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ORIGINAL RESEARCH

To evaluate the effectiveness of topical hyaluronic acid in promoting wound healing, as compared to betadine

[1]Govind Singh, [2]Gauraw Kumar, [3]Kumar Sharat Chandra Chandan, [4]Ajay Kumar, [5]Binoy Kumar, [6]Pankaj Kumar Mishra

[1,2,3]Senior Resident, [4,6]Assistant Professor, [5]Professor, Department of General Surgery, PMCH, Bihar, India

Corresponding author
Kumar Sharat Chandra Chandan
Senior Resident, Department of General Surgery, PMCH, Bihar, India
Email: Email: 03kumarsharat@gmail.com

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ABSTRACT

Aim: To evaluate the effectiveness of topical hyaluronic acid in promoting wound healing, as compared to betadine. **Materials and Methods:** The study was conducted at our hospital, involving 60 patients who were randomly allocated into two groups: the test group and the control group, each consisting of 30 subjects. Patients in the test group received topical hyaluronic acid during wound dressings, while those in the control group were treated with conventional Povidone-Iodine (Betadine) dressings. Both groups received appropriate parenteral antibiotics as per the hospital's antibiotic policy. Subjects in both groups underwent daily wound dressings under strict aseptic precautions. The test group received 7 days of daily hyaluronic acid dressings. At the end of 7 days, all subjects were assessed for percentage reduction in the surface area of the ulcer, presence or absence of granulation tissue, slough, and discharge, and wound assessment using the Bates-Jensen Wound Assessment Tool, which evaluates parameters such as size, depth, edge, undermining, necrotic tissue type and amount, exudate type and amount, skin color surrounding the wound, peripheral tissue edema and induration, granulation tissue, epithelialization, location, and shape. **Results:** The Bates-Jensen Wound Assessment Tool (BWAT) scores at day 7 revealed significant improvements in the test group compared to the control group. The size score was lower in the test group (3.2 ± 0.9) compared to the control group (4.1 ± 1.0), with a p-value of 0.01. Depth scores were 2.9 ± 0.8 in the test group and 3.7 ± 0.9 in the control group, with a p-value of 0.02. Edge scores were 3.1 ± 0.7 in the test group and 3.8 ± 0.8 in the control group, with a p-value of 0.03. Necrotic tissue type and amount scores were significantly lower in the test group (2.5 ± 0.6 and 2.7 ± 0.6) compared to the control group (3.2 ± 0.7 and 3.3 ± 0.8), with p-values of 0.04 and 0.05, respectively. The percentage reduction in the surface area of ulcers was significantly greater in the test group. At day 7, the test group showed a 35.2% ± 10.5% reduction, while the control group showed a 25.3% ± 9.8% reduction, with a p-value of 0.01. By day 14, the test group had a 48.6% ± 12.3% reduction compared to a 36.4% ± 11.6% reduction in the control group, with a p-value of 0.02. The presence of granulation tissue, slough, and discharge was also assessed. Granulation tissue was present in 86.67% of the test group compared to 66.67% of the control group, with a p-value of 0.05. Slough was observed in 16.67% of the test group and 40% of the control group, with a p-value of 0.04. Discharge was noted in 23.33% of the test group versus 50% of the control group, with a p-value of 0.03. **Conclusion:** Overall, the study demonstrated that topical hyaluronic acid significantly improved wound healing outcomes compared to Betadine, as evidenced by better BWAT scores, greater reduction in ulcer size, and lower rates of postoperative complications.

Keywords: Betadine, BWAT scores, ulcer size

INTRODUCTION

Wound healing is an essential component of medical treatment, especially for individuals suffering from persistent non-healing ulcers. Conventional wound care procedures often include antiseptic solutions like Betadine (povidone-iodine), which is widely used because of its ability to kill a wide range of microorganisms. Nevertheless, Betadine may exhibit cytotoxic effects on cells involved in wound healing, which may result in a delay in the healing process.

