wjpmr, 2024, 10(3), 01-06

SJIF Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

THE SAFETY AND EFFICACY OF ZYMALGE GEL IN THE TREATMENT OF CHRONIC VENOUS ULCERS

Ayman Fakhry, MD.[1]* and Sohiel Nagib, MSc., EFVS[2]

[1]Professor of Vascular Surgery, Egyptian Military Academy.
[2]Consultant of Vascular Surgery, Royal Vascular Center, Alexandria- Egypt.

***Corresponding Author: Ayman Fakhry, MD.**

Professor of Vascular Surgery, Egyptian Military Academy.

Article Received on 28/12/2023 **Article Revised on 18/01/2024** **Article Accepted on 08/02/2024**

ABSTRACT

Background: Venous ulcers are characterized by a cyclical pattern of healing and recurrence.[1] The current standard of care for chronic venous ulcers involves the use of compression bandages as a means to reduce ambulatory venous pressure, control edema, and improve venous return. Dressings are applied beneath the compression and are used to control the exudates and to maintain the wound in a moist environment. Since the 1960s it has been accepted that wound healing is optimal when the wound is kept in a moist environment rather than air dried.[2] **Objective:** Detection of the safety and efficacy of *(ZYMALGE GEL)* versus standard dressing for the treatment of chronic venous ulcers. **Patients & Methods:** 40 patients were admitted to the Royal vascular center, with chronic venous ulcer, from 1st January 2023 – 31st December 2023, and randomly classified into 2 groups. - Group A) comprised 20 patients, treated with *(ZYMALGE GEL)*, and compression. - Group B) comprised 20 patients, treated with (*traditional dressing)* and compression. The primary end point was determined as complete wound healing within 3 months of treatment with or without correction of arterial or venous insufficiency. **Results:** Age ranged from 29-63 years and x age 39.8+0.6 years in group A patients and29-63 years and x age 39.8+0.6 years in group B patients. Complete wound healing was observed in 20 patients 100% with a mean duration of 6.03+ 0.8 weeks in group A patients, while only 15 patients 75% gained complete healing within the previously determined duration (3 months), with a mean duration of 9.01+ 0.4 weeks in group A patients. **Conclusion:** Zymalge gel (combination of antimicrobial enzymes, hyaluronic acid, alginate, and moisture agent) is a safe and effective topic treatment for venous ulcer especially when combined with compression, and management of arterial and venous insufficiency.

KEYWORDS: Venous Ulcer/Topical Treatment/Wound Healing.

BACKGROUND

Venous ulceration (VU) is a complex and serious problem that affects 1e2% of the global elderly population (>65 years), and its incidence is constantly increasing.[3] Venous ulcers are characterized by a cyclical pattern of healing and recurrence. The current standard of care for chronic venous ulcers involves the use of compression bandages as a means to reduce ambulatory venous pressure, control edema, and improve venous return. Dressings are applied beneath the compression and are used to control the exudates and to maintain the wound in a moist environment. Since the 1960s it has been accepted that wound healing is optimal when the wound is kept in a moist environment rather than air dried.[4] There are various guidelines around the world for the treatment of VLUs, which leads to a disparity in the treatment of patients worldwide. VLUs may be treated conservatively, with compression bandaging and wound care, medically, surgically, or with a combination of approaches, depending on the etiology, pathology, physiopathology, and the severity of the ulcer and available resources.[5] Dressings are applied beneath the compression and are used to control the exudate and to maintain the wound in a moist environment. In the case of a dry wound, hydrogel and hydrocolloid dressing should be used, whereas highly absorbent dressings such as alginates, hydrofibers, or foam is more appropriate in the case of a highly exuding wound. Dressing changes should be as frequent as necessary.[4] It has been suggested recently that bacterial density is associated with the probability of nonhealing in leg ulcers when infection is detected using swabs or tissue biopsies, and that chronic wound healing may also be influenced by the diversity of microorganisms present and their interactions with one another. On the other hand, antiseptics and antibiotics fail to promote the healing process and to reduce the bacterial density of the wound.[6] The rationale for the use of hyaluronic acid or

collagen is to promote healing because they are present at a very high level in the dermis. Cream, impregnated tulles or dressings containing hyaluronic acid, sometimes in combination with alginates, are available. They have to be changed daily and this may be costly. They are used for mildly exuding chronic wounds at the stage of granulation but may induce a burning sensation.[7] Necrotic tissue left in the ulcer contributes to reduced host resistance to infections because it acts like a foreign body. In this area, there is usually a high concentration of harmful proteases and bacteria that can inhibit wound healing. Skin debridement consists of removing nonviable, nonbleeding slough.

