Oncology
and Radiotherapy©
18(6) 2024: 001-008 • RESEARCH ARTICLE

A comparative study of topical combinations with infrared radiation on non-healing ulcers

Srinivasa B[1], Devika P Jeeragyal[2], M.L.RamyaKrishna[3], J.Anandh Raj[3], S Vaheedha[3], Sai Bhargavi E [4], Gopireddy Likitha[4], K Bhavya Sai Sreeja[5]

[1] Pharmacology Department, Apollo Institute of Medical Sciences and Research Chittoor, India
[2] Community Medicine Department, Apollo Institute of Medical Sciences and Research Chittoor, India
[3] Apollo College of Physiotherapy Chittoor, India
[4] Department of Physiotherapy, School of Paramedical Allied and health care sciences, Mohanbabu University, Tirupati, India
[5] Apollo Institute of Medical Sciences and Research Chittoor, India

ABSTRACT

Background: Various treatment modalities of non-healing ulcers in current setup include topical and systemic antibiotics, surgical debridement, skin grafting, compression stockings, and various types of dressings. The current study evaluates the synergistic effect of topical mupirocin, when used in combination with topical framycetin, placental extract gel and infrared radiation for treating non healing ulcers.

Materials & Methods: Using Chit methods 2 groups were divided. Group "M" was treated by topical 2% mupirocin ointment dressing along with infrared radiation and Group "MFP" by topical combination of 2% mupirocin along with infrared radiation& 1% framycetin ointment with 0.1 g placental extract gel dressing on prospective basis in surgery OPD. Recording of data regarding relevant patient details like date of diagnosis of non-healing ulcer, treatment details and their regular follow up was done for 2 months in preformed data sheet on regular basis. After undergoing a detailed clinical examination, relevant investigations were recorded before and after follow up at 4th week and 8th week. The wound debrided was measured in length x width by digital planimetry. Photographs of ulcers before and after topical treatment dressings were taken. Culture and sensitivity of the ulcers were done for infective ulcers at regular visits of patients.

Results: The important findings like socio-demographic values, number & percentage of reduction in ulcer area of both groups M and MFP noted in the study were expressed efficiently in tables and graphs. For normal data Statistical analysis was done by student's "T" test and for data not following normal, Man Whitney U – test was applied to evaluate the significance of best treatment group over the other group. Reduction in ulcer size at 8th week in group M was 60.17 ± 23.25 and reduction in ulcer size at 8th week in group MFP was 89.8 ± 12.57. There was statistical significance between 2 groups (P value<0.001*, Z value: 4.809). Reduction in ulcer size at 4th week in group M was 31.33 ± 17.17 and reduction in ulcer size at 4th week in group MFP was 49.77 ± 10.62. There was statistical significance between 2 groups (P value<0.001*, Z value: 3.947).

Conclusion: This study concludes that topical combination of mupirocin, framycetin with placental extract gel and infra-red radiation is more effective in treating chronic wounds and non-healing ulcer very rapidly when compared to other modalities of topical treatment which are already present in healthcare. It also gives a great idea or tool for exploration of future novel topical antibiotic combinations to be used in non-healing ulcers especially of infective origin.

Keywords: mupirocin, framycetin, placental extract gel, infrared radiation, non-healing ulcer, topical combination, non-healing wounds

Address for correspondence:
Srinivasa B, Pharmacology Department, Apollo Institute of Medical Sciences and Research Chittoor, India

E-mail: snsrinivasan93@gmail.com

Word count: 4115 **Tables:** 08 **Figures:** 06 **References:** 28

Received: 17 April, 2024, Manuscript No. OAR-24-132437

Editor Assigned: 20 April, 2024, Pre-QC No. OAR-24-132437(PQ)

Reviewed: 03 May, 2024, QC No. OAR-24-132437(Q)

Revised: 10 May, 2024, Manuscript No. OAR-24-132437(R)

