



## TOPICAL USE OF INSULIN IN WOUND MANAGEMENT.

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## KEYWORDS :

## INTRODUCTION

Diabetes is global health crises, which result in major economic consequences for patients, their family and society.

The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030.

Patients with DM are prone to multiple complications such as diabetic foot ulcer (DFU). DFU is a common complication of DM that has shown an increasing trend over previous decades. In total, it is estimated that 15% of patients with diabetes will suffer from DFU during their lifetime [1]. Although accurate figures are difficult to obtain for the prevalence of DFU, the prevalence of this complication ranges from 4%–27%.

To date, DFU is considered as a major source of morbidity and a leading cause of hospitalization in patients with diabetes. It is estimated that approximately 20% of hospital admissions among patients with DM are the result of DFU.

Indeed, DFU can lead to infection, gangrene, amputation, and even death if necessary care is not provided. On the other hand, once DFU has developed, there is an increased risk of ulcer progression that may ultimately lead to amputation. Overall, the rate of lower limb amputation in patients with DM is 15 times higher than patients without diabetes. It is estimated that approximately 50%–70% of all lower limb amputations are due to DFU. In addition, it is reported that every 30 seconds one leg is amputated due to DFU in worldwide.

Furthermore, DFU is responsible for substantial emotional and physical distress as well as productivity and financial losses that lower the quality of life. Common treatment options in patients with diabetic foot ulcers include mechanical and surgical debridement, pressure relief/off-loading, and the use of various dressings and topical agents designed to facilitate wound closure and promote re-epithelialization. Advanced care modalities for the treatment of diabetic foot ulcers include the use of growth factors, bioengineered tissues, electrical stimulation, ultrasound therapy, and negative pressure wound therapy and hyperbaric oxygen therapy.

## AIMS AND OBJECTIVES

- 1) To study the benefits of Topical application of insulin for treating non healing Diabetic ulcers.
- 2) To assess the effect on healing, total number of amputations. Operative procedures Control of infection, and length of hospital stay.

## MATERIAL AND METHODS

Randomized control study that compared the effect on chronic wound healing of treatment with topical insulin and without topical insulin application. 100 diabetic subjects, consecutively hospitalized in our surgical unit, underwent our diagnostic and therapeutic protocol and evaluated for potential inclusion in the investigation.

Diabetic patients were considered eligible if they were at least 12 years of age and if they had a non healing spreading ulcer for at least 3

months despite appropriate local systemic wound care. All patients were assessed by a vascular surgeon at the time of inclusion and only patients with adequate distal perfusion or non-reconstructable peripheral vascular disease were included in the study.

After confirming eligibility, the patients were randomly assigned to the standard treatment group or the standard treatment plus INSULIN group, using a random number table and allocating patients to the treatment groups according to a predetermined sequence wherein consecutively enrolled patients corresponding to an even random number received standard treatment and those corresponding to an odd random number received standard treatment plus topical insulin.

A written valid informed consent was taken from each patient.

## METHODS

Each patient in the INSULIN group received 10 units (0.1 ml) insulin i.e. INJ INSULIN REGULAR (Plain) in solution with 1 cc saline 0.9 % for each 10 cm square of wound as topical injection followed by wet saline gauze dressing once in a day.

Each patient in Conventional group received povidone iodine and salinedressing once in a day.

## Diagnostic and therapeutic protocol

On admission to the hospital, lesions were classified according to Wagner Classification. In our clinical practice, diabetic subjects with full-thickness gangrene (Wagner grade IV) or abscess (Wagner grade III) were admitted to hospital. Subjects with less-deep ulcers (Wagner grade II) were also admitted if the ulcer was large and infected and showed a defective healing in 3 months.

On admission, Glycosylated hemoglobin levels (HbA1c, normal values 4.4-6%) were measured. Specimens of the foot lesion, after decontamination and debridement followed by curettage, were collected for aerobic and anaerobic culture and for antimicrobial susceptibility testing.

Initially, aggressive debridement was performed and the wound was dressed. Dressings were changed at required intervals. After the collection of swabs from the wound, patients were given empirical antibiotic treatment. This was modified if necessary according to the sensitivity tests. Blood glucose levels were optimized with insulin.

