

Topical Therapy for Neuropathic Diabetic Foot Ulcers

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Background: Healing is slow in neuropathic diabetic foot ulcers, using conventional medical treatment. This delayed wound healing is caused mainly by the pressure damages of weight bearing, and sometimes by a tight dressing, on the painless ulcer.

Material and Methods: In our study, we used the dehydrating action of ethyl alcohol to reduce the oedema in the tissue compartments of the foot. This, in turn, reduced pressure on foot micro-vasculature. For this purpose, 60 diabetic subjects with neuropathic infection were rule out. After maximizing diabetic control, they were divided into two comparable groups.

Results: Group A (n=30) patients were treatment with a commonly prescribed broad spectrum antibiotic (tablet ofloxacin 400 mg 12 hourly), and their wounds were dressed daily. In group B (n=30), ulcerated feet were soaked for 20 minutes in a solution of 0.025 L tincture of iodine (U.S.P) in one L of 75% ethyl alcohol. This process was repeated 8 hourly, and the wounds were left open with out any dressing. No systemic antibiotic was used in this group of patients. Time for complete wound healing was compared in the two groups.

Conclusion: Results showed significantly faster wound healing 2.83 weeks vs 5.8 weeks ($p=0.001$) with the used of the proposed therapy, suggested this to be a better treatment option in neuropathic foot ulcers.

Key words: Diabetic foot, neuropathic ulcer, open healing ethyl alcohol, antibiotic, dressing.

Introduction

Diabetes Mellitus is characterized by chronic hyperglycemia produced as a result of insulin deficiency, resistance to its action, or both.¹ While this may result in acute metabolic decompensation, long term complications of this disease lead to significant morbidity and mortality. The foot is a frequent site of disabling complications in diabetic individuals.² About 60% of all lower extremity amputation are performed on patients with diabetes.³ Of these, approximately 85% amputations are precipitated by the deterioration of a foot ulcer.⁴

The aetiology of diabetic foot ulceration involves neuropathy, and or ischaemia. However, neuropathy is more common,⁵ and results in undetected trauma to dry feet with calluses and abnormal pressure areas.

Management is based on ensuring good glycemic control, and intervention directed at risk factor modification. Conventionally, it includes surgical debridement, antibiotics and dressings.⁶

However, routine management of diabetic foot ulcer is seldom cost effective. Healing is slow, and a large percentage of foot ulcers progress to complications.⁷ Reasons for slow healing include continuing mechanical pressure exerted by walking on the painless wound. Thus, despite, treatment, the superficial micro abscesses are pushed deeper into the tissue planes. Oedema of the inflamed tissues in a

restricted compartment adds to the mounting pressure, which compromises the microcirculation, causing tissue hypoxia and damage even when the major blood vessels are patent. We proposed to treat these neuropathic ulcers with a dehydrating agent (75% ethyl alcohol) to relieve the tissue oedema around the microvasculature. This enhanced blood supply in the diabetic foot would revitalize the damaged tissue and result in faster wound healing.

Materials and Methods

This experimental, interventional clinical trial was performed in a tertiary care unit, Services Hospital, Lahore. Ninety eight diabetic subjects with superficial foot ulcers were screened for inclusion from medical indoor, outdoor and emergency departments. A total of 60 subjects completed this trial.

Inclusion Criteria

- Eighteen to seventy years old diabetic adults with superficial foot ulcers (Wagner's grade 1&2) appendix.^{1,8,9}
- Presence of motor and sensory distal symmetrical polyneuropathy, as evidenced by each of the following clinical findings. Absent of diminished ankle reflex, loss of vibration sense on the big toe, diminished joint position sense in the foot, loss of foot temperature sense, and absent or diminished pin

prick sensation on the foot.

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Palpable posterior tibial and dorsalis pedis artery, as well as evidence of more than 90% vessel patency on Doppler blood flow studies of the lower limbs.

Exclusion Criteria

- Bone involvement, as detected by plain radiograph of the ulcer area.
- Patients with severe or systemic infection, as confirmed by presence of any three of; fever, enlarged and tender regional lymph nodes, a raised leukocyte count or ESR,
- Concomitant interfering conditions like anaemia (HB<10 in females and <12 in males), clinical evidence of vasculitis, malignancy or immune deficiency state, uncompensated heart failure (basal crepitations), uncontrolled hypertension (above 160 systolic or 100 diastolic), hepatic failure or liver enzymes above three times normal, renal impairment with serum creatinine >1.0mg/dl.
- Hypersensitivity to any of the used treatment options.
- History of epilepsy or psychiatric illness.

After written informed consent by the subjects and approval by the local ethics committee, necessary clinical assessment and investigations were carried out to confirm the selection criteria in all the subjects. The patients were educated about their disease and the importance of good glycaemic control was emphasized. Their hypoglycemic management was intensified with an aim to achieve as near normoglycemia as possible. A special effort was made to explain the principals of offloading in diabetic feet, and patients in both the groups were advised complete avoidance of weight bearing on their ulcerated feet. The patients' attendants were additionally targeted to ensure better compliance.

