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ORIGINAL ARTICLE

Effect of Topical Insulin on Wound Healing in Diabetic Foot Ulcer

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ABSTRACT

Background: Diabetic foot ulcers (DFU) are a serious side effect of diabetes mellitus that are associated with high rates of morbidity, mortality, and medical costs worldwide. The purpose of this study was to determine the optimal topical insulin dressing technique for diabetic foot ulcers in terms of the amount of time needed for ulcer healing and the effectiveness of insulin in comparison to conventional techniques.

Methods: This prospective clinical trial was conducted at the Vascular Surgery Department, Zagazig University Hospitals, included 42 diabetic foot ulcer patients randomly assigned into two equal groups: Group A received topical insulin dressing, while Group B received saline dressing. All patients underwent thorough clinical evaluation, ulcer assessment, ABPI measurement, and baseline investigations. Topical insulin dressing was applied daily for one week followed by saline dressing for three weeks, in a repeated 12-week cycle. Ulcer dimensions (area, length, width, depth) and healing progression were assessed weekly. **Results:** The insulin group demonstrated significantly faster and greater reductions in ulcer area, length, width, and depth starting from the second week and persisting throughout the 12-week follow-up ($p<0.05$). The median healing time was significantly shorter in the insulin group (40 days) compared to the saline group (66 days) ($p=0.003$). Notably, 61.9% of insulin-treated ulcers achieved complete healing within 30–40 days versus none in the saline group ($p=0.016$). Both groups maintained adequate glycemic control throughout the study without significant adverse effects.

Conclusion: These findings affirm topical insulin as an optimal dressing strategy, offering enhanced efficacy and faster recovery.

Key words:Diaabetic foot ulcer, Topical insulin, Wound healing

INTRODUCTION

One of the earliest known illnesses in the world is diabetes mellitus. The prevalence of diabetes has shockingly increased worldwide due to a combination of lifestyle changes, physical inactivity, and obesity .Every year, over 18.6 million people worldwide get diabetic foot ulcers. These ulcers appear prior to 80% of lower leg amputations in diabetics and are linked to a higher chance of passing away [1].

Diabetic foot is a common complication of diabetes, where delayed wound healing is influenced by several factors, including impaired angiogenesis, excessive fibrous tissue deposition, and elevated blood glucose levels both at the local and systemic levels [2].

The management of diabetic foot ulcers includes blood sugar monitoring, strict blood sugar control, infection control by local wound care, unloading the area with the proper therapeutic footwear, debriding the wound, and frequent antibiotic treatment (if necrotic tissue is present), and peripheral artery evaluation [3].

According to a previous animal study, insulin may hasten burn wound healing by reducing inflammation and encouraging the formation of collagen. Moreover, the re-epithelialization of the wound can be accelerated by a diffuse insulin injection. This could be the result of insulin encouraging the creation of proteins, which implies that insulin might be involved in the healing process of wounds. Numerous studies have been conducted on the local application of insulin to treat refractory wounds; however, it is unclear what the safe dosage and effective concentration of insulin are [4,5].

The safety of the most recent therapeutic approaches, such as the use of growth factors and stem cells, has not yet been determined, and they are costly. Considering its role in regulating cell differentiation, protein synthesis, and energy consumption, and growth, insulin may also be a crucial hormone in controlling wound healing. In addition to influencing keratinocyte, endothelial, and fibroblast proliferation, migration, and secretion, insulin promotes the growth and development of other cell types. It appears that a method for treating chronic wounds that is both clinically simpler and financially advantageous for patients is required **[4].**

METHODS

This prospective clinical trial study was conducted at the vascular surgery department Zagazig university hospitals, period from March 2024 to March 2025. The series has a six-month follow-up period. All patients gave their informed consent, and the study was approved by the Zagazig University Faculty of Medicine's Research Ethics Council (IRB# 11354). The World Medical Association's Code of Ethics for Human Studies, known as the Declaration of Helsinki, was followed when conducting the inquiry.

Patients who regularly attended the diabetic foot clinic and had a diagnosis of diabetic foot as defined by the 2010 Edition of the American Diabetes Association's Clinical Practice Guidelines for the Prevention and Management of Diabetes Foot Complications were eligible to participate in this study. In addition to being able to go daily for wound dressings or agree to inpatient admission for the course of therapy, participants had to voluntarily volunteer to participate in the trial. Eligible patients had foot ulcers on the dorsal or plantar aspect of the foot, below the ankle, that were no larger than 5 cm in diameter. Only ulcers that met Wegener's Classification's Grade I or Grade II criteria and lacked radiographic signs of osteomyelitis or extensive granulation tissue were included. Additionally, the ulcer had to have been present for fewer than three months at the time of enrollment.