A chronic wound has to be converted by debridement to an acute wound and hence it can proceed through the normal healing phases. Removal of necrotic and devitalized tissue can be achieved through mechanical, autolytic, or enzymatic, and biological debridement.[7] The skin surrounding the ulcer can be damaged due to excess moisture, wound fluid proteases and adhesives present in the dressings. Barrier creams and ointments are available, which protects the skin around the ulcer.[8]

OBJECTIVE

Detection of the safety and efficacy of *(ZYMALGE GEL)* versus standard dressing for the treatment of chronic venous ulcers.

PATIENTS AND METHODS

40 patients were admitted to the Royal vascular center, with chronic venous ulcer, from 1st January 2023 – 31st December 2023, and randomly classified into 2 groups. - Group A) comprised 20 patients, treated with *ZYMALGE GEL (Enzymatic combination as antimicrobial, alginate as debridement agent, hyaluronic acid and moisture)*[9] and compression. - Group B) comprised 20 patients, treated with (*traditional dressing)* and compression. The primary end point was determined as complete wound healing within 3 months of treatment with or without correction of arterial or venous insufficiency. - All patients were subjected to: - Informed consent - Careful history taking and General examination - ABI & Duplex examination of arterial and venous systems of both extremities - Plain X-ray of the affected lower limb - wound examination and classification according to Texas classification. Fig 1.[9]

	GRADE				
STAGE		0	1	2	3
	A	Pre-ulcerative lesions No skin break	Superficial wound No penetration	Wound penetrating tendon or capsule	Wound penetrating bone or joint
	B	With infection	With infection	With infection	With infection
	C	With ischemia	With ischemia	With ischemia	With ischemia
	D	With infection and ischemia	With infection and ischemia	With infection ad ischemia	With infection and ischemia

Fig 1: Texas Wound Classification.

RESULTS

In the present study we compared 2 different2 groups of chronic venous ulcer patients. - Group A) comprised 20 patients, treated with *(ZYMALGE GEL),* and compression. - Group B) comprised 20 patients, treated with *traditional dressing (Normal saline, antiseptic solution)* and compression. The age ranged from 29-63 years and x age 39.8+0.6 years in group A patients and29-63 years and x age 39.8+0.6 years in group B patients. All patient in group A) completed follow up, while 19 patients (95% reached the primary end point and only one patient (5%) withdrew from the study due to his travelling after 23 days from the beginning .Complete wound healing was observed in 20 patients 100% while only 15 patients 75% gained complete healing within the previously determined duration (3 months), Male/female was (12/8 & 14/6) in both groups. The wound was located on the right lower limb in 11 (55%) & 13 (65%) patients, and on left lower limb in 3 (15%) & 2 (10%) patients while bilateral leg wound was noticed in 7(35%) & 4 (20%) patients. Table- 1.

Table. 1: Side affected.

	A	B
Right lower limb	11 (55%)	13 (65%)
Left lower limb	3 (15%)	2 (10%)
Bilateral	7(35%)	4 (20%).

According to Texas wound classification, 9 Patients in both groups 45% were in grade (a), 6&7 patients in grade b in both groups, 4 & one patient in grade c, while 1&3 patients in graded. Table -2a Staging of the wound revealed that 8&11 patients were in stage 1, 8&4 patients in stage 2, while 4&5 patients were in stage 3 Fig 2b.

Table. 2a: Wound grades.

Grade	A	B
A	9 patients	9 patients
B	6 patients	7 patients
C	4 patients	one patient
D	one patient	3 patients

Table. 2: Wound stages.

Stage	A	B
1-	8 patients	11 patients
2-	8 patients	4 patients
3-	4 patients	5 patients

Infection was noticed in 11 patients 55%, but the toxic manifestations and toxemia was shown in 3 patients 15% in group A, and 2 patients 10% in group B isolation of the organisms and organism frequency was shown in table 3 a&b. We had used antibiotics (Tavacin + Targocin) only in 3 patients with toxemia in group A, but we used antibiotics (Tavacin +Targocin) in 2 patients with toxic manifestations in group B in addition to 5 patients with more severe infection in group B. Table 3 a&b.

Table 3a: Organisms Frequency in group (A).