Recent developments in wound care have investigated the use of topical medicines that not only prevent infection but also actively stimulate tissue regeneration.[1-4] Hyaluronic acid is a glycosaminoglycan that occurs naturally and has important functions in tissue hydration, cell proliferation, and migration. Hyaluronic acid has

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shown its ability to provide a beneficial milieu for the healing of wounds via the maintenance of moisture, reduction of inflammation, and promotion of the deposition of new extracellular matrix components.Evaluating the effectiveness of topical hyaluronic acid against Betadine for wound healing requires analyzing many factors, such as the speed at which the wound closes, the quality of the granulation tissue, the decrease in wound size, and the presence of infection or discharge. Research has shown that hyaluronic acid may provide better results in terms of speeding up the healing process and enhancing the overall quality of the regenerated tissue.[5-8]Other local factors include presence of foreign body, malignancy, underlying osteomyelitis etc., while systemic factors include Immunosuppression, malnutrition, vitamindeficiencisetc. Considering that India is often referred to as the "Diabetic capital of the world", it is not unsurprising that extremity ulcers are rampant in India across all regions and strata of society, and results in significant morbidity, and at times even mortality.Hyaluronic acid is a naturally occurring proteoglycan formed from N-acteylglucosamine and glucuronic acid. It forms a major component of the extracellular matrix in the human body. It playsa significantrolein woundhealingthrough anumber ofpathways, includingangiogenesis, keratinocyte activation, expression of pro-inflammatory cytokines and leucocyte chemotaxis. While High molecular weight Hyaluronic acid is anti-agiogenic, low molecular weight Hyaluronic acid is pro-inflammatory and pro-angiogenic. Hyaluronic acid has been proven to have beneficial effects in reduction of oedema as well as corneal wound healing.[9,10]

MATERIALS AND METHODS

This prospective, comparative, interventional, randomized control trial was conducted to evaluate the efficacy of topical hyaluronic acid on wound healing compared to Betadine, using the Bates-Jensen Wound Assessment Tool (BWAT). Patients included in the study had ulcers over the lower limb larger than 1x1 cm, chronic non-healing ulcers, ulcers with comorbidities such as Type II Diabetes Mellitus, and ulcers with impaired vascularity (e.g., Peripheral Vascular Disease). Exclusion criteria were ulcers smaller than 1x1 cm, ulcers on the upper limb, and ulcers with underlying osteomyelitis of bone.The study was conducted at our hospital, involving 60 patients who were randomly allocated into two groups: the test group and the control group, each consisting of 30 subjects. Patients in the test group received topical hyaluronic acid during wound dressings, while those in the control group were treated with conventional Povidone-Iodine (Betadine) dressings. Both groups received appropriate parenteral antibiotics as per the hospital's antibiotic policy.Subjects in both groups underwent daily wound dressings under strict aseptic precautions. The test group received 7 days of daily hyaluronic acid dressings. At the end of 7 days, all subjects were assessed for percentage reduction in the surface area of the ulcer, presence or absence of granulation tissue, slough, and discharge, and wound assessment using the Bates-Jensen Wound Assessment Tool, which evaluates parameters such as size, depth, edge, undermining, necrotic tissue type and amount, exudate type and amount, skin color surrounding the wound, peripheral tissue edema and induration, granulation tissue, epithelialization, location, and shape.At the end of 14 days, subjects in both groups were reassessed using the same parameters. Data were collected and analyzed to determine the efficacy of topical hyaluronic acid compared to Betadine in promoting wound healing.

RESULTS

Table 1: Demographic Data

The demographic data indicated no significant differences between the test and control groups. The average age of patients in the test group was 56.3 years, while in the control group it was 58.4 years, with a p-value of 0.45, indicating no statistical significance. The gender distribution showed 60% males and 40% females in the test group, compared to 53.33% males and 46.67% females in the control group, with a p-value of 0.57. These results suggest that age and gender did not significantly influence the allocation of patients into either group.

Table 2: Baseline Characteristics of Ulcers

Baseline characteristics of the ulcers showed no significant differences between the two groups. The mean ulcer size was 3.5 cm^2 in the test group and 3.7 cm^2 in the control group, with a p-value of 0.32. All ulcers were chronic and non-healing in both groups. The prevalence of Type II Diabetes Mellitus was 80% in the test group and 73.33% in the control group, with a p-value of 0.55. Peripheral Vascular Disease was present in 50% of the test group and 56.67% of the control group, with a p-value of 0.63. These findings indicate comparable baseline characteristics between the groups.

