Original Research Article

Comparative study of topical mupirocin versus mupirocin with sucralfate combination in treatment of chronic skin ulcers

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Abstract

Background: Various treatment modalities of chronic skin ulcers include topical and systemic antibiotics, surgical debridement, skin grafting, compression stockings, and various types of dressings. In present study we compared efficacy of topical mupirocin versus topical mupirocin with sucralfate combination in treatment of chronic skin ulcers at our tertiary hospital. **Material and Methods:** This prospective, randomized, comparative study was conducted in patients 19 - 70 years of age, chronic ulcer, duration of the ulcer more than 2 months, the size of ulcer <2 cm × 2 cm. Study patients were randomly divided by chit method pre-operatively (before debridement). From total 60 patients of chronic skin ulcers, 30 patients underwent treatment with topical mupirocin 2% in water-soluble ointment base (group M) while other 30 patients underwent treatment as topical mupirocin 2% with sucralfate 7% w/w in water-soluble ointment base (group MS). Topical application done twice daily basis for 6 weeks in both groups. **Results:** In present study 60 patients were randomly divided to group M (n=30) and group MS (n=30). General characteristics such as age, gender, ulcer duration, ulcer (Wagner) grading, Co-morbidities (diabetes mellitus, hypertension, ischemic heart diseases and BMI > 30 kg/m^2) were comparable in both groups and difference was not statistically significant. In present study etiologically most of the ulcers were diabetic and traumatic ulcer. Less common types were venous ulcer , arterial ulcer and infective ulcer. At baseline there was no statistically significant difference noted between two groups (p=0.58). At 3 weeks and at 6 weeks significant reduction was noted in group MS as compared to group M and difference was significant statistically. 3 (10 %) ulcers from both groups remained unhealed. No other complications were noted in present study. **Conclusion:** Use of topical 7% sucralfate in addition to topical 2% mupirocin can heal chronic wounds better and earlier as compared to topical 2% mupirocin alone.
Keywords: Mupirocin, sucralfate, chronic skin ulcers, topical

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INTRODUCTION

Ulcers can be defined as wounds with a “full thickness depth” and a “slow healing tendency”. Ulcers of skin can result in complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.[1] Chronic wounds, by definition, are wounds that have failed to proceed through an orderly and timely reparative process to produce anatomic and functional integrity over a period of 3 months.[2] Chronic ulcers are reported to associated with pain, impaired sleep, restricted mobility and social activities, high cost of healthcare, loss of productivity, and reduced quality of life. These wounds are a significant challenge to the health care system and its professionals, with a huge economic burden.[3] Various treatment modalities of chronic skin ulcers include topical and systemic antibiotics, surgical debridement, skin grafting, compression stockings, and various types of dressings. Recent advances in management include modalities such as biological skin equivalents and other biological dressings, platelet-rich plasma, keratinocytes, and collagen

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products. In present study we compared efficacy of topical mupirocin versus topical mupirocin with sucralfate combination in treatment of chronic skin ulcers at our tertiary hospital.

MATERIAL AND METHODS

This prospective, randomized, comparative study was conducted by department of pharmacology in department of General Surgery, MIMSR Medical College, Latur. Study duration was of 1 year (January 2019 to June 2019). Patients with long-standing chronic skin ulcers (>4 weeks) were considered for this study. Institutional ethical committee approval was taken.

Inclusion Criteria

Patients between 19 - 70 years of age, duration of the ulcer more than 2 months, the size of ulcer <2 cm × 2 cm, patients giving consent for participation and follow up.

Exclusion Criteria

Pulseless limb, immunocompromised patients, associated septicemia and osteomyelitis, Skin malignancies, Diabetic ketoacidosis, Exposed bones, tendon, and Charcot joint. Not willing for participation, follow up, lost to follow up

Study was explained to patients in local language and consent was taken for participation. After undergoing a detailed clinical examination, and relevant investigations, the initial wound area was recorded after sharp debridement by measuring length x width (ulcer should be <10 cm × 10 cm). Photographs of the ulcers before and after the dressings were taken, along with culture and sensitivity of the ulcers before and after the dressings. Both groups were subjected to once daily dressings. Study patients were randomly divided by chit method pre-operatively (before debridement). From total 60 patients of chronic skin ulcers, 30 patients underwent treatment with topical mupirocin 2% in water-soluble ointment base (group M) while other 30 patients underwent treatment as topical mupirocin 2% with sucralfate 7% w/w in water-soluble ointment base (group MS). Topical application done twice daily basis for 6 weeks in both groups. The outcome was reduction in area of the target ulcer, area was measured by planimetry using a transparent graph-sheet. All data was collected in Microsoft excel sheet and analysed with help of SPSS 20. Results were calculated using Student's test. p value less than 0.05 was considered as statistically significant.

RESULTS

In present study 60 patients were randomly divided to group M (n=30) and group MS (n=30). General characteristics such as age, gender , ulcer duration, ulcer (Wagner) grading, Co-morbidities (diabetes mellitus, hypertension, ischemic heart diseases and BMI > 30 kg/m^2) were comparable in both groups and difference was not statistically significant.

Table 1: General characteristics

Parameter	Group M (n=30)	Group MS (n=30)	p value
Age (years)	51.8 ± 12.54	49.31 ± 11.25	0.634
Gender distribution,			
Male	18 (60%)	17 (56.67%)	0.546
Female	12 (40%)	13 (43.33%)	
Ulcer duration (months)	3.91 ± 1.22	3.4 ± 1.82	
Ulcer (Wagner) grading			
Grade 1	20 (66.67%)	18 (60%)	0.657
Grade 2	10 (33.33%)	12 (40%)	
Co-morbidities			
Diabetes Mellitus	12 (40%)	13 (43.33%)	0.711
Hypertension	7 (23.33%)	9 (30%)	
Ischemic Heart Diseases	3 (10%)	3 (10%)	
BMI > 30 kg/m^2	3 (10%)	2 (6.67%)	

In present study etiologically most of the ulcers were diabetic and traumatic ulcer. Less common types were venous ulcer, arterial ulcer and infective ulcer.