Organism	Patients	Toxic manifestations
Staph aureus	4 patients	no
Citrobacter freundii	One patient	no
Klebsiella	2 patients	no
Pseudomonas	One patients	no
MRSA + E.coli	3 patients	yes

Table 3b: Organisms Frequency in group (B).

Organism	Patients	Toxic manifestations
Staph aureus	3 patients	no
Staph aureus + coliform species	2 patients	yes
Proteus mirabilis	One patient	no
Pseudomonas	2 patients	no
MRSA	3 patients	no

The duration of the wound duration varied from 4-11 & 5- 10 weeks and mean duration of 6.8+9 &7.1+0.4 months in both groups. Wound measurements in all patties were done; the mean length was 8&7.6+0.9&1.02 CM in group A&B width was 6.2&5.8 +0.8&0.76 CM in group A&B patient. Fig 2a, the depth of the wound was 1.9 & 1.7 + 0.4 &0.6 CM in group A &B patients. Fig 3b.

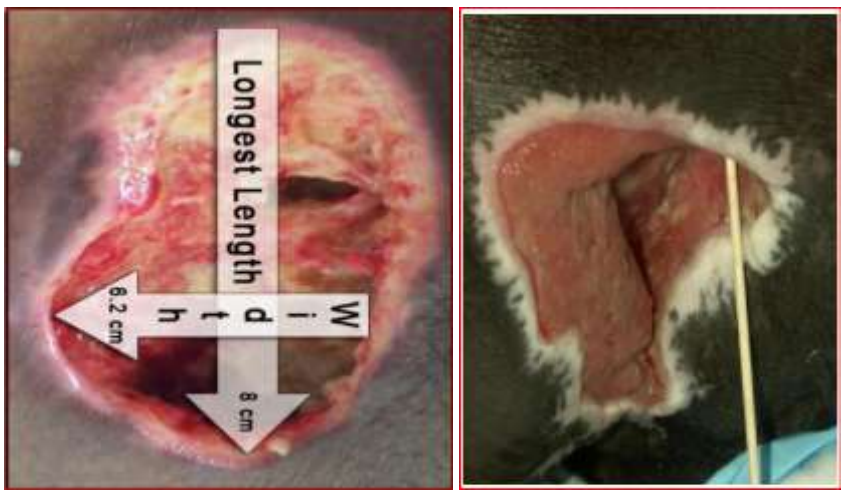


Fig 3 a & b Wound Measurements.

Arterial assessment of all patients was done, and ABI was 0.9 & 0.87 in group A & B patients, ischemic manifestations were detected in 2 patients 10 % in both group and revisualization was performed before wound care management and compression. Fig 4 & 5.

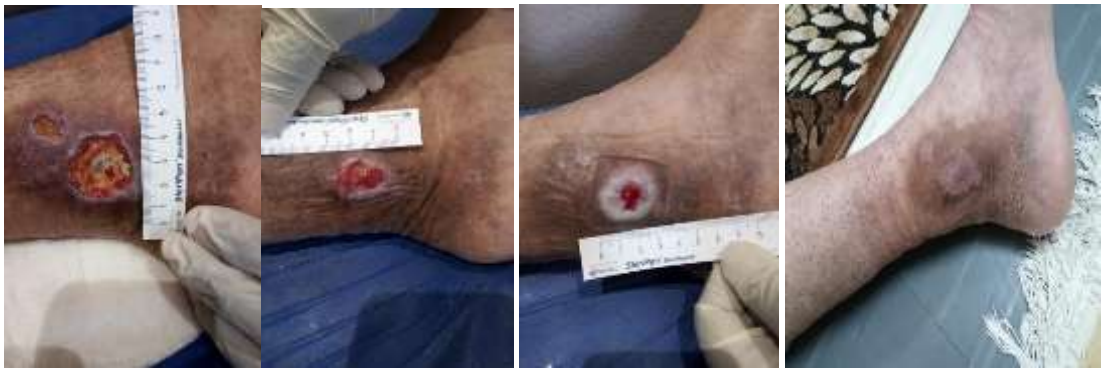


Fig 4: Venous ulcer in ischemic limb, before and after revascularization.

