

# To Assess Wound Healing of Lower Limb Ulcers in Patients Treated with Local Application of Collagen Particles with Mupirocin and Metronidazole Powder Dressing

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**Abstract:** An ulcer is defined as a breach in the continuity of epithelium or mucosa characterized by destruction of the surface epithelium and a granulating base. Lower limb ulcers are most commonly due to neuropathic, venous, or arterial causes. Most commonly in India, the lower limb ulcers are due to a venous pathology whereas in Karnataka the most common cause of lower limb ulcers was found to be diabetes mellitus. Various factors affect wound healing which include immunosuppression, co - morbidities, presence of foreign body, lack of hygiene, lack of knowledge, delayed hospital visits, infection, etc. Chronicity of wounds occurs due to persistence of infection. Hence treatment for such ulcers focuses on treatment of infection with antibiotics. This study aims to assess use of local application of collagen particles with mupirocin and metronidazole powder over the ulcers for wound healing and thus to assess the decrease in pus culture reports post - treatment with collagen particles with mupirocin and metronidazole. There is a need to explore the different moralities available for the treatment of diabetic foot, as it is the leading cause of lower limb ulcers in the locality. It not only affects the individual but the family associated too. Chronicity leads to financial burden, psychological problems and dependency. Hence treating them earliest aids in improvement in all aspects. **Materials and Methods:** This study is a prospective comparative study that was conducted over 6 months, with 50 patients participating in the study amongst which 25 patients underwent betadine dressing (Group A) and 25 patients underwent collagen particles with mupirocin and metronidazole dressing (Group B). After the patient was selected, the ulcer was scored according to BWAT score (– Bates – Jensen Wound assessment tool) and considered the ulcer's baseline score. Under sterile precautions, the ulcer was cleaned and thorough debridement will be done. Daily such dressings was done and the ulcer healing was assessed on 3<sup>rd</sup>, 5<sup>th</sup>, and 7<sup>th</sup> day using BWAT scoring system. Culture swabs was taken from ulcers site of individuals in groups A and B on day 8. **Results:** The study showed a significant decrease in size of the ulcer, in exudate amount, in peripheral tissue edema and induration in patients treated with Collagen particles with mupirocin and metronidazole dressing compared to ulcers treated with betadine dressing. There was also significant increase in granulation tissue for the ulcers treated with Collagen particles with mupirocin and metronidazole dressing. 52% patients who underwent Collagen particles with mupirocin and metronidazole dressing were found have no growth in the pus culture implying reduction in bacterial load of the ulcer. Also 12 patients (48%) underwent split skin grafting within 1 month of Collagen particles with mupirocin and metronidazole dressing. **Conclusion:** Collagen particles with mupirocin and metronidazole is a cheap local antibiotic which is easily available all over India. Local application of Collagen particles with mupirocin and metronidazole is an easy method of local antibiotic application to treat lower limb ulcers to hasten the process of wound healing and decrease the need for debridement and prepare the ulcers earlier for Split split - thickness skin Grafting.

**Keywords:** Lower limb ulcers, Diabetic foot, chronic non - healing ulcer, BWAT scoring, Collagen particles, Mupirocin, metronidazole

## 1. Introduction

Ulcer is defined as breach in epithelium or mucosa. Prevalence of ulcers is 1 % in the adult population and 3 - 5 % in the population above 65 years of age. <sup>(1)</sup> It has been reported that lower limb ulcers related to venous insufficiency constitutes 70% of cases, arterial disease 10%, ulcer of mixed aetiology 15% and 5% of lower limb ulcers occur due to lesser - known pathophysiological causes. <sup>(1)</sup> In Karnataka, the most common cause of lower limb ulcers has been found to be diabetes mellitus <sup>(2)</sup>. Various factors are involved in healing of an ulcer such as nutrition, co - morbidities, presence of foreign body, location of the ulcer, status of ulcer, etc.