Published: 15 May, 2024, Invoice No. J-132437

INTRODUCTION

It is estimated that 1% to 2% of the population in developed countries will suffer from a chronic wound in their lifetime [1]. Ulcers can be defined as wounds with a "full thickness depth" and a "slow healing tendency". 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 associate with pain, impaired sleep, restricted mobility and social activities, high cost of healthcare, loss of productivity, and reduced quality of life. Non healing wounds pose a very big challenge for the treating physician and huge economic burden for the patients. Various treatment modalities of non-healing 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 products. Mupirocin stimulates the production of Tumor Necrosis Factor (TNF)-α in RAW 264.7 cells. TNF-α is a critical cytokine involved in the inflammatory stage of wound healing [3]. Mupirocin plays a significant role in wound healing by increasing proliferation of human keratinocytes and enhancing the production of several growth factors [4]. Conventional treatments include local antiseptic agents and antibiotics. Antiseptic agents include hydrogen peroxide, chlorhexidine, triclosan, iodophors (povidon iodine). Antibiotics include aminoglycosides (viz., Framycetin, Neomycin, etc.) and Polymyxin B, Bacitracin, etc. [5]. Placental extract is well known for its effects on wound healing with anti-inflammatory, antiplatelet, and angiogenic effects and is also a biogenic modulator [6]. Human placental extract activates a wide array of gene expressions related to skin functions [7]. Though there are various alternative topical therapies available for treating non-healing ulcers of various causes, none of them have high potential to completely cure the ulcer and overcome the anti-bacterial resistance when they are used in monotherapy. This scope for discovery of novel topical anti-bacterial combinations motivated us to do the study which could be of great value in treating non-healing ulcers of various causes more importantly infective cause, in a most effective way. Despite the development of modern diagnostic tools and remarkable therapeutic improvement, many chronic leg ulcers do not heal satisfactorily in an outpatient clinic within a certain time period [8].

Topical antibiotics such as mupirocin, fusidic acid, neomycin, gentamicin, bacitracin and polymyxin B combination, and metronidazole are widely used for superficial skin ulceration with inflammation. Faced with increasing bacterial resistance to antimicrobials, prescribing guidelines now indicate that antibacterial formulations should not be used for bacterial colonization alone but only in cases of clinically evident infection [9].

Among various biological agents currently applied topically to chronic wounds, human amniotic membrane has been considered safe and effective as it promotes angiogenesis in chronic wounds, reduces pain at the local site and promotes rapid epithelialization [10-12].

Placentalextract gel and cream are both effective topical agents for chronic non-healing wounds [13]. Mupirocin (Bactroban, Beecham Laboratories) is currently formulated as a 2% ointment in a water-miscible polyethylene glycol base. The drug is a unique antimicrobial agent because of its structure and mechanism of action. Mupirocin apparently exerts its antimicrobial activity by reversibly inhibiting isoleucyl-transfer RNA, thereby inhibiting bacterial protein and RNA synthesis. Mupirocin has excellent in vitro activity against *staphylococci* and most *streptococci* but less activity against other gram-positive and gram-negative bacteria. The drug will only be used topically because of its rapid and extensive systemic metabolism. Several controlled clinical trials documented that mupirocin was significantly better than the polyethylene glycol vehicle alone or *ampicillin* and as effective as cloxacillin, dicloxacillin, or erythromycin in producing clinical and bacteriological cures in patients with impetigo and wound infections caused by gram-positive pathogens [14].

Infrared radiation therapy is beneficial in improving wound healing in pressure ulcer. The infrared energy for 30 minutes every session, application was done 5 times per week for 6 weeks as a total period of treatment in addition to their medical treatment, the control group who not received the monochromatic infrared energy but they just received standard medical treatment [15]. Infrared radiation therapy plus conventional dressing on diabetic foot ulcers grade 1 and 2, accelerates the ulcer healing, improves granulation tissue formation and diminishes wound exudation and inflammation [16].

The randomized controlled trial data on the effectiveness and safety of topical antimicrobial treatments for diabetic foot ulcers is limited by the availability of relatively few, mostly small, and often poorly designed trials. Based on our systematic review and analysis of the literature, we suggest that: 1) use of an antimicrobial dressing instead of a non-antimicrobial dressing may increase the number of diabetic foot ulcers healed over a medium-term follow-up period (low-certainty evidence); and 2) there is probably little difference in the risk of adverse events related to treatment between systemic antibiotics and topical antimicrobial treatments based on the available studies (moderate-certainty evidence) [17].