According to Wegener's Classification, patients who had Grade III, IV, or V ulcers at presentation were not allowed to participate in the study. Patients with peripheral limb ischemia that was clinically or radiologically verified by arterial Duplex ultrasonography and the Ankle-Brachial Pressure Index (ABPI) were also not included. Additionally omitted were those who were unable to sustain consistent daily dressing changes or were not receiving frequent follow-up care at the diabetic foot clinic. Patients with significant or total limb necrosis that required immediate amputation upon admission, those who experienced systemic diabetes problems that prevented treatment continuation, and any patients who experienced local or systemic complications during the research.

The two equal groups of eligible patients were divided at random into an interventional group (topical insulin) and a placebo group (topical saline). In addition to their designated local treatment, all participants got normal medical care.

All patients had a thorough clinical evaluation upon registration, which included a thorough medical history that covered demographic information (age, sex), presenting complaints, previous surgery history, and any chronic conditions that may have been linked to the patient, such as respiratory, hepatic, or cardiac conditions. To ensure suitability for the surgery, a comprehensive general checkup was performed to evaluate vital signs and systemic health state. The site, size, depth, shape, consistency, and signs of healing were all evaluated during the local inspection of the ulcer. For uniformity, the paper ruler method was used to measure each ulcer's size. Ten minutes prior to and one hour following

topical insulin application, patients in the interventional group had their blood glucose levels randomly checked using a glucometer to ensure the safety of the procedure, even though topical insulin has very little systemic absorption.

Routine laboratory tests, including complete blood count (CBC), coagulation profile, glycosylated hemoglobin (HbA1c), random blood glucose (RBG), fasting blood glucose (FBG), kidney function tests, and liver function tests, were performed on all patients as part of their baseline investigations. Furthermore, the Ankle-Brachial Pressure Index (ABPI) was computed to rule out substantial peripheral artery disease, and a Duplex ultrasonography examination was conducted to evaluate limb vascularity.

Technique:

Before applying the dressing, local preparation steps were taken in both groups. In order to maximize the healing of the wound bed, this involved surgically debriding the necrotic tissue, removing any fibrotic or scarred tissue, and cleaning the ulcer's margins. Using the Paper Ruler method, the length, width, and depth of each ulcer were measured in cm.

To create a combination for the interventional group, 1 mL of regular insulin was diluted with 10 mL of normal saline. The cost of the 10 mL insulin vial was 55 LE. For seven days in a row, sterile dressings were soaked in this combination and applied directly to the ulcer once every day. Random blood sugar (RBS) measurements were used to check blood glucose levels before and two hours after each dressing application, and then as needed to guarantee patient safety.

Patients in both groups kept using daily saline dressings for the next three weeks after this seven-day intervention period. For a total trial period of 12 weeks, this monthly treatment cycle one week of topical insulin followed by three weeks of saline was repeated three times.

The same procedure was performed in the placebo group, except during the intervention and follow-up phases, only regular saline was administered.

Follow up:

Regular follow-up visits were used to track the development of ulcers in all patients. Clinical assessment of granulation tissue production, healing, and epithelialization, as well as changes in ulcer size (length, width, and depth) using the Paper Ruler method, were the main criteria evaluated. For a total of 12 weeks, the follow-up regimen included daily dressings for 7 days, followed by once-weekly assessments for the next 3 weeks.

Statistical Analysis

The data collected was computerized and statistically analyzed using software known as the Statistical Package for Social Sciences (SPSS) version 2010 for Windows. While continuous quantitative data were presented as mean ± standard deviation (SD) and median when appropriate, categorical variables were shown as frequencies and percentages. Two independent groups with properly distributed data were compared using the Independent Samples Student's t-test. When working with continuous data that wasn't regularly distributed, the Mann-Whitney U test was employed. To ascertain relationships between categorical variables, the Chi-square test or, if appropriate, Fisher's Exact test were used to examine categorical data. The P-value (P-value < 0.05) was fixed at 5%.

RESULTS.

Table 1 shows that, in terms of demographic factors like age and gender, there was no statistically significant difference between the groups under study. Similarly, baseline clinical indicators such as the Ankle-Brachial Pressure Index (ABPI), HbA1c, and random blood sugar (RBS) at baseline and follow-up did not significantly differ between the groups. Over the course of the trial, a notable decrease in RBS was observed within each group, nevertheless. Additionally, there was no discernible difference between the two groups in terms of ulcer-related traits such as the ulcer's length, Wagner grade, or lesion side.

