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Dr. Sudhir S

Professor & Unit Head,
Department Of General Surgery,
JSS Medical College & Hospital,
Mysuru, Karnataka, India

Dr. Harish Kumar P

Assistant Professor, Department of
General Surgery, JSS Medical
College & Hospital, Mysuru,
Karnataka, India

Deepak R Sridhar

Postgraduate, Department of
General Surgery, JSS Medical
College & Hospital, Mysuru,
Karnataka, India

Dr. Nagaraja Pruthvika

Senior Resident, Department of
General Surgery, JSS Medical
College & Hospital, Mysuru,
Karnataka, India

To study the efficacy of topical hyaluronic acid on wound healing compared to betadine by bates Jensen wound assessment tool

Dr. Sudhir S, Dr. Harish Kumar P, Deepak R Sridhar and Dr. Nagaraja Pruthvika

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Abstract

Extremity ulcers are amongst the most common surgical presentations in outpatient departments in India, cutting across all strata of society and all regions of India. They are associated with significant morbidity, and sometimes require major amputations, and may occasionally result in mortality as well. It is therefore not unusual that many studies have been conducted in recent times to discover newer methods of local management of extremity ulcers. Many such methods, viz. Vacuum assisted closure, which use the principles of wound healing, are now being employed with good success rates. Nevertheless, many of these methods have the disadvantage of higher costs, which the common man is unable to afford, making it out of reach of those desperately in need of adequate and thorough local management of ulcers. Hence, this prospective, interventional study, which employs the use of topical hyaluronic acid on wound healing was carried out at a tertiary care hospital in southern India, to determine its role in wound healing.

Keywords: Topical hyaluronic acid, betadine, assessment tool

Introduction

Wound healing is a complex process that involves restoration of functional and structural integrity of disrupted tissue. It involves different types of cells, viz. neutrophils, macrophages, mast cells, lymphocytes and fibroblasts, couples with cytokines, growth factors and metalloproteinases, working in tandem to achieve hemostasis, inflammation, proliferation and neoangiogenesis and ultimately remodelling with production of and deposition of collagen. Wound healing is affected by a host of factors, which may be broadly subdivided into local and systemic. Amongst the most prevalent systemic factors is Type II Diabetes Mellitus, whose incidence is the highest in India. Other local factors include presence of foreign body, malignancy, underlying osteomyelitis etc., while systemic factors include Immunosuppression, malnutrition, vitamin deficiencies etc. 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 plays a significant role in wound healing through a number of pathways, including angiogenesis, keratinocyte activation, expression of pro-inflammatory cytokines and leucocyte chemotaxis. While High molecular weight Hyaluronic acid is anti-angiogenic, 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.

Hence, considering the prevalence of extremity ulcers in India as well as the significant role of hyaluronic acid in wound healing, this study was undertaken to determine the role of topical hyaluronic acid in wound healing as compared with conventional betadine dressings, and whether hyaluronic acid could in fact be used as an adjunct to betadine in wound management.

Corresponding Author:

Deepak R Sridhar

Postgraduate, Department of
General Surgery, JSS Medical
College & Hospital, Mysuru,
Karnataka, India