Wound healing is a multistep procedure involving various inflammatory cells, eventually leading to wound contraction in a favourable environment. Appropriate treatment and wound care accelerate the healing process and prevention of infection and chronicity of the wound. Management of ulcer requires a multisystem approach which includes nervous,

vascular, skeletal and immune system. Various techniques for wound dressing have been established till date such as betadine dressings, mupirocin dressing alone, oxum dressings, autolyse dressing, etc. Chronic wounds are always colonized by bacteria and infection can be present with various clinical signs <sup>(2)</sup>. Treatment with topical antibiotics should be considered for wounds which are not healing despite good quality regular dressing and IV antibiotics. Local application of antibiotic help in achieving higher concentration of the antibiotic at the ulcer site for faster action against the bacteria.

Collagen particles with mupirocin and metronidazole is composed of Collagen, Metronidazole, and Mupirocin. Collagen promotes wound healing by laying down a collagen matrix in the wound bed, thus aiding the formation of granulation tissue and epithelialization <sup>(3)</sup>. Metronidazole belongs to the class of drugs called nitroimidazole antimicrobials. It exerts bactericidal in action and inhibits bacterial DNA synthesis and cell growth. Mupirocin is an antibacterial drug. It prevents the synthesis of essential proteins required by bacteria to carry out their vital functions,

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thus preventing bacterial growth. Mupirocin and metronidazole being broad spectral antibiotics helps in reducing the bacterial load of the ulcer and acts against mainly staphylococcus aureus, pseudomonas, gram negative bacteria as well <sup>(3)</sup>. Thus, Collagen particles with mupirocin and metronidazole powder can be used as local application for ulcers to fasten the healing by reducing bacterial load of the ulcer.

## 2. Materials and Methodology

This hospital - based, Prospective comparative study was conducted at Akash Medical College Hospital between October 2023 and March 2024.

(a) **Study Design:** Prospective comparative study

(b) **Study Duration:** Maximum of 6 months.

The sample size - 50

(c) **Study setting and Method of collection of data:**

This shall be a comparative study which shall include 50 individuals based upon the inclusion and exclusion criteria and then divided into 2 groups using the lottery method.

### Subject Eligibility

#### 1) Inclusion Criteria

- Individuals with lower limb ulcers
- Size of the ulcer should be more than 1x1cm
- One or more ulcers without evidence of osteomyelitis
- Post op SSG cases with ulcers between the skin grafting sites.

#### 2) Exclusion Criteria

- Ischemic lower limb ulcers (ankle brachial index less than 0.7)
- Healing lower limb ulcers with culture showing no growth in 48 hours.
- Pregnant females
- Malignant ulcers proven by biopsy
- Known case of liver disease or patient with deranged LFT

### Methodology

After patient have been selected in Group A due consent will be taken and the wound will be examined thoroughly. The ulcer will be scored according to BWAT score and that will

be considered the baseline score of the ulcer. Under sterile precautions the ulcer will be cleaned and thorough debridement will be done. Saline wash will be given and the wound will be dried using a sterile gauze piece. Collagen particles with mupirocin and metronidazole powder will be used for the local application over the ulcer. The dosage will vary according to the surface area of the ulcer. The surface of the ulcer will be completely covered by collagen particles with mupirocin and metronidazole powder and a dry gauze piece will be then placed over it and the ulcer will be then covered in layers and sterile dressing will be done. Daily such dressings will be done and the ulcer healing will be assessed on 3<sup>rd</sup>, 5<sup>th</sup> and 7<sup>th</sup> day using BWAT scoring system. Thorough saline wash will be given before assessment of wound healing. This shall be compared with healing that occurs in ulcers being treated with betadine dressing. Culture swabs will be taken from ulcers site of individuals in group A and B on day 8. The hospital stay duration for the patients in Group A and B will also be compared.

**Study Population and source of data:** Total number of subjects included in the study will be 50 (25 in each group) of any sex, race or age which includes all patients with lower limb ulcers admitted in the Akash hospital surgery wards for management of the lower limb ulcer after fulfilling the inclusion and exclusion criteria will be interviewed to obtain complete clinical details. For patients agreeing for the participation in the study thorough general, physical and systemic examination along with thorough wound examination will be done and valid consent will be taken for the management for the ulcer.