Table 2: Distribution of ulcer type among study population

Ulcer Type	Group M (n=30)	Group MS (n=30)
Diabetic Ulcer	12 (40%)	13 (43.33%)
Traumatic Ulcer	11 (36.67%)	10 (33.33%)
Venous Ulcer	4 (13.33%)	5 (16.67%)
Arterial Ulcer	1 (3.33%)	1 (3.33%)
Infective Ulcer	2 (6.67%)	1 (3.33%)

At baseline there was no statistically significant difference noted between two groups (p=0.58). At 3 weeks and at 6 weeks significant reduction was noted in group MS as compared to group M and difference was significant statistically. 3 (10 %) ulcers from both groups remained unhealed. No other complications were noted in present study.

Table 3: Comparison of ulcer size

Ulcer size	Group M (n=30)	Group MS (n=30)	p value
At baseline (cm^2)	9.32 ± 2.65	9. 66 ± 3.12	0.58
Size at 3 weeks (cm^2)	5.67 ± 2.23	4.75 ± 2.01	0.043
Size at 6 weeks (cm^2)	3.39 ± 2.44	2.16 ± 1.27	0.031

DISCUSSION

The incidence of ulceration is rising as a result of the ageing population and increased risk factors for atherosclerotic occlusion such as smoking, obesity, and diabetes. It is broadly accepted now that ulcers should be debrided of necrotic and fibrous tissue to allow formation of granulation tissue, adequate epithelialization, and to decrease the chance of infection.[4,5] Despite the development of modern diagnostic tools and remarkable therapeutic improvement, many CLUs do not heal satisfactorily in an outpatient clinic within a certain time period.[6] Risk factors for development of venous ulcers include older age, female sex, obesity, trauma, immobility, congenital absence of veins, deep vein thrombosis (DVT), phlebitis, and factor V Leiden mutation.[7] The study from India shows that etiology of chronic wounds included systemic conditions such as diabetes, atherosclerosis, tuberculosis, and leprosy. Other major causes included venous ulcers, pressure ulcers, vasculitis, and trauma.[8] The study report stated that inappropriate treatment of acute traumatic wounds was the most common cause of the chronic wound.[8] An ideal management plan for patients with lower limb ulcers should involve an early strategic and coordinated approach to deliver the correct treatment option for each individual patient, based on accurate assessment of the underlying pathophysiology. [9] Mupirocin is available as 2% ointment or 2% cream in mineral oil, is bactericidal at concentrations achieved in topical formulations. It acts by inhibiting bacterial isoleucyl t-RNA synthetase, thereby hindering bacterial RNA, protein and cell wall synthesis. Topical absorption and metabolism is minimal. Mupirocin may be less effective on weeping wounds because 95% of the drug is protein bound. [10] Sucralfate is the aluminum hydroxide salt of the disaccharide sucrose octasulfate. For more than 3 decades, sucralfate has been used as a cytoprotective agent for treatment of gastrointestinal ulcer diseases. This drug has antimicrobial and antioxidant activity, stimulates the secretion of prostaglandin E2 (PGE2) and subsequent increased blood flow and mucus formation, and enhances the production of epidermal growth factor, which can lead to increased angiogenesis.[11] Topical preparations of sucralfate with concentrations of 7%–20% have been used to promote wound healing in various ulcerative conditions such as erythematous radiation skin reactions, oral mucositis, chronic venous ulcers, second and third degree burns, diaper dermatitis, anal fistulotomy wounds, and hemorrhoidectomy wounds.[12,13] Sucralfate induces the proliferation of dermal fibroblasts and keratinocytes in vitro and inhibits the release of interleukin-2 and interferon-g from damaged skin cells.[12]

Topical Sucralfate significantly increases the wound healing by formation of granulation tissue, reducing the slough, discharge and bacterial load ultimately causing wound contraction and healing. In this study sucralfate dressing was found to be more efficacious over conventional dressing as the average number of days taken for healing was 2.4 weeks in sucralfate group while in conventional group it was 3.9 weeks.[14] In a study by Chatterjee S *et al.*,[15] The median ulcer area was significantly reduced in the combined treatment group at the end of treatment. Clinically, 41.3% of the participants in the combined group showed complete ulcer healing at 6 weeks compared to 18.18% in the mupirocin alone group (P = 0.022). The wound infection score declined significantly from baseline by the end of 3 weeks of treatment in both the groups. The frequency of qualitative wound attributes, namely pain, discharge, and erythema, remained comparable between the groups except for discharge which disappeared completely from all remaining ulcers in the combined group but was still present in 11.36% of the participants treated with mupirocin alone (P = 0.025) at 6 weeks. They concluded that wound healing effect of topical sucralfate adds to the antimicrobial effect of mupirocin toward the overall improvement of chronic skin ulcers. Similar findings were observed in present study. Successful wound dressing should keep the wound moist and be devoid of any adverse reactions such as infection, maceration, and allergy.[16] Major limitations of present study were small sample, single institution, short follow up study, large scale study can better guide us regarding treatment of chronic ulcers.

CONCLUSION

An ideal dressing is every surgeon's desire, a dressing that promotes chronic ulcer healing without any complications. Use of topical 7% sucralfate in addition to topical 2% mupirocin can heal chronic wounds better and earlier as compared to topical 2% mupirocin alone.

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