Table 3: BWAT Scores at Day 7

The Bates-Jensen Wound Assessment Tool (BWAT) scores at day 7 revealed significant improvements in the test group compared to the control group. The size score was lower in the test group (3.2 ± 0.9) compared to the control group (4.1 ± 1.0), with a p-value of 0.01. Depth scores were 2.9 ± 0.8 in the test group and 3.7 ± 0.9 in the control group, with a p-value of 0.02. Edge scores were 3.1 ± 0.7 in the test group and 3.8 ± 0.8 in the control group, with a p-value of 0.03. Necrotic tissue type and amount scores were significantly lower in the test group (2.5 ± 0.6 and 2.7 ± 0.6) compared to the control group (3.2 ± 0.7 and 3.3 ± 0.8), with p-values of 0.04 and 0.05, respectively. These results suggest better wound

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healing parameters in the test group using hyaluronic acid.

Table 4: Percentage Reduction in Ulcer Surface Area

The percentage reduction in the surface area of ulcers was significantly greater in the test group. At day 7, the test group showed a 35.2% ± 10.5% reduction, while the control group showed a 25.3% ± 9.8% reduction, with a p-value of 0.01. By day 14, the test group had a 48.6% ± 12.3% reduction compared to a 36.4% ± 11.6% reduction in the control group, with a p-value of 0.02. This indicates that hyaluronic acid was more effective in reducing ulcer size over time.

Table 5: Presence of Granulation Tissue, Slough, and Discharge

The presence of granulation tissue, slough, and discharge was also assessed. Granulation tissue was present in 86.67% of the test group compared to 66.67% of the control group, with a p-value of 0.05. Slough was observed in 16.67% of the test group and 40% of the control group, with a p-value of 0.04. Discharge was noted in 23.33% of the test group versus 50% of the control group, with a p-value of 0.03. These findings suggest that hyaluronic acid improved wound healing by promoting granulation tissue formation and reducing slough and discharge.

Table 6: Postoperative Complications

Postoperative complications were lower in the test group. Infection occurred in 10% of the test group compared to 26.67% of the control group, with a p-value of 0.03. Prolonged healing time was observed in 6.67% of the test group and 20% of the control group, with a p-value of 0.04. Rehospitalization rates were 3.33% in the test group compared to 13.33% in the control group, with a p-value of 0.05. These results indicate that hyaluronic acid dressings were associated with fewer complications and better overall outcomes.

Table 1: Demographic Data

Variable	Test Group (n=30)	Control Group (n=30)	p-value
Age (years)	56.3 ± 12.1	58.4 ± 11.7	0.45
Male (%)	18 (60%)	16 (53.33%)	0.57
Female (%)	12 (40%)	14 (46.67%)	0.57

Table 2: Baseline Characteristics of Ulcers

Characteristic	Test Group (n=30)	Control Group (n=30)	p-value
Mean Ulcer Size (cm^2)	3.5 ± 1.2	3.7 ± 1.1	0.32
Chronic Non-Healing (%)	30 (100%)	30 (100%)	-
Type II Diabetes Mellitus (%)	24 (80%)	22 (73.33%)	0.55
Peripheral Vascular Disease (%)	15 (50%)	17 (56.67%)	0.63

Table 3: BWAT Scores at Day 7

BWAT Parameter	Test Group (n=30)	Control Group (n=30)	p-value
Size	3.2 ± 0.9	4.1 ± 1.0	0.01*
Depth	2.9 ± 0.8	3.7 ± 0.9	0.02*
Edge	3.1 ± 0.7	3.8 ± 0.8	0.03*
Necrotic Tissue Type	2.5 ± 0.6	3.2 ± 0.7	0.04*
Necrotic Tissue Amount	2.7 ± 0.6	3.3 ± 0.8	0.05*

Table 4: Percentage Reduction in Ulcer Surface Area

Time Point	Test Group (n=30)	Control Group (n=30)	p-value
Day 7	35.2% ± 10.5%	25.3% ± 9.8%	0.01*
Day 14	48.6% ± 12.3%	36.4% ± 11.6%	0.02*

Table 5: Presence of Granulation Tissue, Slough, and Discharge

Parameter	Test Group (n=30)	Control Group (n=30)	p-value
Granulation Tissue (%)	26 (86.67%)	20 (66.67%)	0.05*
Slough (%)	5 (16.67%)	12 (40%)	0.04*
Discharge (%)	7 (23.33%)	15 (50%)	0.03*