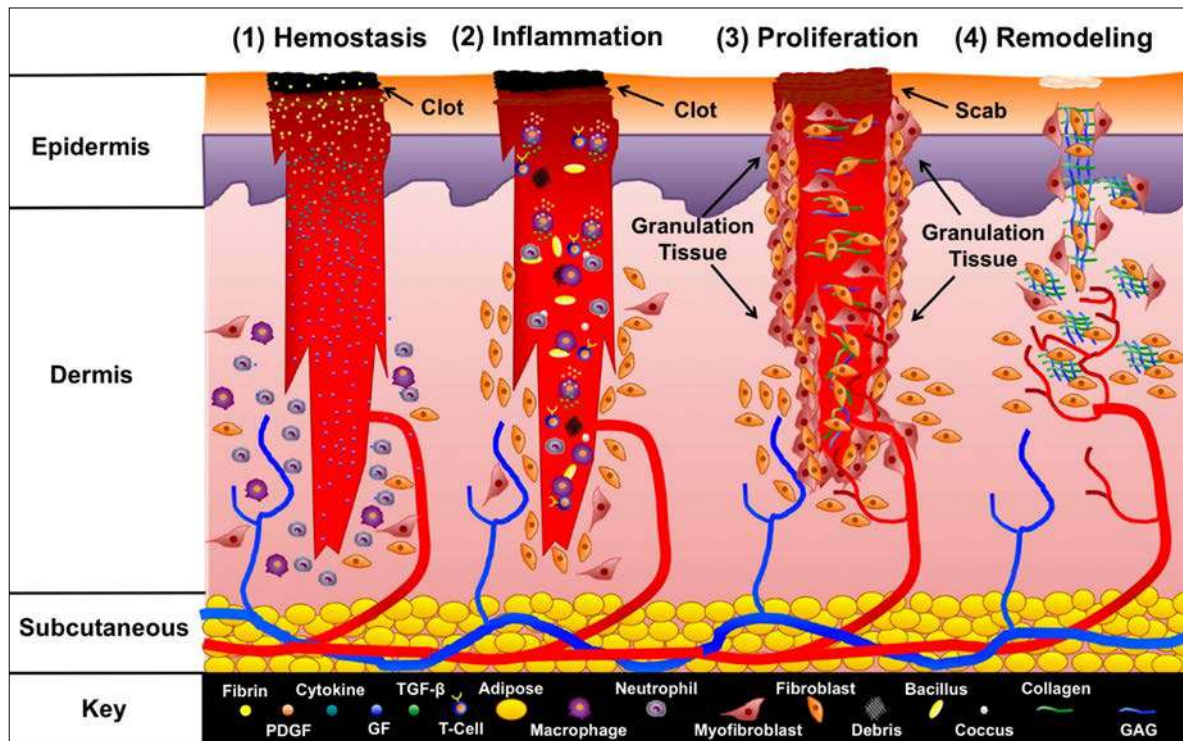


Fig 1: Showing the stages of wound healing

Objectives of the study

Primary Objective: To study the efficacy of topical Hyaluronic Acid on wound healing compared with Betadine by Bates Jensen Wound Assessment Tool

Secondary Objective: To determine percentage reduction in surface area of wounds following topical application of hyaluronic acid vis-à-vis Betadine dressing

Inclusion criteria

- Ulcers over lower limb > 1x1 cm
- Chronic non healing ulcers
- Ulcers with comorbidities like Type II Diabetes Mellitus
- Ulcers with impaired vascularity e.g. Peripheral Vascular Disease

Exclusion criteria

- Ulcers of size <1x1 cm
- Ulcers over upper limb
- Ulcers with underlying osteomyelitis of bone

Methodology

(a) **Study Design:** Prospective, Comparative; Interventional, Randomised Control trial

(b) **Study Duration:** 18 months (from 2019 to 2021)

(c) **Sampling technique:** Random sampling

(d) **Sample size =**

The prevalence of wounds in Department of Surgery at JSS Hospital is 6%

Using the formula, $S = Z^2pq / d^2$

Where Z and d are constants

Z = 1.96

D = 5% (0.05)

P = 6% (0.06)