The main objective of this study is to compare the effect of topical combination of mupirocin, infrared radiation and framycetin ointment with placental extract gel on non-healing ulcers vs topical mupirocin and infrared radiation in tertiary care hospital.

MATERIALS AND METHODS

This nonrandomized interventional clinical research was conducted in department of General Surgery, AIMSR; Chittoor by abiding ICH-GCP guidelines [18]. Study duration was of 2 months done between August and October 2023. Patients with non-healing ulcer for more than 4 weeks were considered for this study.

Institutional ethical committee approval was taken (No.UG/06/IEC/AIMSR/2023).

Informed consent was taken prior the study from all patients in both groups by explaining the complete study procedure, advantages and complications in their own understandable language and documented [19-22].

Inclusion criteria

Patients of age more than 18 years of either sex, duration of the ulcer more than 1 month, the size of ulcer more than or equal to 2 cm^2 were taken.

Exclusion criteria

Not willing for participation, pulseless limb, maggots in limbs, immunocompromised patients, sepsis, Pregnancy, Skin malignancies, Diabetic ketoacidosis, Exposed bones, tendon, and Charcot joint.

After obtaining informed consent from all study participants in their own understandable language, Using Chit methods groups were divided. Total number of patients included in study were 60. Sample size was choosen based on sample size taken from similar studies and also consideration of prevalence of non-healing ulcers in current study area was given during sample size estimation. Group "M" was treated by topical 2% mupirocin ointment dressing along with infrared radiation and lamp was placed at a distance of 90 cm and 45° angulation from ulcer for 30 minutes and Group "MFP" by topical combination of 2% mupirocin, infrared radiation and lamp was placed at a distance of 90 cm and 45° angulation from ulcer for 30 minutes and 1% framycetin ointment with 0.1 g placental extract gel dressing on prospective basis in surgery OPD. Total no of patients studied in group M were 30 and total no of patients studied in group MFP were 30. Recording of data regarding relevant patient details like date of diagnosis of non-healing ulcer, treatment details and their regular follow up was done for 2 months in preformed data sheet on regular basis. After undergoing a detailed clinical examination, relevant investigations, initial wound was recorded after sharp debridement by measuring length x width by digital planimetry. Photographs of the ulcers before and after the topical treatment dressings were taken, along with culture and sensitivity of the ulcers before and after topical treatment dressings. Topical application of drugs mentioned above were done in both groups twice daily basis for 8^{th} weeks.

The outcome was reduction in area of the target ulcer and the same was measured at 4^{th} week & 8^{th} week by digital planimetry and a transparent graph-sheet. Data was collected in Microsoft excel sheet and analyzed with help of SPSS 20. Results was calculated using Student's test. P value less than 0.05 was considered as statistically significant.

RESULTS

In the current study, 60 patients following inclusion and exclusion criteria were randomly divided into 2 groups n=30 in each group (Group M & Group MFP). As shown in the table 1 and figure 1, general characteristics like age and gender were comparable in both groups and the difference was not statistically significant.

Tab. 1. Age distribution

Age Distribution					
Characteristic	**Mean ± SD**	**Median**	**IQR**	**Z statistic**	**P value**
Group M-Age	48.33 ± 9.94	48	18.5	0.03	0.976
Group MFP-Age	48.67 ± 11.38	47	20.5		

Fig. 1. Gender distribution

As shown in the table 2, non-healing ulcer duration (in weeks) of group M did not vary much while group MFP did very much. The common non-healing ulcer duration in group MFP was found to be 6 weeks and 12 weeks while in group M, it was found to be 6 weeks.

