	-0.1014	0.9013
Week 1	50	26.92	50	33.66	-6.74	0.0008
Week 2	50	46.82	50	59.22	-12.4	<.0001
Week 3	50	66.66	50	81.9	-15.24	<.0001
Week 4	50	85.9	41	95.0976	-9.1976	<.0001
Week 5	40	97.55	16	98.875	-1.325	0.2704

Table 1. Distribution of Week-Wise Granulation-Tissue Formation

- There was a significant difference in the percentage increase in granulation tissue in the papaya group compared to the normal saline group.
- Week wise comparison between the two groups showed that papaya showed better granulation tissue formation after 2nd, 3rd & 4th weeks when compared to normal saline group.
- p - Value was less than 0.0001 at the end of the fourth week.

Timepoint	Normal Saline		Papaya		Difference	P-Value
	N	Mean	N	Mean		
Week 1	31	0.9087	34	0.8929	0.0158	0.8858
Week 2	49	1.4339	49	1.63	-0.1961	0.3065
Week 3	50	2.1564	50	2.5062	-0.3498	0.2158
Week 4	50	3.0306	50	3.6966	-0.666	0.0866

Table 2. Distribution of Reduction of Ulcer Size in the Study

Week wise comparison of reduction in the size of the ulcer did not show any significant difference.

There is no significant difference in the reduction of slough / necrotic tissue between diabetes and non-diabetes patients.

Diabetes Status	Time Point	N	Mean	S.D.	Min.	Max.	Difference from Baseline
Yes	Baseline	23	12.1304	3.8412	6	19	
	Week 1	30	32.1667	11.0706	12	57	24.3913
	Week 2	30	56.9667	11.4786	34	79	48.4783
	Week 3	30	78.6667	10.8924	56	100	68.087
	Week 4	28	94.2143	7.4851	79	100	82.8571
	Week 5	12	98.5	3.5291	90	100	89.3333
No	Baseline	14	12.7143	2.9982	8	19	
	Week 1	20	35.9	12.0783	14	58	28.5
	Week 2	20	62.6	11.2034	42	78	52.2143
	Week 3	20	86.75	11.5434	60	100	75.0714
	Week 4	13	97	4.761	88	100	82.25
	Week 5	4	100	0	100	100	87.75

Table 3. Distribution of Granulation Tissue Formation in Diabetic vs Non-Diabetic Patients in Papaya Group

There is no significant difference in the information on granulation tissue between diabetic and non-diabetic patients.

Diabetes Status	Timepoint	N	Mean	S.D.	Min.	Max.	t-Value
Yes	Week 1	20	0.964	0.4304	0.41	2.11	10.02
	Week 2	29	1.709	1.0265	0.4	4.37	8.97
	Week 3	30	2.6383	1.5577	0.5	7.32	9.28
	Week 4	30	3.919	2.1519	0.86	10.12	9.98
No	Week 1	14	0.7914	0.365	0.32	1.54	8.11
	Week 2	20	1.5155	0.9152	0.32	3.16	7.41
	Week 3	20	2.308	1.4357	0.84	5.27	7.19
	Week 4	20	3.363	2.0424	1.12	8.31	7.36

Table 4. Reduction of Ulcer Size in Diabetic vs. Non-Diabetic Patients in Papaya Dressing

There was no significant reduction in ulcer size between diabetic and non-diabetic patients.

There was a significant difference in percentage reduction in slough necrotic tissue in the papaya group compared to the normal saline group.

The disappearance of slough/necrotic tissue was significant in the papaya group in the 3rd and fourth week when compared to the normal saline group.

- In the third month, follow up showed 78% of wounds treated with papaya wholly healed, and 22% were recovering.
- 72% of wounds treated with normal saline wholly healed and 28% were healing.
- 22 patients underwent SSG in the normal saline group and 19 patients in the papaya group
- Five patients underwent secondary suturing in the normal saline group and four patients in the papaya group
- 23 patients in the normal saline group and 27 patients in the papaya group did not require any additional treatment.
- There was a significant difference in the percentage increase in granulation tissue in the papaya group compared to the normal saline group.
- Week wise comparison between the two groups showed that papaya showed better granulation tissue formation after 2nd, 3rd & 4th weeks when compared to normal saline group.
- p-Value was less than 0.0001 at the end of the fourth week.
- Week wise comparison of reduction in the size of the ulcer did not show any significant difference.
- There is no significant difference in the reduction of slough/necrotic tissue between diabetes and non-diabetes patients.
- There is no significant difference in the information on granulation tissue between diabetic and non-diabetic patients.
- There was no significant reduction in ulcer size between diabetic and non-diabetic patients.
- There was a significant difference in percentage reduction in slough necrotic tissue in the papaya group compared to the normal saline group.
- The disappearance of slough/necrotic tissue was significant in the papaya group in the 3rd and fourth week when compared to the normal saline group.
- In the third month, follow up showed 78% of wounds treated with papaya wholly healed, and 22% were recovering.
- 72% of wounds treated with normal saline wholly healed and 28% were healing.
- 22 patients underwent SSG in the normal saline group and 19 patients in the papaya group
- Five patients underwent secondary suturing in the normal saline group and four patients in the papaya group
- 23 patients in the normal saline group and 27 patients in the papaya group did not require any additional treatment.