Wound index of all participants was recorded using the formula:

Wound index = ulcer length (mm) ulcer breadth (mm) ulcer grade. Minimal necessary surgical wound debridement was carried out to speed up healing in cases of chronic, non-healing ulcers.

The patients were divided randomly into two groups, A and B. Further management was as follows:

Group A

- Patients in this group received twice-daily dressing of their ulcers with sterilized gauze using topical silver-sulphadiazine.
- They were also given oral ofloxacin in a dose of 400 mg 12 hourly (800 mg daily)

Group B

- Ulcerated feet were soaked in a solution of 75% ethyl alcohol and tincture of iodine (in a ratio of 1 l ethyl alcohol: 0.025 L tincture of iodine U.S.P.) for a duration of 20 minutes. After air drying, local silver-sulphadiazine was applied as in the group A. this soaking process was repeated eight hourly.
- Following the procedure, the surrounding skin was covered with soft paraffin to avoid undue dehydration of normal skin.
- No dressing was applied and no systemic antibiotics were used in this group of patients. No time limit was set, and the recruited subjects were followed up weekly until complete healing of their wounds (Wagner's grade 0 ulcer). Their wound index, glycaemic control, compliance to treatment and off loading was recorded at each visit.

Results

Of 98 recruitments, a total of 60 subjects completed this clinical trial with 30 in each treatment group (Table 1).

Table 1: Dropout Details.

	Group A- Antibiotic+ Dressing	Group B- Alcohol Dip + Open Healing
Total recruitment	47	51
(n) failure to follow up non compliance	05 11 01	10 08 03
complication		
Complete Data	30	30

Dropouts included:

- Failure to follow up mostly <1 cm ulcers superficial ulcers.
- Non compliance to therapy or off loading,
- Myocardial infarction (group A),

- Severe urinary tract infection necessitating antibiotic treatment (two patients in group B).
- Haemorrhagic stroke (group B).

In either group, there was no apparent association between study discontinuations and adverse effects of treatment offered.

Mean baseline variables likely to influence outcome were similar in both the groups (Table 2).

Table 2: Comparison of variables likely to affect outcomes.

Variables		Group A	Group B	P-Value
Mean wound index		2202.20	2519.67	N/S
Mean HbA1c		7.73	8.01	N/S
Mean age		52.43	51.13	N/S
Protein urea (n)	Positive	11	10	NS
	Negative	19	20	
Anti diabetic Treatment (n)	Oral	09	11	NS
	Insulin	21	19	
Gender (n)	Male	22	19	NS
	Female	08	11	

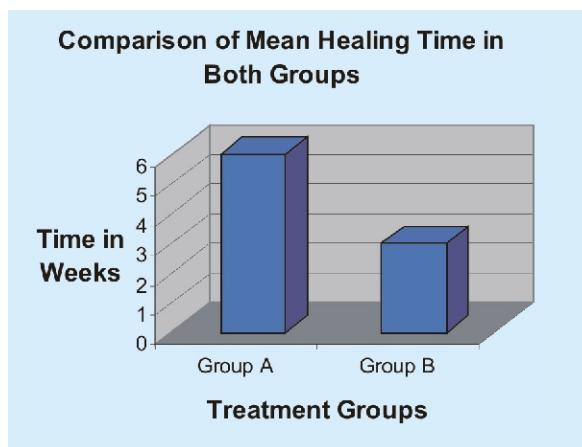


Fig. 1: Comparison of mean healing time in both groups.

These included size and extent of the wound, glycaemic control as judged by glycosylated haemoglobin, age, kidney function judged by proteinuria, and anti-diabetic treatment. Gender distribution was also similar among the two groups. Compliance to off loading and treatment was noted, however, to be much better in subjects on proposed therapy.

The mean healing time in subjects treated conventionally 9 dressings + oral antibiotic) was 5.8 weeks; while the mean time taken by the group on proposed open treatment was 2.83 weeks (graph 1, 2).

Thus, healing in neuropathic, non inchaemic, superficial diabetic foot ulcer was found to be significantly faster ($p=0.001$) with open care using ethyl alcohol and tincture on iodine 'dips', when compared with dressings and oral antibiotics.

Discussion

This study, aimed at finding a better treatment option for diabetic foot ulcers, is based upon our current knowledge of the pathophysiological mechanisms involved in the progression of neuropathic foot ulceration. Sensory loss makes diabetic feet prone to repeated and undetected trauma.¹⁰ Autonomic neuropathy makes the skin dry,¹¹ so it loses its suppleness and thus becomes vulnerable to fissuring. Motor neuropathy results in altered biomechanics of the foot leading to the development of high pressure pints and calluses on the plantar surface.¹² These may later ulcerate and become infected with microorganisms. The insensate foot allows the patient to ignore this pathological process, so that he continues to use the damaged for walking and weight bearing. The resultant puncture wounds or cracks to deepen and pus tracks up into the inner tissue planes.¹³ Oedema of these deep tissues, surrounded by bones or tight fascia, results in the build up of high pressures, compromising local microvasculature. This may result in ischaemic necrosis even when the macro vascular status of the affected limb is normal.