Patients were discharged only if their wound swabs were negative for organisms, or had a very healthy healed ulcer with granulation tissue and no slough and patient was willing to do regular cleaning & dressing with regular follow up. Each patient was followed up regularly till 6 months following discharge. The end point of the study was healing (conversion of a non healing, spreading ulcer to a healing ulcer), graft/flap closure, amputation or no change. Non healing spreading type of ulcer was defined as a painful one with inflamed, edematous and ragged edge with floor covered with slough and pus/thick discharge without granulation tissue and surrounding skin being inflamed. Healing ulcer was defined as one with reddish edge and granulation, and bluish margin with growing epithelium with floor covered with red healthy granulation tissue and scanty serous discharge. Statistical significance was defined at 5 % (p value <0.05).

**INCLUSION CRITERIA**

Patients above 18 yrs suffering from type 1/2 diabetes mellitus.

Patients having chronic non healing ulcers i.e.:- more than 6 weeks and non healing for more than 3 months.

Patients with ulcers of Wagner's grade 2, 3, 4.

**EXCLUSION CRITERIA**

Patients on chemotherapy or suffering from malignancy.

Patients with high grade fever, COPD, Upper respiratory tract infection.

Patients with untreated pneumothorax.

Patients with seizure disorder.

Pregnant patients.

Patients who required vascular intervention or who have had vascular Surgery in the lower limbs in the past. Suspected poor compliance.

**RESULT**

A total of 100 patients were eligible for participation in this study. Two groups divided as INSULIN – GROUP (A) 50% and CONVENTIONAL- GROUP (B) 50%.

Data was collected and analyzed.

**TABLE 1. AGE DISTRIBUTION**

AGE GROUP (IN YEARS)	INSULIN (50)	CONVENTIONAL (50)
< 30	02	01
31-45	09	07
46-60	21	24
>60	18	18

**TABLE 2. SEX DISTRIBUTION**

SEX	INSULIN (50)	CONVENTIONAL (50)	P VALUE
MALE	38(76%)	34(68%)	0.3730
FEMALE	12(24%)	16(32%)	

**TABLE 3. ULCER WAGNER GRADE**

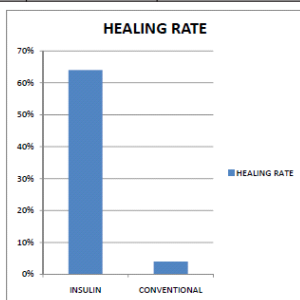
WAGNER GRADE	INSULIN (50)	CONVENTIONAL (50)	P VALUE
1	5(10%)	7(14%)	0.772
2	13(26%)	14(28%)	
3	32(64%)	29(58%)	

**TABLE 4. INFECTION AND ITS RECOVERY**

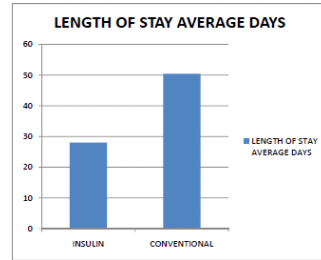
	INSULIN (50)	CONVENTIONAL (50)	P VALUE
INFECTION	43	42	0.779
INFECTION RECOVERY	33(76.74%)	20(47.61%)	0.0055

**TABLE 5. OPERATIVE PROCEDURE**

OPERATIVE PROCEDURE	INSULIN (50)	CONVENTIONAL (50)	P VALUE
CRAFT/FLAP CLOSURE	4	2	0.399
PROXIMAL AMPUTATION	3	18	0.001
DISTAL AMPUTATION	8	13	0.22
DEBRIDEMENT	0	9	0.001
TOTAL	15(30%)	42(84%)	0.0001



**CHART 1. HEALING RATE**



**CHART 2. AVERAGE LENGTH OF HOSPITAL STAY**

**DISCUSSION**

One of the most destructive complications of diabetes is loss of a limb. Three factors lead to tissue necrosis in the diabetic foot- neuropathy, infection and ischemia. Peripheral ischemia may also result from small vessel disease.

However, it is unlikely that the micro vascular disease itself is responsible for foot ulcers. Anaerobic bacteria coexist with aerobic bacteria in most of the cases.