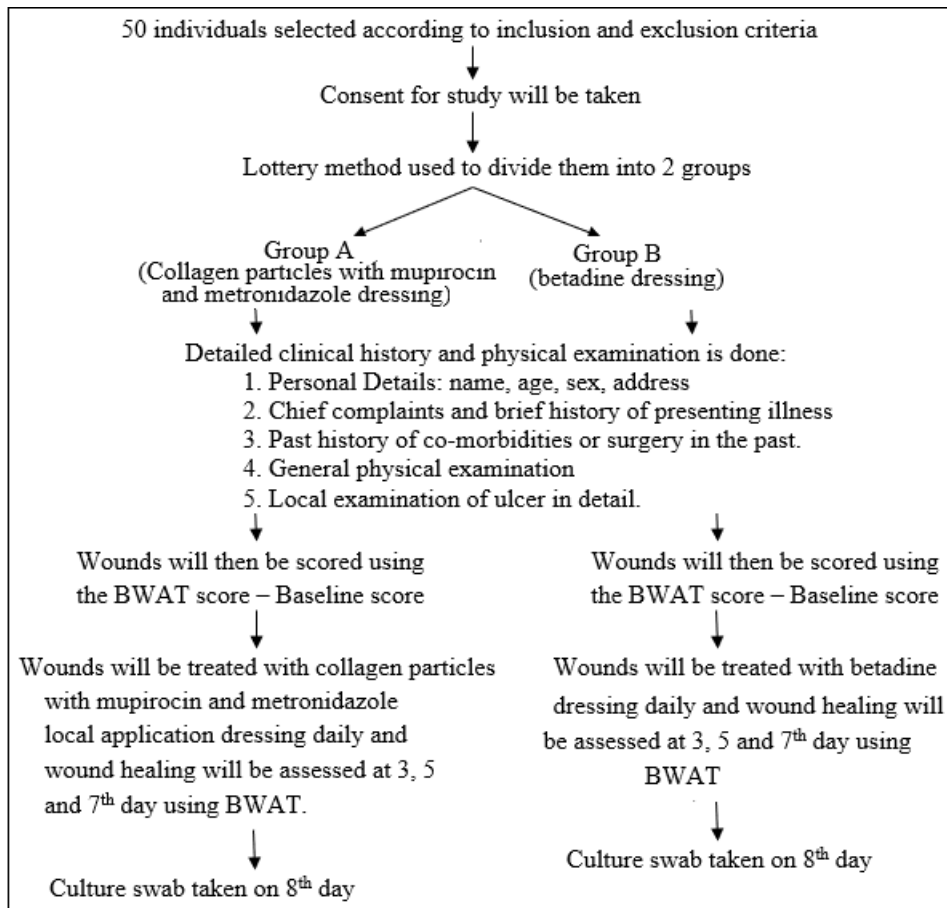
**Study Assessments of end points:** When there is evidence of granulation tissue formation, decrease in the size and depth of the wound, decrease in the amount of exudate, peripheral tissue induration and an increase in epithelisation of the wound as assessed by the BATES - JENSEN WOUND ASSESEMENT TOOL.

A score of 13 according to the BWAT score indicates wound regeneration.

A score of 60 according to the BWAT score indicates wound degeneration.

## 3. Study Conduct

This shall be a Prospective interventional study with Purposive sampling.