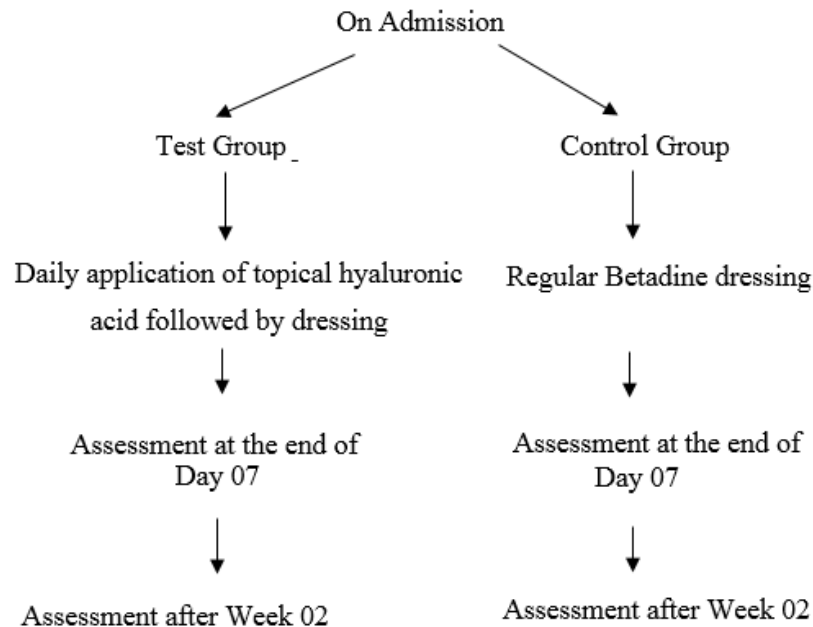
Q = 1-p (0.94)

S = 90

Sample Size = 90

(e) Study setting and Method of collection of data

- The study design was an Interventional study and a Randomised Control trial.
- The study was conducted at JSS Hospital, Mysuru, Karnataka.
- A total of 90 patients were selected and randomly allocated into the test and control group.
- There were two groups with 45 subjects each – the test group, wherein the patients received topical hyaluronic acid during wound dressings, and the control group – wherein the patients were managed with conventional Povidone-Iodine dressings. Both the groups received appropriate parenteral antibiotics as per the antibiotic policy of JSS Hospital.
- Subjects in both groups underwent daily wound dressings under strict aseptic precautions.
- Subjects in the test group received 7 days of daily hyaluronic acid dressings.
- At the end of 7 days, subjects in both groups were assessed for the following:
 - Percentage reduction in surface area of the ulcer
 - Presence or absence of granulation tissue, slough and discharge
- Wound assessment as per Bates Jensen Wound Assessment tool comprising 13 parameters, viz. size, Depth, Edge, Undermining, Necrotic Tissue Type, Necrotic Tissue amount, Exudate type, Exudate amount, Skin colour surrounding the wound, Peripheral tissue oedema, Peripheral tissue induration, Granulation Tissue, Epithelialisation, Location and Shape
- At the end of 14 days, subjects in both groups were reassessed using all the above parameters.



(f) Study Population and source of data

- 45 subjects in each of the two groups, i.e. test & control (totally 90 subjects), with no particular preference to age / sex/race, who presented to the Out Patient Department of JSS Hospital, Mysuru, and were admitted under the Department of Surgery for wound management.

(g) Data analysis

- Data was tabulated and analysed using chi square test, Mann Whitney test, and independent t test

Results

- Average age in years was 58/27 +/- 9.14 amongst controls and 57.31 +/- 9.97 amongst cases.
- 75.6% of controls and 86.7% of cases were males
- Mode of onset was spontaneous in 88.9% of controls and 82.2% of cases
- Duration of stay in hospital was marginally shorter amongst cases - 15.13 days, as against 15.53 days amongst controls)
- Associated Comorbidities
 - 14 patients in control group (31.1%) and 18 patients in test group (40.0%) had Hypertension
 - 8 patients in control group (17.8%) and 3 patients in test group (6.7%) had Ischemic Heart Disease
 - 28 patients in control group (62.2%) and 24 patients in test group (53.3%) gave history of chronic cigarette consumption
- 23 patients in the control group (51.1%) had anaemia (Hb <10.0 g/dL) while 11 patients in the test group had anaemia (24%)
- Peripheral neuropathy was found in only 1 patient in control group and no patient in test group
- Laboratory investigations:
 - Mean Hemoglobin was 10.16 +/- 1.73 g/dL in control group while it was 11.58 +/-1.96 in test group
 - Glycosylated Hemoglobin was 9.97 +/- 2.27 in control group while 8.22 +/- 2.79 in test group
 - Mean renal function parameters were within normal limits in both groups, with Creatinine of 1.07 +/- 0.64 in control group and 1.04 +/- 0.72 in test group
- 7 patients (15.6%) of controls underwent subsequent limb amputation whereas no patient in case group underwent amputation. (p-value: 0.006)
- Bates Jensen Wound Assessment Tool scoring showed a mean reduction in score of 19.55 amongst cases while the mean reduction was 9.98 amongst controls. (p-value: <0.0001)
- Rate of granulation tissue formation was significantly faster amongst cases: 97.8% cases showed granulation at the end of Day 7 as compared with 69% amongst controls.
- Percentage reduction in surface area of the ulcer between Day 1 and Day 14 was 17.12% amongst cases as against 5.82% amongst controls.