Tab. 2. Non-healing ulcer duration in weeks

Weeks	No of patients in Group M	Percentage (%)	No of patients in Group MFP	Percentage (%)
5	-	-	1	3.3
6	6	20	8	26.7
7	1	3.3		
8	3	10	2	6.7
9	3	10	3	10
10	3	10	3	6.7
11	3	10	3	10
12	3	10	7	23.3
14	3	10	3	10
18	3	10	1	3.3
19	1	3.3	-	-
24	1	3.3	-	-
Total	30	100	30	100

As shown in table 3 and figure 2, most of the non-healing ulcers in both the groups were found to be of grade 1. There was no statistical significance in other grades (2,3,4) between 2 groups (P value: 0.719 and Chi Square value: 1.344).

Tab. 3. Wagner's ulcer grading

	Group M (%)	Group MFP (%)	Chi square	P Value
Grade 1	20 (66.7)	16 (53.3)	1.344	0.719
Grade 2	4 (13.3)	6 (20)		
Grade 3	3 (10)	5 (16.7)		
Grade 4	3 (10)	3 (10)		

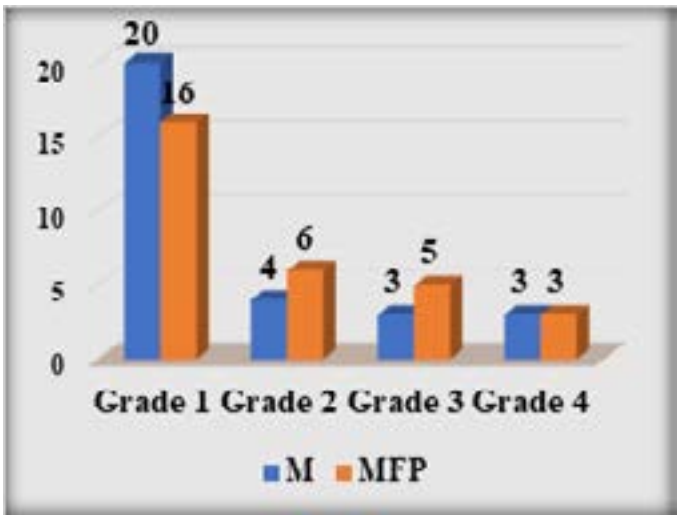

Fig. 2. Graphical representation of Wagner's Ulcer Grading

As shown in table 4 and figure 3, common co-morbidity associated with non-healing ulcer in both the groups (Group M: 60%, Group MFP: 56.7%) is diabetes with obesity following the next common co-morbidity associated with non-healing ulcers in both groups (23.3%).

Tab. 4. Co-morbidities

	Group M (%)	Group MFP (%)	Chi square	P Value
Diabetes	18 (60)	17 (56.7)	0.362	0.948
Hypertension	4 (13.3)	4 (13.3)		
IHD	1 (3.3)	2 (6.7)		
Obesity	7 (23.3)	7 (23.3)		
Total	30 (100)	30 (100)		

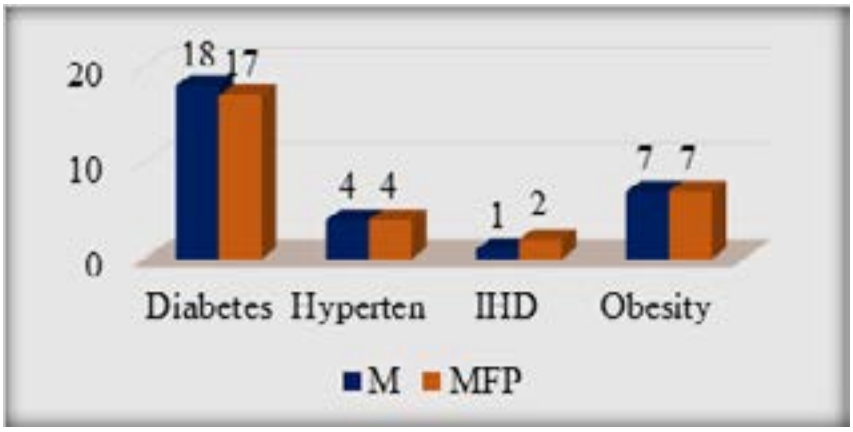

Fig. 3. Graphical representation of co-morbidities

As shown in table 5 and figure 4, most common etiological type associated with non-healing ulcer in both the groups (Group M: 60%, Group MFP: 60%) is diabetic ulcer. There was no statistical significance between 2 groups (P value: 0.219 and Chi Square value: 5.749).