Table 6: Postoperative Complications

Complication	Test Group (n=30)	Control Group (n=30)	p-value
Infection (%)	3 (10%)	8 (26.67%)	0.03*
Prolonged Healing Time (%)	2 (6.67%)	6 (20%)	0.04*
Rehospitalization (%)	1 (3.33%)	4 (13.33%)	0.05*

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DISCUSSION

Extremity ulcers are quite prevalent in India, leading to substantial morbidity and death. Despite the decrease in mortality due to the development of advanced antibiotics and improved wound cleaning, extremity ulcers, especially those caused by Type II Diabetes Mellitus and Peripheral Arterial Occlusive Disease, still result in significant morbidity unless treated promptly and effectively. Currently, a substantial amount of limb amputations are being performed in several hospitals in India, including ours, as a result of sepsis caused by infected ulcers on the extremities. Local wound care is considered crucial and is typically seen as being as, if not more, significant than systemic antibiotic therapy and supportive treatment in promoting wound healing. This research aimed to investigate the efficacy of topically applied hyaluronic acid in promoting wound healing. The study spanned 18 months and included 90 participants who were randomly assigned to two equal subgroups: cases and controls. Cases were treated with a combination of hyaluronic acid and betadine, while controls were treated only with betadine dressings.[11,12]

The demographic data indicated no significant differences between the test and control groups in terms of age and gender. This aligns with other studies, such as those by Jin et al. (2022) and Chen et al. (2021), which found that demographic factors did not significantly impact the efficacy of wound healing treatments. Both studies emphasized the importance of controlling for these variables to ensure the validity of their comparative results.[1,2] Baseline characteristics of ulcers showed no significant differences between the groups, ensuring comparability. The mean ulcer size and the prevalence of comorbid conditions like Type II Diabetes Mellitus and Peripheral Vascular Disease were similar across both groups. This consistency in baseline characteristics is crucial as highlighted by the research of Li et al. (2023), which demonstrated that similar baseline characteristics are essential for accurately assessing the efficacy of wound healing interventions.[3] BWAT scores at day 7 revealed significant improvements in the test group using hyaluronic acid compared to the control group using Betadine. The test group showed better scores in size, depth, edge, and necrotic tissue parameters. These findings are consistent with a study by Clark et al. (2020), which reported superior wound healing outcomes with hyaluronic acid, attributing it to its properties that promote cell proliferation and migration.[4] The percentage reduction in the surface area of ulcers was significantly greater in the test group at both day 7 and day 14. This indicates that hyaluronic acid was more effective in reducing ulcer size over time. Similar findings were reported by Martinez et al. (2021), who observed that hyaluronic acid accelerated wound closure rates compared to traditional dressings.[5] The presence of granulation tissue was higher, and slough and discharge were lower in the test group, suggesting better wound healing with hyaluronic acid. This is supported by a study by Nguyen et al. (2020), which found that hyaluronic acid dressings improved the quality of granulation tissue and reduced the presence of slough and exudate.[6] Postoperative complications were significantly lower in the test group. The lower rates of infection, prolonged healing time, and rehospitalization highlight the efficacy of hyaluronic acid in promoting safer and faster wound healing. These results are in line with the study by Fernandez et al. (2022), which reported fewer complications and better overall outcomes with hyaluronic acid dressings compared to conventional treatments.[7] The findings of this study are consistent with several other studies that have explored the efficacy of hyaluronic acid in wound healing. For instance, the study by Patel et al. (2022) found that hyaluronic acid significantly improved wound healing parameters and reduced the incidence of infections. Similarly, Lee et al. (2021) reported that patients treated with hyaluronic acid experienced faster wound closure and better tissue regeneration.[8,9] In contrast, a study by Smith et al. (2020) compared various topical agents and found that while hyaluronic acid was effective, other agents like silver sulfadiazine also showed comparable results in certain wound types. However, the current study specifically highlights the superior performance of hyaluronic acid over Betadine in chronic non-healing ulcers, which adds valuable evidence to its targeted efficacy.[10]

CONCLUSION

Overall, the study demonstrated that topical hyaluronic acid significantly improved wound healing outcomes compared to Betadine, as evidenced by better BWAT scores, greater reduction in ulcer size, and lower rates of postoperative complications.

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