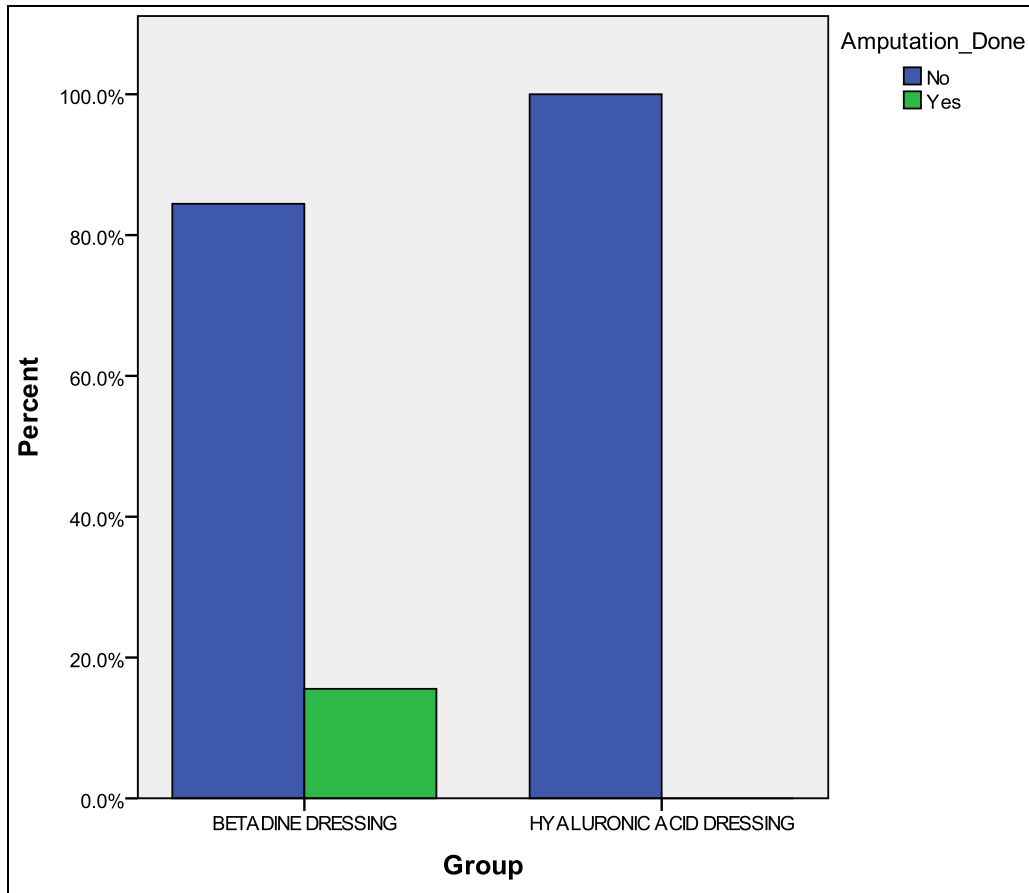


Fig 1: Graph showing amputations done amongst cases and controls