Tab. 5. Etiological type of non-healing ulcer

	Group M (%)	Group MFP (%)	Chi square	P Value
Arterial	2 (6.7)	1 (3.3)	5.749	0.219
Diabetic	18 (60)	18 (60)		
Infective	3 (10)	0 (0)		
Traumatic	3 (10)	8 (26.7)		
Venous	4 (13.3)	3 (10)		
Total	30 (100)	30 (100)		

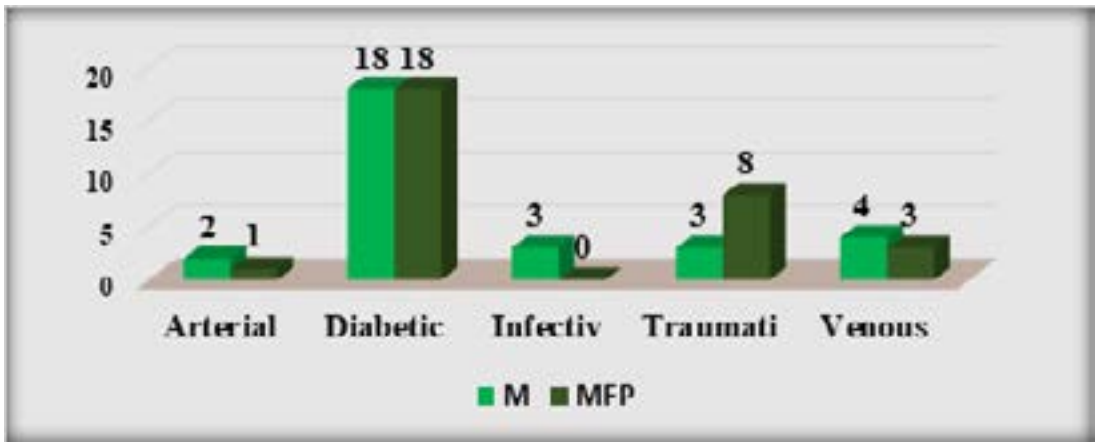

Fig. 4. Etiological type of non-healing ulcer

As shown in table 6, most common ulcer size range (in cm^2) in both groups was from 2 cm^2-3.9 cm^2. There was no statistical significance between 2 groups (P value: 0.67 and Chi Square value: 0.503).

Tab. 6. Ulcer size differentiation between group m and group MFP at baseline

Ulcer size at baseline	Group M (%)	Group MFP (%)
2 cm^2-3.9 cm^2	14 (46.67)	17 (56.67)
4 cm^2-5.9 cm^2	12 (40)	7 (23.33)
6 cm^2-7.9 cm^2	0	3 (10)
8 cm^2- 12 cm^2	4 (13.33)	3 (10)

As shown in table 7 and figure 5 and 6, ulcer size in group M at 4th week was 3.06 ± 1.81 and ulcer size in group MFP at 4th week was 2.08 ± 1. 24. There was statistical significance between 2 groups (P value: 0.006*, Z value: 2.727). As shown in table 7, ulcer size in group M at 8th week was 1.68 ± 1.21 and ulcer size in group MFP at 8th week was 0.52 ± 0.81. There was statistical significance between 2 groups (P value<0.001*, Z value:4.201).
As the data was not normal, non-parametric test Mann Whitney 'U' test has been applied to find the difference between median values of percentage reduction in ulcer size at 4th week as well as 8th week in both the groups. There is a significant difference between the median values.