4. Observations and Results

	DAY 1				DAY 3				DAY 5				DAY 7			
	Group A		Group B		Group A		Group B		Group A		Group B		Group A		Group B	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Size score	3.1	1.08	2.7	1.08	3.1	1.09	2.7	1.03	3.1	1.05	2.7	1.06	3.04	0.99	2.4	1.1
Depth score	2.7	0.7	2.7	0.6	2.7	0.6	2.7	0.7	2.3	0.6	2.5	0.4	2.1	0.5	2.2	0.3
Edges score	2.5	0.7	2.8	0.5	2.4	0.7	2.8	0.5	2.1	0.5	2.5	0.6	1.7	0.5	2.06	0.5
Undermining score	2.1	1.08	2.2	1.1	2.04	0.9	2.1	1	1.6	0.9	1.9	0.7	1.3	0.7	1.6	0.5
Necrotic tissue type	3.2	0.6	3.08	0.6	3	0.5	2.9	0.6	2.4	0.5	2.7	0.7	1.9	0.7	2.2	0.6
Necrotic tissue amount score	3.1	1.01	3.4	0.7	2.8	0.9	3.2	0.6	2.4	0.7	2.9	0.7	1.9	0.9	2.3	0.6
Type of exudate score	4.02	0.7	3.6	0.8	3.5	0.6	3.4	0.6	2.9	0.6	3.1	0.7	2.4	0.9	2.7	0.7
Exudate amount score	3.4	0.8	3.1	0.6	3	0.6	3.2	0.5	2.6	0.7	2.8	0.6	2.1	0.7	2.4	0.5
Surrounding skin colour score	2.4	0.9	2.6	0.8	2.2	0.8	2.5	0.6	1.9	0.8	2.2	0.7	1.3	0.9	1.8	0.6
Peripheral tissue edema score	2.6	1.06	2.9	0.8	2.5	0.9	2.7	0.7	2.02	0.9	2.4	0.7	1.5	0.8	2.02	0.7
Induration score	2.4	1.1	2.1	0.7	2.2	0.9	2.2	0.6	1.6	0.9	1.9	0.6	1.1	0.8	1.6	0.5
Granulation tissue score	3.7	0.6	4.7	0.6	3.2	0.7	4.2	0.6	2.5	0.6	3.6	0.7	2.2	0.7	3.2	0.6
Epithelialisation score	5	0	5	0	5	0	5	0	4.8	0	5	0.47	4.1	0.3	4.9	1
Total BWAT score	40.22	6.5	40.88	7.7	37.64	5.9	39.6	4.7	32.22	5.4	36.2	4.6	26.64	6.4	31.38	5.04

Pus culture taken of Day 8 report analysis amongst the study group:

		Group		Total
		Group A	Group B	
Alpha hemolytic Streptococci	Count	1	1	2
Beta hemolytic streptococci	Count	0	1	1
E coli	Count	1	1	2
Enterococci	Count	1	1	2
Klebsiella pneumoniae	Count	1	3	4
MRSA	Count	0	1	1

No growth	Count	17	3	20
Proteus mirabilis	Count	1	3	4
Pseudomonas aeruginosa	Count	2	4	6
Staphylococcus aureus	Count	1	5	6
Streptococcus sp.	Count	0	2	2
Total	Count	25	25	50

**Comparison between the 2 groups of patients who required debridement within 3 months:**

			Group		Total
			Group A	Group B	
Debridement required patients	No	Count	22	22	44
	Yes	Count	3	3	6
Total		Count	25	25	50

**Comparison between the 2 groups of patients who underwent SSG within 3 months:**

			Group		Total
			Group A	Group B	
Patients who underwent SSG	Yes	Count	19	13	32
	No	Count	12	24	36
Total		Count	25	25	50

**5. Discussion**

It is estimated that 1 to 2 percent of the population in developed countries will suffer from a chronic wound in their lifetime. The incidence of chronic wounds is expected to increase as our population ages leading to chronic pain, loss of function and mobility, increased social stress and isolation, depression and anxiety, prolonged hospitalization, financial burden, morbidity and mortality<sup>(4)</sup>. Although there is no clear consensus on the duration of a wound that defines chronicity, a range of 4 weeks to 3 months has been used to define chronic wounds.<sup>(5)</sup>

Most commonly the cause of these lower limb ulcers includes diabetes mellitus, varicose veins, peripheral vascular disease and trauma.<sup>(6, 7)</sup> India being diabetes mellitus capital significantly contribute to lower limb ulcers. The main cause of chronicity of ulcers includes persistent infection of the ulcers.<sup>(8, 9, 10)</sup> Due to persistence of infection the ulcers require surgical debridements or amputations. Various methods have been tried for treatment for the same and this study too aims in reducing the bacterial load of the ulcers and thus hasten the wound healing. Local application of antibiotics helps in achieving higher concentration of the antibiotic at the ulcer site for faster action against the bacteria. Various antibiotics like gentamicin, amikacin, neomycin, and Fucidin have been used for local application over ulcers.