Conventional Versus Proposed Treatment

On first presenting to the health care worker, most of the diabetic foot wounds are superficial and uncomplicated, neuropathic damage being the only underlying pathology. Conventionally, these are treated with extensive, repeated debridement, dressing and systemic antibiotics.⁶ Extensive debridement, while effectively achieving wound toilet, results in a much larger foot ulcer than before, and unless the neuropathic patient shows excellent compliance regarding off-loading, the same vicious cycle is again set up with mechanical stress, continuing trauma and further tissue damage.

Dressings are an essential part of routine wound care. However, in the setting of neuropathy, a few points need to be considered regarding their use. In order to protect ourselves form noxious stimuli, we depend heavily on our five senses, with pain and

vision playing a major role in saving us from under harm. The patient with diabetic neuropathy has no pain sensation in his feet. The dressing, while protecting the ulcer from environmental contamination, hides the ulcer allows his a false sense of security regarding the state of his ulcer. If he cannot see or feel his ulcer, then he is unlikely to be able to care for it. This may cause the patient to neglect his ulcer as he again starts bearing weight on his wound. This not only delays wound healing, but also promotes further tissue breakdown, with resultant increased risk of amputation. Additionally, since there is no pain, the patient may not notice that his dressing has been applied too tightly; this adds to the pressure damage, while at the same time impeding the drainage of pus from the ulcer.

In contrast, his study aims at achieving open wound healing in uncomplicated neuropathic ulcers. The proposed treatment utilizes ethyl alcohol, which is a dehydrating agent, to reduce tissue oedema by actively getting rid of infected tissue exudates through the open ulcer crater. As a result, almost all of the patients with locally infected ulcers reported profuse drainage of purulent discharge from their wounds after soaking them in ethyl alcohol for the first few times; soon afterwards, the ulcers dry out, oedema and internal tissue pressures subside, the compromised blood supply is restored, and the damaged tissues start to revitalizes. In this way, the need for deep release incisions is avoided; a small wound remains small, and therefore heals quickly. This treatment is tolerated well by diabetic patients, because underlying neuropathy numbs the irritation caused by topical ethanol.

Alcohol additionally denatures surface proteins by forming a superficial crust on the wound surface, which becomes iodized by tincture of iodine. This iodized crust acts as a barrier to bacterial invasion. Thus, the ulcer is allowed to heal in a safe, protected environment. This natural aseptic dressing is comparable to a physiological scab. The risk of alcohol related tissue damage has been proposed as a big disadvantage. In our experience, this tissue damage is minimal, as alcohol penetration to the health tissue is negligible after crust formation

The Use of Systemic Antibiotics

The common pathogens in uncomplicated skin and skin related structures include staphylococci (*S. Aureus*, coagulase negative staphylococci), and group A, B C and G streptococci. Mild or non-limb threatening infections of the diabetic foot are usually treated with oral antibiotics including quinolones

(including ofloxacin), cephalosporins, clindamycin and amoxicillin/clavulanate. Recommended daily dose of ofloxacin in skin and soft tissue infections is 800 mg.

Appendix 1: The Meggfit Wagners classification of foot ulcers.

Grade 0	Intact skin
Grade 1	Superficial ulcer of skin/subcutaneous tissue
Grade 2	Ulcer extends into tendon, bone or capsule
Grade 3	Deep ulcer with osteomyelitis
Grade 4	Gangrene of toes or forefoot
Grade 5	Mid food or hind foot gangrene

However, diabetic foot infection starts as a localized pathology and remains as such unless it spills over into the systemic circulation, as evidenced by pyrexia, lymph node involvement, and raised leukocyte counts. Thus, in the absence of signs and symptoms of systemic disease, the ulceration can be safely labeled as a localized pathology, which should, as a rule respond to local measures. Systemic therapy with antibiotics in this situation should only be reserved for those having systemic signs of infection, or in cases with osteomyelitis. The proposed therapy not only reduces the total cost of treatment significantly, but also reduces the morbidity related to the potential side effects of antibiotics.

Conclusion

The significantly faster healing ($P= 0.001$) shown by ulcers soaked in 75% ethyl alcohol and tincture iodine proves that this is a better option, when compared with conventionally prescribed dressings. Results also show that oral antibiotics can be safely avoided in uncomplicated diabetic foot ulcers if there is no evidence of systemic infection.

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Picture Quiz

What is the diagnosis?



Answer on page 41.