Tab. 7. Comparison of ulcer size of both groups at different time intervals

	Mean ± SD	Median	IQR	Z statistic	P value
Group M-Ulcer size at baseline in cm^2	4.48 ± 2.59	4	1.52	0.67	0.503
Group MFP-Ulcer size at baseline in cm^2	4.09 ± 1.95	3.5	1.67		
Group M-Ulcer size at 4th week in cm^2	3.06 ± 1.81	2	2.1	2.727	0.006*
Group MFP-Ulcer size at 4th week in cm^2	2.08 ± 1.24	1.8	0.55		
Group M-Ulcer size at 8th week in cm^2	1.68 ± 1.21	1.1	2.1	4.201	< 0.001*
Group MFP-Ulcer size at 8th week in cm^2	0.52 ± 0.81	0.1	0.85		

There is a significant difference between median values of ulcer size at 4th week in both the groups. There is a significant difference between median values of ulcer size at 8th week in both the groups. In other variables, there is no difference.

Fig. 5. Ulcer size at 4th week in cm^2

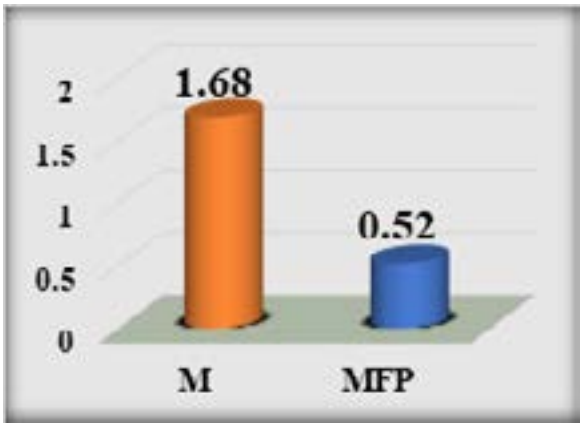

Fig. 6. Ulcer size at 8th week in sq cm

As shown in table 8, reduction in ulcer size at 4th week in group M was 31.33 ± 17.17 and reduction in ulcer size at 4th week in group MFP was 49.77 ± 10.62. There was statistical significance between 2 groups (P value <0.001*, Z value: 3.947).

As shown in table 8, reduction in ulcer size at 8th week in group M was 60.17 ± 23.25 and reduction in ulcer size at 8th week in group MFP was 89.8 ± 12.57. There was statistical significance between 2 groups (P value <0.001*, Z value: 4.809).

Tab. 8. Percentage reduction in ulcer size at various time intervals

	Mean ± SD	Median	IQR	Z statistic	P value
Group M -% Reduction in ulcer size at 4th week	31.33 ± 17.17	33	27	3.947	<0.001
Group MFP-% Reduction in ulcer size at 4th week	49.77 ± 10.62	53	17		
Group M-% Reduction in ulcer size at 8th week	60.17 ± 23.25	63.5	36	4.809	<0.001
Group MFP-% Reduction in ulcer size at 8th week	89.8 ± 12.57	96	17		

DISCUSSION

As evident from the above findings, there is highly significant difference between groups in reducing the ulcer size at 4th week as well as 8th week, where non-healing ulcers treated with topical mupirocin plus framycetin plus placental extract have healed almost completely at around 8th week of follow-up with median value of 96 in table 8. These findings clearly state that topical combination have significant edge in treating non-healing ulcer effectively over using topical monotherapy. The reason could be due to presence of different mechanisms of each drug in combination act synergistically which may inturn provide broad anti-bacterial spectrum, thereby providing best anti-bacterial cover for wound healing as well as completely destroying the already present organisms in the wound. Though the patients with non-healing ulcer in group M were treated with topical mupirocin and infrared radiation, they also recovered at around 8th week near completely but not more than in group MFP (% Reduction in ulcer size at 8th week in group M – approx 63.5% compared to approx 96% in group MFP). During the course of the study, it was found out there were no adverse effects with any of the topical drugs used and even there were nil drug–drug interactions with any systemically used concomitant drugs in both the groups. In a study done by Patil K S et.al, comparison was done for 7% topical sucralfate plus 2% mupirocin to 2% mupirocin alone in which case also the combination was effective than topical mupirocin alone. Furthermore, when we compared to same study, the present study had most favourable results and still more quite effective in treating resistant non-healing ulcers of various etiologies.