The beneficial effects of INSULIN therapy may be explained on the following grounds. Insulin improves micro vascular supply by increasing & promoting angiogenesis & the amount of oxygen so that gaseous diffusion can occur in relatively avascular or ischemic areas. Normal fibroblast proliferation and collagen production requires a local oxygen tension level of 20 - 40 mm of Hg.

Insulin by its hormonal action stimulates greater degree of neovascularisation which may favor definitive local healing and increase relative increase in oxygen tension per surface area. Oxygen is bactericidal to certain anaerobic or microaerophilic organisms because they lack the appropriate enzymes (superoxide dismutase and catalase) necessary to protect them in highly oxygenated environments.

The findings in the study are significant because it overall decreases the total morbidity associated with diabetic foot ulcers.

**SUMMARY**

This is a prospective study conducted in the Department of General Surgery in a tertiary referral hospital, to evaluate the role of topical application of insulin in chronic non healing diabetic foot ulcers.

Patients in the study group were treated with topical insulin while those in the control group were treated with conventional dressing.

A total of 100 patients participated in the study out of which 50 patients belongs to the study group and 50 patients to the control group.

The patients in both the groups were in the range of 29 – 69 years.

In both the groups, males outnumbered the females. 76 % in the insulin group and 68% in the conventional group were males.

On admission, patients' ulcers were classified according to Wagner's classification and patients belonging to Wagner's grade 2, 3 and 4 were included in the study. Maximum patients in both groups belonged to Wagner's grade 4 i.e. 64% in insulin group and 58% in conventional group.

Patients were evaluated on the basis of presence of risk factors like, HbA1c levels, ankle-brachial index, duration of diabetes mellitus, type of anti diabetic medication, presence of retinopathy, Proteinuria, renal impairment, hypertension, hyperlipidemia, obesity, smoking, coronary artery disease, prior stroke, osteopenia, presence of infection. There were no statistically significant differences in the HBOT and non-HBOT group with regards to these risk factors.

The rate of infection recovery in the insulin group was 76.74% (33 out of 43) whereas in the conventional group, it was 47.61% (20 out of 42). The result was found to be statistically significant favoring insulin group.

Healing rate in insulin group was 64% (32 out of 50) and 4% (2 out of 50) in conventional group. The result was found to be statistically significant favoring insulin group.

In the insulin group, 22% (11 out of 50) patients underwent amputation while in the conventional group 62% (31 out of 50) underwent amputation. The result was statistically significant favoring insulin group. Amputations included both proximal and distal.

30% patients (15 out of 50) in the insulin group underwent operative procedures whereas 84% patients (42 out of 50) in the conventional group underwent operations. The difference was statistically significant. Operative procedures included amputations, graft/flap closure and debridement in the operating room.

The average length of stay in hospital in the insulin group was 28 days and it was 50.42 days in the conventional group. The result was statistically significant favoring insulin group.

## CONCLUSION

Topical application of insulin offers a significant advantage over the conventional method of treatment of diabetic foot ulcers. The overall rate of recovery from infection is definitely higher among patients receiving topical insulin.

Patients undergoing insulin therapy have a higher rate of healing as compared to those being subjected to standard therapy, as insulin by acting as hormone helps in angiogenesis. Patients subjected to insulin therapy have a lesser chance of undergoing amputation. Thus, topical insulin therapy can save a patient from the lifelong physical, social and mental handicap, disability and depression as it helps in reducing the number of amputations. Topical insulin helps in reducing the total number of costly operative procedures that a patient may be subjected to, which include amputations, graft/flap closures, debridement. Thus can save a patient from exposure to risks of anesthesia and other operative risks and it indirectly has an effect on the hospital expenses of the patient. The length of stay in hospital is reduced in patients undergoing insulin therapy thus reducing the inconvenience and expenses of a patient allowing effective utilization of hospital resources and an early return to normal life.

Topical insulin enhances the healing of ischemic, non-healing diabetic leg ulcers and may be used as a valuable adjunct to conventional therapy when reconstructive surgery is not possible.

There is certainly a reason in continuing the use of topical insulin for diabetic foot ulcers as an adjunct to the standard therapy.

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