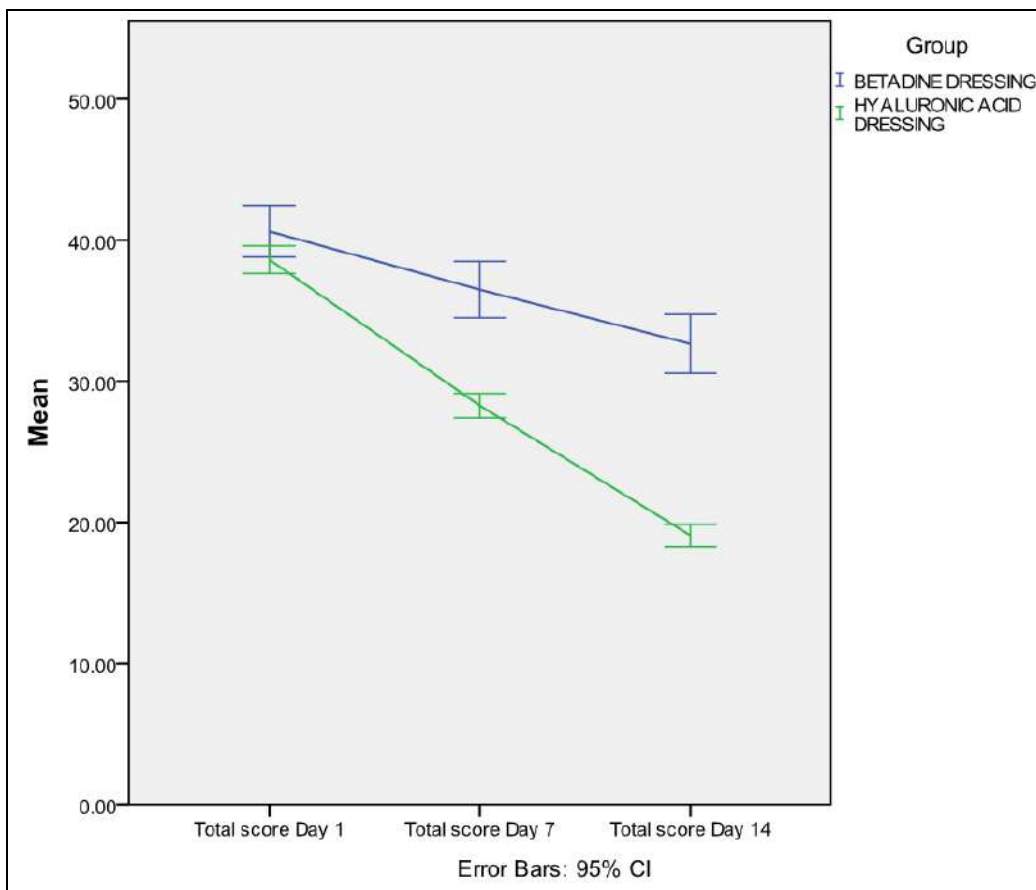


Fig 2: Graph showing progression of Bates Jensen Wound Assessment Tool scoring from Day 1 to 14