In a similar study done by Pote MP et al, for comparative evaluation of povidone iodine ointment and placentrex gel as topical agents in superficial burns inflicted non-healing wounds, it was found that patients treated with placentrex gel, wounds healed significantly than those with povidone – iodine ointment. The findings in the study are comparable with the present study findings.

In another study done by subramanium et al, it was observed that in indolent ulcers – placentrex gel dressing seems to free the lesion from infection and then produces adequate granulation tissue formation and healing enough to facilitate, if necessary, skin grafting [23, 24].

The findings of above study also justify the use of placentrex gel in our study. The effectiveness of mupirocin in combination with various topical antibiotics have been assessed in comparison with placebo and monotherapy in various studies [25-28].

The added advantage of using framycetin, topical aminoglycoside in the combination is significant which could be due to providing of antibacterial cover to gram –ve organisms while mupirocin will be covering gram +ve spectrum. Topical absorption and metabolism of mupirocin is minimal. Mupirocin may be less effective on weeping wounds because 95% of the drug is protein bound. Mupirocin resistance encountered in strains of Methicillin Resistance *Staphylococcus* Aureus (MRSA) and Methicillin Resistance *Staphylococcus Epidermidis* (MRSE) and prior exposure is a strong predictor of resistance.

But once the resistance is assessed with better clinical judgement and culture sensitivity, it is better advisable for early change over topical mupirocin to effective one.

Strengths of study

This treatment modality of combining topical and infrared radiation is a very new approach in treating non-healing ulcers effectively. The combination of topical mupirocin plus infrared radiation plus framycetin plus placental extract gel had significant impact on resistant non-healing ulcers which were refractory to other topical antibiotics. The study signifies that non-healing ulcers were recovering in very small time period. The current study also signifies there were nil adverse effects with better patient compliance for topical medicines along with regular wound dressing.

Limitation of study

Small sample size was included due to logistics problem, single centre study and short follow up. There were few extreme values in the results which could be due to inadequate sample size, there by affecting standard deviation, but it is noteworthy to mention that median values and IQR (Inter Quartile Range) values calculated in results are enough able to substantiate the findings.

CONCLUSIONS

Topical combination of mupirocin, framycetin with placental extract gel and Infra-red radiation was more effective in treating chronic wounds and non-healing ulcer very rapidly when compared to other modalities of topical treatment which are already present in healthcare. It is also important to note here that the current study also indicates the above treatment modality combining topical plus infrared radiation could eliminate the potential of non-healing ulcers conversion to skin carcinogenicity. Once the above said limitations will be countered in near future, the study done could be a major tool for successive studies and a better guide for surgeons to treat non-healing ulcer more effectively and faster.

CONFLICT OF INTEREST

Nil

SOURCES OF FUNDING

None declared

IEC PERMISSION

Approval taken (No.UG/06/IEC/AIMSR/2023).