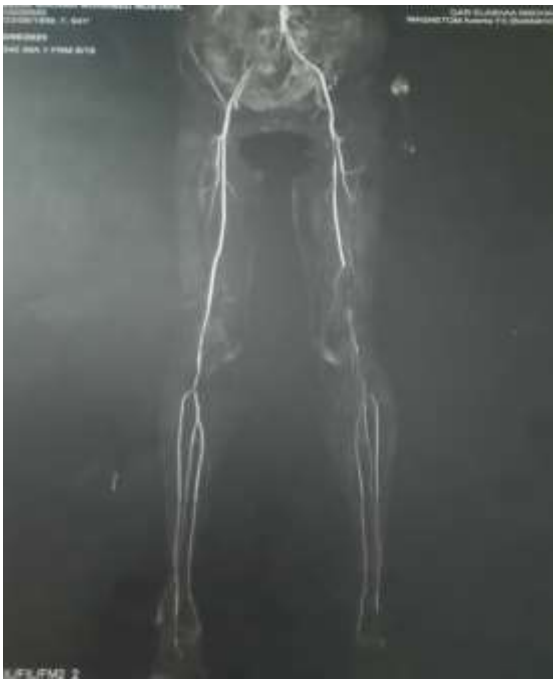


Fig 5: CT Angiogram before revascularization.

Venous duplex showed significant reflux in the great saphenous vein in 3&2 patients 15 & 10% and one patient with incompetent SPJ (5%) in group A) patients, that was treated by ablation of the GSV &SSV and improving venous pathology, while post thrombotic changes were detected in further 2 & 3 patients 10 & 15% that was counteracted by wearing elastic compression type III (40 mm Hg). Fig 6a & b).

Fig 6a: Venous ulcer.

Fig 6b: Venous ulcer & compression dressing.

Duration of the wound healing ranged from 4 -16 & 3-18 weeks with a mean duration of 6.03+ 0.8 weeks in group A) patients and a mean duration of 9.01+ 0.4 weeks in group B) patients. Wounds were healed spontaneously in 20 patients (100%) in group A) and. On the other hand, Wounds were healed spontaneously in 15 patients (75%) in group B patients and skin graft was successfully taken in 3 patients(15%)% ingroup B) patients. Fig 7.

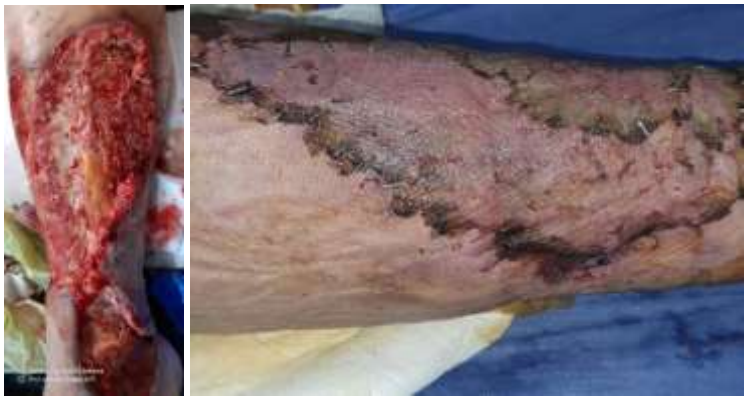
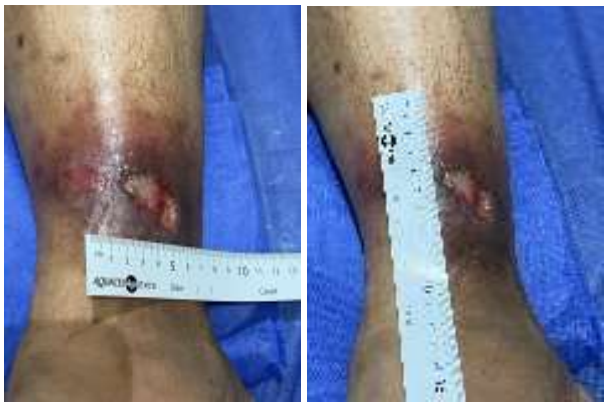


Fig 7: Post Thrombotic Ulcer Healed Using Skin Graft.

In the present study all venous ulcers in group A) patients were healed spontaneously without any allergic manifestation nor deterioration in natural status of the venous ulcer during the dressing and follow up period.