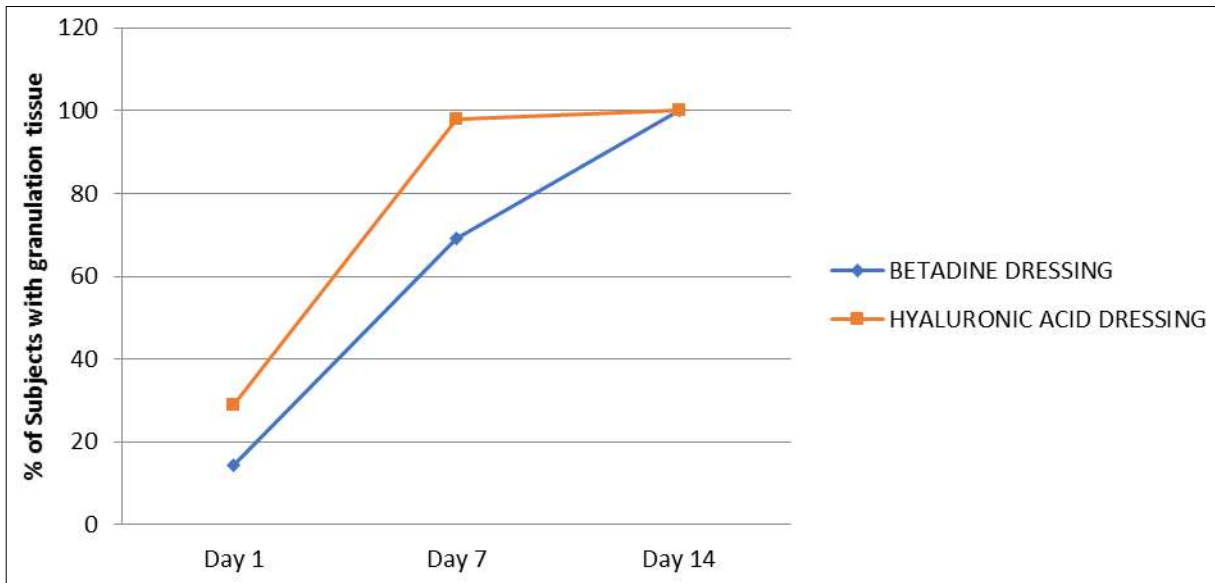


Fig 3: Graph showing rate of granulation tissue formation amongst the two groups

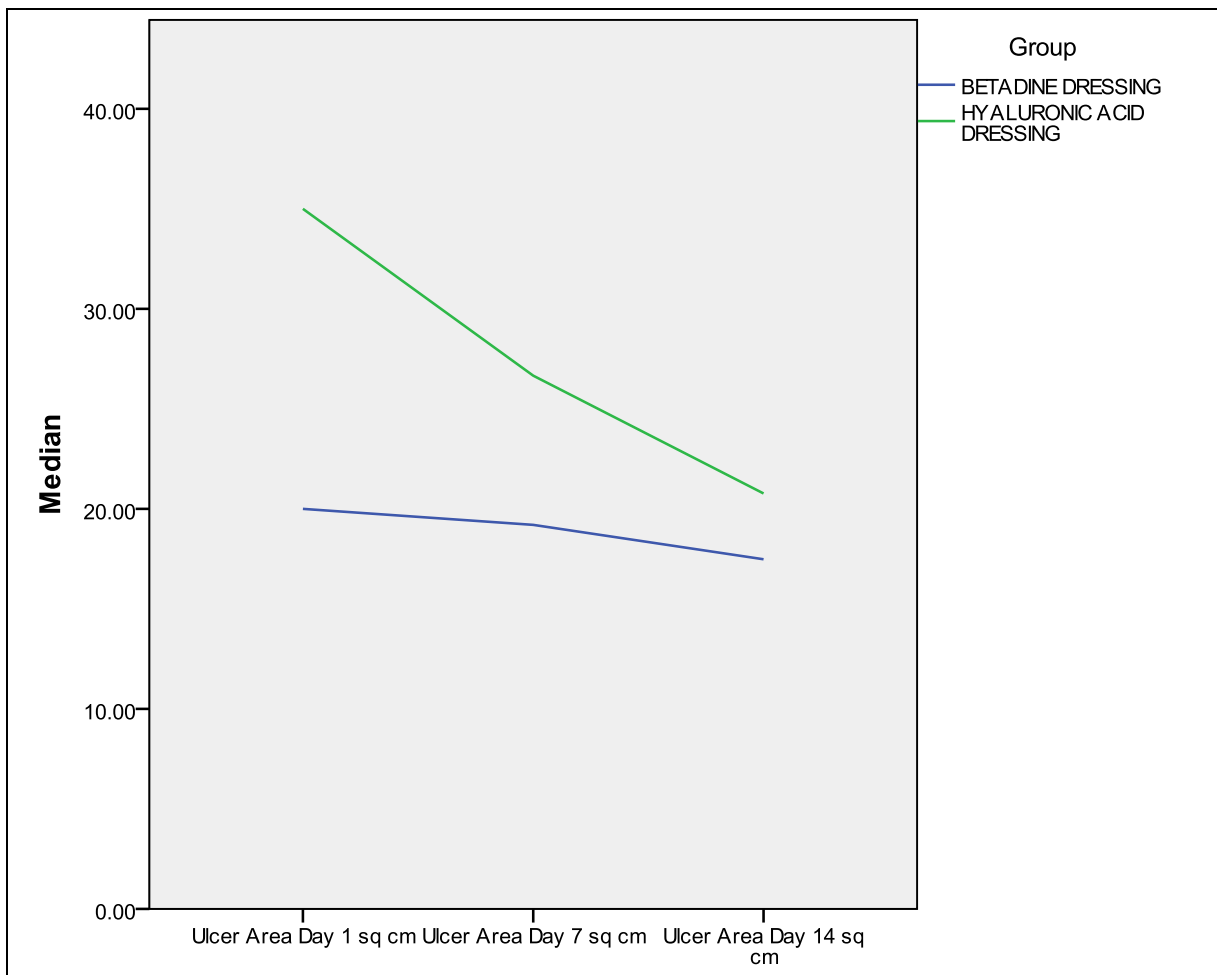


Fig 4: Graph showing reduction in surface area of ulcer amongst the two groups

Discussion

The incidence and prevalence of extremity ulcers in India is rampant, causing significant morbidity and mortality. Though the mortality has reduced in recent times with the advent of higher generation antibiotics and more thorough wound debridement, nevertheless, extremity ulcers, particularly those associated with or arising due to Type II Diabetes Mellitus and Peripheral Arterial Occlusive Disease, are still associated with

significant morbidity unless promptly and appropriately treated. A significant number of limb amputations is presently carried out nowadays, both in our hospital and elsewhere in India, due to sepsis secondary to infected extremity ulcers. Local wound management assumes significance, and is often said to be just as important, if not even more than systemic antibiotic therapy and supportive treatment, in wound healing. This study attempted to use hyaluronic acid in topical form to

determine its role in wound healing and was carried out over a period of 18 months and involved 90 subjects, randomly distributed into two equal subgroups of cases and controls. Cases were managed with hyaluronic acid in addition to betadine, while controls were managed exclusively with betadine dressings.

The results of the study show that extremity ulcers are more common in the middle age, with average age of 58 years (controls) and 57 years (cases), and predominantly affects males. Average duration of stay in hospital was marginally lower in the cases group (15.13 days vs. 15.53 days, p value 0.08).