DISCUSSION

Enzymatic compound debriding agents like collagenase, pure papain, and papain urea blends are used for wound bed readiness. Enzymatic debridement with papaya is a practical, effective, accessible and is eco amicable.

The concept of using papaya as a debriding agent came from observing the use of papaya latex as a debriding agent in Ayurvedic practice by local Ayurvedic physicians. This was based on Bhavaprakasham Nighantu, an Ayurvedic classic written in the sixteenth century by Bhava Mishra. It describes the characteristics and the use of various plants and minerals in medicine. Wound cleansing effect of papaya is mentioned in this.

Carica papaya has a long history of being a very effective medicinal plant. It is considered to have significant wound healing properties. It contains the proteolytic enzymes,

papain, and chymopapain in various levels in the fruit, latex, leaves, stems, and roots. Its proteolytic action is marked in acid, alkaline, and neutral solutions and has a digestive power at a wide range of temperatures and pH.[9] Studies at the University of Nigeria, Nigeria have revealed that extracts of papaya fruits are active against gram - positive bacteria and strong doses effective against gram - negative bacteria. Very significant antibacterial activity was found on Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa etc. The activity of papain is higher in extracts from the younger fruit than the older fruit.[10]

A point by point writing search uncovered a few episodic reports, different survey articles, and barely any practical examinations which have dissected the enzymatic activity of organic papaya products, in diabetic ulcers, postoperative wound dehiscence in western population and diabetic rodents. Given these reports, it was chosen to consider the impacts of papaya in wound bed planning.

Gurung S, Et Al. (2013) conducted a group study to investigate the healing efficiency of papaya latex formulated as 1.0 and 2.5% hydrogels.[11]

Burns were induced in swiss albino mice divided into five groups as following; group - I (negative control) received no treatment. Group - ii was treated with Carbopol 974p nf empty gel. Groups - iii and - IV were treated with Carbopol gel containing 1.0 and 2.5 % of dried papaya latex, respectively.

Group - v (positive control) received the standard drug (silver sulphadiazine and chlorhexidine gluconate cream). The efficacy of treatment was evaluated based on the hydroxyproline content, wound contraction and epithelialization time. Results show that hydroxyproline content was found to be significantly increased in the group-iii. Significant increase in percentage wound contraction was observed from day 12 in group - iv and from day 20 in groups iii and - v. the epithelialization time was found to be the shortest in group - iv. The study concluded that papaya latex formulated in the Carbopol gel is effective in the treatment of burns and thus supports its traditional use.

Murthy, Mangala. R et al (2012) et al done a interventional study related to comparison of safety and efficacy of papaya dressing with hydrogen peroxide solution on wound bed preparation in clients with wound gape.[12] The results Revealed that papaya dressing is more efficacious and equally safe as compared to hydrogen peroxide dressing when used for wound bed preparation in clients with postoperative wound gape.

In present study investigation results have indicated that there is a critical distinction (p value < 0.001) in granulation tissue development with papaya dressing when contrasted with typical saline dressing in the third and fourth weeks. This credit of granulation tissue arrangement actuated by Papain and chymopapain. Slough reduction decrease with papaya was likewise critical, as 96 % of the patients were cleared of slough toward the finish of the fourth week when contrasted with 36 % with ordinary saline dressing. The p-value was (0.0082) significant during the second, third, and fourth seven day stretch of the papaya dressing.

There was no significant reduction in ulcer size (p-value of 0.086) when compared to normal saline. Reductions in ulcer size in both groups were similar. In well - controlled diabetes mellitus, papaya can be used as a debriding agent safely. Wet to dry ordinary saline dressings are routinely utilized for ulcer dressings, as it is readily available and effectively accessible. Be that as it may, in contrast with papaya, it takes a more extended span for ulcer healing and tedious.There were no hypersensitivity, tolerability, or side effects in both the groups, as previous studies have already confirmed the safety and tolerability aspects of papaya. It reported that some pure papain preparations associated with pain, itching, and hypersensitivity reactions. Despite such concerns, no such hypersensitivity seen in this study. The patient has to be clearly educated that use of semi-ripe papaya application is associated with itching.

Limitations of this study are related to the lack of standardized methods of papaya preparation. The enzymatic content of papaya is said to decrease as the fruit ripens, suggesting a better efficacy in semi-ripe papaya. Despite the difference in enzyme content as the fruit ripens, previous studies confirm that there is no difference is in antibacterial activity in ripe and unripe fruit.

Papaya dressing can be encouraged as papaya is readily available in India throughout the year and cost-effective also. Preparation and application of papaya dressing are also comfortable and done by unskilled personnel. Thus, in terms of efficacy, Papaya dressing can be a good and better dressing method compared to normal saline dressing.

CONCLUSIONS

Papaya dressing and normal saline dressing have proven efficacy in debridement of wounds. Papaya dressing is a better enzymatic agent when compared to wet to dry normal saline mechanical debridement Papaya dressing was found to remove slough and necrotic tissue more rapidly when compared to normal saline as per this study. Wounds treated with papaya dressing had a faster granulation tissue formation compared to normal saline dressing. There was no significant difference in the reduction in ulcer size between the two groups in this study. The overall response to treatment with papaya dressing was significantly better when compared to normal saline dressing.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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