In one such cohort study of diabetic foot osteomyelitis, a significantly lower rate of a combined amputation or mortality endpoint was observed in those treated with rifampin (26.9%) was noted.<sup>(11)</sup>

In another study, rifamycin was used locally. Although the difference in rate of superficial sternal wound infection (SSWI) in the rifamycin and control groups was not statistically significant, locally applied rifamycin SV during closure of the sternum in the CABG operation may have had a protective effect against SWI.<sup>(12)</sup>

Another study of topical collagen particles with mupirocin and metronidazole reduce the risk of surgical field infection in hernia repair showed that applying rifampicin locally can decrease surgical field infection.<sup>(13)</sup>

This study focused on use of Collagen particles with mupirocin and metronidazole powder as local applicant over the ulcer for 7 days and assess the wound healing using Bates

- Jensen Wound assessment tool. This study was performed over a period of 6 months with 50 patients included in the study who were randomly grouped into 2 groups of betadine dressing and collagen particles with mupirocin and metronidazole dressing.

The study concluded that lower limb ulcers are more common in middle age population with mean age of 57 years amongst controls and mean age of 58 years amongst cases with male predominance in both groups. Among the controls 98% and among cases 72% were diabetic patients.

BWAT used 13 parameters to assess the wound healing and the reduction of score represented healing of ulcers. Hence reduction in scores in both groups were compared and found to have significant reduction in score in collagen particles with mupirocin and metronidazole dressing patients implying faster healing process.

The study showed significant decrease in BWAT score in the patients who underwent collagen particles with mupirocin and metronidazole dressing implying faster wound healing with reduction in size of ulcer, exudate amount and peripheral tissue edema with induration.

52% patients who underwent collagen particles with mupirocin and metronidazole dressing were found have no growth in the pus culture implying reduction in bacterial load of the ulcer. Also 12 patients (48%) underwent split skin grafting within 1 month of collagen particles with mupirocin and metronidazole dressing as the wounds were found healing.

Thus, Collagen particles with mupirocin and metronidazole powder can be used as local application agent in case of wounds found non - healing or infected to help the wound healing process by killing the bacteria locally. Thus, patients can undergo SSG earlier.

No side effects of local application of collagen particles with mupirocin and metronidazole powder were reported. Hence collagen particles with mupirocin and metronidazole can be safely used in patients with lower limb ulcers with normal liver function tests and with no vascular compromise.

**6. Conclusion**

Lower limb ulcers can be treated in various ways which include surgical debridement, regular dressing, antibiotics, etc to promote wound healing.<sup>(14)</sup> This study concluded that use of collagen particles with mupirocin and metronidazole powder for local application over the ulcer help in reduction of size of the ulcer, undermining of the ulcer, exudate amount, surrounding induration, peripheral tissue edema. The study also concluded that collagen particles with mupirocin and metronidazole dressing helps to increase the granulation tissue of the ulcer, promotes epithelialisation, changes the type of necrotic tissue thus promoting wound healing. The study showed significant decrease in positive pus culture reports in patients treated with collagen particles with mupirocin and metronidazole dressing. Due to faster wound healing and decrease in bacterial load of the ulcer, 48% of the patients who underwent collagen particles with mupirocin

and metronidazole dressing could undergo SSG within 1 month. Collagen particles with mupirocin and metronidazole is a cheap drug which is easily available all over India. Local application of collagen particles with mupirocin and metronidazole is an easy method of local antibiotics application to treat the lower limb ulcers.

**Ethical clearance:** Taken from ethical committee of institute

**Source of funding:** none

**Conflict of Interest:** Nil

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