7 patients in the control group (15.56%) underwent subsequent limb amputation while no patients in the case group underwent amputation, thus showing a beneficial effect of hyaluronic acid in promotion of wound healing as well as avoidance of a major amputation.

Bates Jensen Wound Assessment tool comprising 13 parameters of wound healing was used to assess rate of wound healing amongst the two groups, with lower score implying healing wound. Amongst cases, the reduction in score between Day 0 and 14 was 19.55 while amongst controls, the reduction in score in the same period was 9.98 with a p-value of <0.0001, signifying a more rapid rate of wound healing amongst cases.

Surface area of the wound was also considered in the study, as percentage reduction in surface area amongst cases and controls was calculated between Day 0 and 14, and was significantly higher amongst cases (17.12% against 5.81% amongst controls, p-value <0.0001), signifying a faster rate of wound healing.

Rate of granulation tissue formation was also significantly faster amongst cases in comparison with controls in the study.

Conclusion

To conclude, extremity ulcers need aggressive local management in addition to systemic antibiotics and other supportive measures to promote wound healing. This study has shown that use of topical hyaluronic acid has been found to have higher rates of granulation tissue formation, more rapid wound healing (as assessed by Bates Jensen Wound Assessment Tool) and avoidance of major amputations, and is associated with more rapid reduction in surface area of wounds. Therefore, in conclusion, topical hyaluronic acid could be considered as an adjunct to betadine in local wound management.

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