DISCUSSION

This study, applying a clear definition for chronicity, provides a comparison of the effectives of*(ZYMALGE GEL),* and compression versus *traditional dressing (Normal saline, antiseptic solution)* and compression in the healing process of chronic wounds. Age of the patients was (&) in both groups which was the in agreement with Salomoni et al[11] in his study for foot ulcer, and much younger than those patients in Lipsky B, et study for chronic wound management using Nano silver colloid.[12] Initially, the wound starts unintentionally, therefore wounds are colonized with microorganisms causing a serious diabetic foot infection once the wound becomes infected with purulent exudate

and inflammation may lead to diffuse infection and ends by leg amputation.[12] Practically, selecting a suitable type of advanced antimicrobial dressing to play a key part of DFU treatment as Honey-impregnated dressings, Iodine-Impregnated dressing, and silver-impregnated dressing.[10] About 45% of the patients in both groups in this study had clinical manifestations of infection and the frequency of organisms was done with systemic antibiotic therapy in 10% of cases in group A patients while it was used in 15% of patients in group B without toxic signs . Recently, the integration of silver with nanoparticles displays a significant novel and distinguish of physical, chemical, and biological characteristics, meanwhile, the magic nanoscale size provides a unique tool in tissue repair and overall wound management.[11] Duration of the wound healing ranged from 4 -16 & 3-18 weeks in patients of both groups and wounds were healed spontaneously in all patients in group A). On the other hand, Wounds were healed spontaneously in 15 patients (75%) in group B patients and skin graft was successfully taken in 2 patients 10%. Evans reported that: After the implementation of the hydrogel-based dressing on patients with chronic leg ulcer of the present study, the findings illustrated that use of hydrogel wound dressing compared to the traditional dressing showed a more significant reduction in the area when the initial wound area is compared to the subsequent area measurements expressed as the initial percentage and their findings proved that the healing rate was statistically significant and the healing rate per week and the complete recovery was achieved with hydrogel dressing.[3]

CONCLUSION

Zymalge gel (combination of antimicrobial enzymes, hyaluronic acid, alginate, and moisture agent) is a safe and effective topic treatment for venous ulcer especially when combined with compression, and management of arterial and venous insufficiency.

REFERENCES

1. Patricia Senet. Local treatment of venous leg ulcers. Phlebolymphology, 2010; 17(2): 87-94.
2. Vuerstaek JD, Vainas T, Wuite J, Nelemans P, Neumann MH, Veraart JC.State-of-the-art treatment of chronic leg ulcers: a randomized controlled trial comparing vacuum-assisted closure (VAC) with modern wound dressings. J Vasc Surg, 2006; 44: 1029-1038.
3. C.J. Evans, F.G.R. Fowkes, C.V. Rockley, A.J. Lee, Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population: Edin- burgh Vein Study, J. Epidemiol. Community Health, 1999; 53: 149-153.
4. Singer AJ, Clark RAF. Cutaneous wound healing. N Engl J Med, 1999; 341: 738-746.
5. Lazareth I, Meaume S, Sigal-Grinberg ML, et al. The role of a silver releasing lipido-colloid contact layer in venous leg ulcers presenting inflammatory signs suggesting heavy bacterial colonization: results of a randomized controlled study. Wounds, 2008; 20: 158-166.
6. Hansson C, Faergemann J. The effect of antiseptic solutions on microorganisms in venous leg ulcers. Acta Derm Venereal, 1995; 75: 31-33.
7. Ubbink DT, Westerbos SJ, Nelson EA, Vermeulen H. A systematic review of topical negative pressure therapy for acute and chronic wounds. Br J Surg, 2008; 95: 685-692.
8. Bishop SM, Walker M, Rogers AA, Chen WY. Importance of moisture balance at the wound-dressing interface J Wound Care, 2003; 12: 125–8.
9. Rose A Cooper. Inhibition of biofilms by glucose oxidase, lactoperoxidase and guaiacol: the active antibacterial component in an enzyme algin gel. International Wound Journal © 2013 Medicalhelplines.com Inc and John Wiley & Sons Ltd, 630-35.
10. Duncan Stang and Matthew Young. Selection and application of a diabetic foot ulcer classification system in Scotland: part 2 The Diabetic Foot Journal, 2018; 21(2): 100-106.
11. Salomoni R, Léo P, Montemor AF, Rinaldi BG, Rodrigues M (2017) Antibacterial effect of silver nanoparticles in Pseudomonas aeruginosa. Nanotechnol Sci Appl, 10: 115-121.
12. Lipsky B, Berendt A, Cornia P, Pile J, Peters E, Armstrong D, Deery G, Embil J, Joseph W, Karchmer A, Pinzur M,11 and Senneville E. 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections. IDSA Guideline for Diabetic Foot Infections, CID, 2012; 54: 1679-1684.