REFERENCES

1. Jarbrink K, Ni G, Sönnergren H, Schmidtchen A, Pang C, et al. Prevalence and incidence of chronic wounds and related complications: a protocol for a systematic review. Syst rev. 2016;5:1-6.
2. Patil KS, Muglikar A. Comparative study of topical mupirocin versus mupirocin with sucralfate combination in treatment of chronic skin ulcers. MedPulse Int J Pharmacol. 2019;12:28-31.
3. Kamlungmak S, Nakpheng T, Kaewpaiboon S, Bintang MA, Prom-In S, et al. Safety and biocompatibility of mupirocin nanoparticle-loaded hydrogel on burn wound in rat model. Biol Pharm Bull. 2021; 44:1707-1716.
4. Twilley D, Reva O, Meyer D, Lall N. Mupirocin promotes wound healing by stimulating growth factor production and proliferation of human keratinocytes. Front Pharmacol. 2022;13:862112.
5. Nipanikar SU, Gajare KV, Vaidya VG, Kamthe AB, Upasani SA, et al. An open label, randomized, comparative, parallel group, multicenter, prospective, interventional, clinical study to evaluate efficacy and safety of "AHPL/AYTOP/0113" in comparison with "Framycetin sulphate cream" in acute wounds. Anc Sci Life. 2017;36:117-128.
6. Thakur G, Thomas S, Bhargava D, Pandey A. Does topical application of placental extract gel on postoperative fibrotomy wound improve mouth opening and wound healing in patients with oral submucous fibrosis?. J Oral Maxillofac Surg. 2015;73:1439-1441.
7. Chang PY, Chin LC, Kimura K, Nakahata Y. Human placental extract activates a wide array of gene expressions related to skin functions. Sci Rep. 2022;12:11031.
8. Bradley M, Cullum N, Nelson EA, Petticrew M, Sheldon T, et al. Systematic reviews of wound care management:(2) dressings and topical agents used in the healing of chronic wounds. 1999.
9. Chatterjee S, Sen S, Hazra A, Das AK. Randomized controlled trial of topical mupirocin versus mupirocin with sucralfate combination in chronic skin ulcers. Indian J Pharmacol. 2019;51:316-322.
10. Ramakrishnan KM, Jayaraman V. Management of partial-thickness burn wounds by amniotic membrane: a cost-effective treatment in developing countries. Burns. 1997;23:33-36.
11. Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. Bmj. 1997;315:576-580.
12. Somerville PG. The possible use of amniotic membrane in chronic leg ulcers. Phlebologie. 1982;35:223-229.
13. Tiwary SK, Shukla D, Tripathi AK, Agrawal S, Singh MK, et al. Effect of placental-extract gel and cream on non-healing wounds. J wound care. 2006;15:325-328.
14. Parenti MA, Hatfield SM, Leyden JJ. Mupirocin: a topical antibiotic with a unique structure and mechanism of action. Clin Pharm.1987;6:761-770.
15. Noseir Aa, Ahmed Me, Asmaa Ef, Mahmoud Ah. Efficacy of Monochromatic Infrared Energy on Pressure Ulcer Healing. Med J Cairo Univ. 2019;87:2403-2407.
16. Saad AY, Desoky GM. Effect of Infrared Radiation on Healing of Diabetic Foot Ulcer. Alex Sci Nurs J. 2017;19:69-86.
17. Dumville JC, Lipsky BA, Hoey C, Cruciani M, Fiscon M, et al. Topical antimicrobial agents for treating foot ulcers in people with diabetes. Cochrane Database Syst Rev. 2017.
18. Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. Physiol Rev. 2003;83:835-870.
19. https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf
20. Pote MP. Comparative evaluation of povidone-iodine ointment and human placental extract as topical agent for treatment in superficial burn. Ind Med Gaz Dev Mod Med Surg. 2004;7:351-354.
21. Subramanian T, Vijayarathinam P, Sathyavan V, Navaneethakrishnan S, Anugraham S, et al. Effects of placental dressing indolent ulcers. J Indian Med Assoc. 1990;88:314-316.
22. Gilbert M. Topical 2% mupirocin versus 2% fusidic acid ointment in the treatment of primary and secondary skin infections. J Am Acad Dermatol. 1989;20:1083-1087.
23. Morley PA, Munot LD. A comparison of sodium fusidate ointment and mupirocin ointment in superficial skin sepsis. Curr Med Res Opin. 1988;11:142-148.
24. White DG, Collins PO, Rowsell RB. Topical antibiotics in the treatment of superficial skin infections in general practice—a comparison of mupirocin with sodium fusidate. J Infect. 1989;18:221-229.
25. Koning S, van der Wouden JC. Treatment for impetigo. Bmj. 2004;329:695-696.
26. Velappan R, Ramasamy S, Venu S, Chandrasekar M.A randomised open label comparative study evaluating the effectiveness, adherence and safety between 2% mupirocin ointment and 2% fusidic acid cream in children with impetigo. Int J Res Dermatol 2019;5:511-516.
27. Bork K, Brauers J, Kresken M. Efficacy and safety of 2% mupirocin ointment in the treatment of primary and secondary skin infections--an open multicentre trial. Br J Clin Pract. 1989;43:284-288.
28. Parenti MA, Hatfield SM, Leyden JJ. Mupirocin: a topical antibiotic with a unique structure and mechanism of action. Clin Pharm. 1987;6:761-770.