Table 2 revealed that, both at the beginning of the first week and at the end of the first visit, there was no statistically significant difference in the ulcer area between the groups. But starting in weeks

two, three, four, eight, and twelve, the insulin group's ulcer area was noticeably smaller. There is a considerable area of ulcer depth within each group.

Table 3 revealed that the length of the ulcer during the initial visit and the first week varied statistically not significantly across the groups. Although the insulin group's ulcer was significantly shorter in length, the groups' ulcer areas varied statistically significantly during the course of the second, third, eighth, fourth, and twelve weeks. There is a notable reduction in ulcer length among each group.

Table 4 revealed that the groups' differences in ulcer width at the first visit were statistically insignificant. Nonetheless, there was a statistically significant difference in the ulcer's area between the groups at the second, third, fourth, eighth, and twelve-week marks (the insulin group's ulcer's breadth was significantly smaller during all visits). The ulcer's breadth significantly decreases within each group.

Table 5 showed that the depth of the ulcer at the first visit was statistically non-significant, but the area of the ulcer at the first, second, third, and fourth weeks, as well as the eighth and twelveth weeks, was statistically significant (the width of the ulcer was significantly lower among insulin group all over visits). The ulcer's depth significantly decreases throughout each group.

Table 6 showed that there was statistically **significant** difference between groups regarding time till ulcer healing. In the first 40 days, almost 62% of patients who took insulin experienced healing, compared to 0% in the saline group. Patients in the experimental and control groups did not report any study-related adverse effects or problems during the six-month follow-up period. This might have something to do with our inclusion and exclusion criteria, which only included people who were generally healthy and infrequently experienced major issues. Additionally, the local administration of insulin might have helped to prevent difficulties. Similar techniques used in other earlier research did not reveal any adverse effects from the local insulin.

Case 1 (Insulin Group): A diabetic foot ulcer on the stump of the left little toe after amputation was discovered in a 52-year-old female patient with a 10-year history of diabetes mellitus on insulin therapy and a history of hypertension. The ulcer's initial measurements were 3.2cm × 2.1cm × 1.2cm. When topical insulin was used for a week, the ulcer's size shrank to 3.0cm by 2.0cm by 0.4cm. By the conclusion of the fourth week, the dimensions had shrunk to 1.8 cm by 0.5 cm. By the sixth week, the ulcer was barely 0.7 cm × 0.3 cm and had healed considerably. At the start of the seventh week, full recovery was attained.

Table (1) : Comparison between the studied groups regarding demographic data:

	Insulin group n=21 (%)	**Saline group n=21 (%)**	χ^2	**p**
Gender Male Female	 12 (57.1%) 9 (42.9%)	 11 (52.4%) 10 (47.6%)	0.096	0.757
	Mean ± SD	**Mean ± SD**	t	p
Age (year)	52.29 ± 3.02	52.05 ± 4.99	0.187	0.853
investigations	**Mean ± SD**	**Mean ± SD**	t	P
ABPI	1.1 ± 0.09	1.06 ± 0.05	1.46	0.155
HbA1c (%)	7.44 ± 0.32	7.32 ± 0.4	1.065	0.293
Baseline RBS (mg/dl)	185.71 ± 10.28	193.81 ± 18.57	-1.748	0.09
RBS at last FUP	181.67 ± 5.32	183.1 ± 16.01	-0.388	0.701
P	0.02*	<0.001**		
disease-specific data	**Insulin group n=21 (%)**	**Saline group n=21 (%)**	χ^2	P
Side				

	Insulin group n=21 (%)	**Saline group n=21 (%)**	χ^2	**p**
Left Right	17 (81%) 4 (19%)	13 (61.9%) 8 (38.1%)	1.867	0.172
Wagner grade First Second	 4 (19%) 17 (81%)	 5 (23.8%) 16 (76.2%)	Fisher	>0.999
	Median (range)	**Median (range)**	Z	p
Duration of ulcer	6(4 – 120)	7(2 – 120)	-1.078	0.281

χ^2Chi square test t independent sample t test , Z Mann Whitney test
t independent sample t test $^{\infty}$p for paired sample t test between baseline and last visit

Table (2) : Comparison between the studied groups regarding area of ulcer over time

	Insulin group Median (range)	**Saline group Median (range)**	**Z**	**p**
First visit	9(6 – 24)	8.7(4.18 – 22.05)	-1.078	0.281
First week	5(3.2 – 14.4)	6.5(3.4 – 18.86)	-1.224	0.221
Second week	2.34(1.43 – 7.5)	5.06(2.38 – 15.91)	-2.785	**0.005***
Third week	1.2(0.66 – 6.9)	3.8(1.43 – 12.16)	-2.693	**0.003***
Fourth week	0.56(0.2 – 5.25)	3(0.72 – 9.6)	-3.791	**<0.001****
Eighth week	0.18(0.03 – 1.5)	2.28(0.4 – 8.25)	-5.172	<0.001**
Twelve week	0.09(0.02 – 0.5)	3.23(1.2 – 4.14)	-3.722	**<0.001****
p^{∞}	<0.001**	<0.001**		

Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant $^{\infty}$p for Wilcoxon signed rank test between baseline and last visit

Table (3) : Comparison between the studied groups regarding length of ulcer over time

	Insulin group Median (range)	**Saline group Median (range)**	**Z**	**p**
First visit	4(3 – 5)	3(2.2 – 5)	-1.503	0.133
First week	2.7(2 – 4)	2.7(2 – 4.7)	-0.699	0.485
Second week	2.1(1.1 – 3)	2.6(1.7 – 4.5)	-2.109	0.035*
Third week	1.7(0.8 – 3)	2.1(1.3 – 3.8)	-2.893	0.004*
Fourth week	1(0.4 – 2.5)	2(0.9 – 3.4)	-4.119	<0.001**
Eighth week	0.5(0.1 – 1.5)	1.8(0.5 – 3.3)	-5.027	<0.001**
Twelve week	0.25(0.1 – 1)	1.8(0.6 – 2.3)	-3.583	**<0.001****
p^{∞}	<0.001**	<0.001**		

Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant $^{\infty}$p for Wilcoxon signed rank test between baseline and last visit

Table (4) : Comparison between the studied groups regarding width of ulcer over time

	Insulin group Median (range)	**Saline group Median (range)**	**Z**	**p**
First visit	2.1(2 – 4.8)	2.9(1.9 – 4.5)	-0.257	0.797
First week	2(1.5 – 3.6)	2.5(1.7 – 4.1)	-2.042	**0.041***
Second week	1.3(1 – 2.7)	2.2(1.4 – 3.7)	-2.956	**0.003***
Third week	1(0.6 – 2.3)	1.9(1.1 – 3.2)	-2.964	**0.003***
Fourth week	0.7(0.5 – 2.1)	1.5(0.8 – 3)	-3.459	**<0.001****
Eighth week	0.4(0.3 – 1)	1.4(0.8 – 2.6)	-4.94	**0.042***
Twelve week	0.25(0.1 – 0.8)	1.9(1.1 – 2)	-3.746	**<0.001****
p^{∞}	**<0.001****	**<0.001****		

Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant $^{\infty}$p for Wilcoxon signed rank test between baseline and last visit

Table (5): Comparison between the studied groups regarding depth of ulcer over time

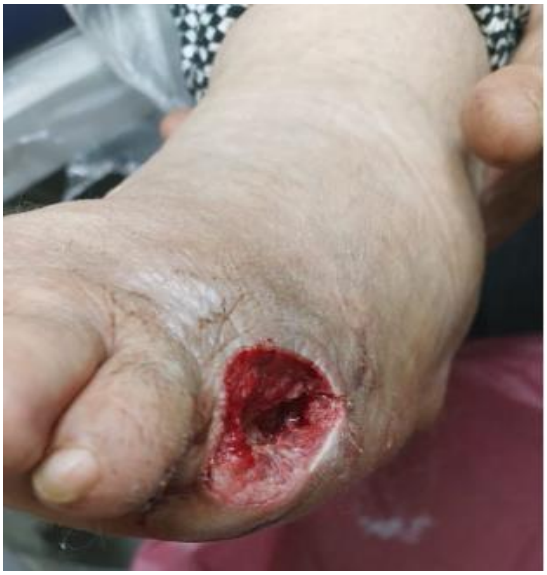
	Insulin group Median (range)	**Saline group Median (range)**	**Z**	**p**
First visit	1(0.5 – 2)	1.9(0.5 – 4)	-1.766	0.077
First week	0.5(0.4 – 1.5)	1.6(0.4 – 3.5)	-3.487	**<0.001****
Second week	0.3(0.2 – 1.2)	1.4(0.3 – 3)	-4.185	**<0.001****
Third week	0.25(0.1 – 0.9)	1(0.3 – 2.7)	-4.407	**<0.001****
Fourth week	0.2(0.1 – 0.6)	0.6(0.2 – 2.1)	-3.352	**<0.001****
Eighth week	0.1(0.1 – 0.2)	0.5(0.1 – 2)	-2.776	0.006*
Twelve week	0.1(0.1 – 0.2)	0.75(0.3 – 1.8)	-2.756	0.004*
p^{∞}	<0.001**	<0.001**		

Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant $^{\infty}$p for Wilcoxon signed rank test between baseline and last visit

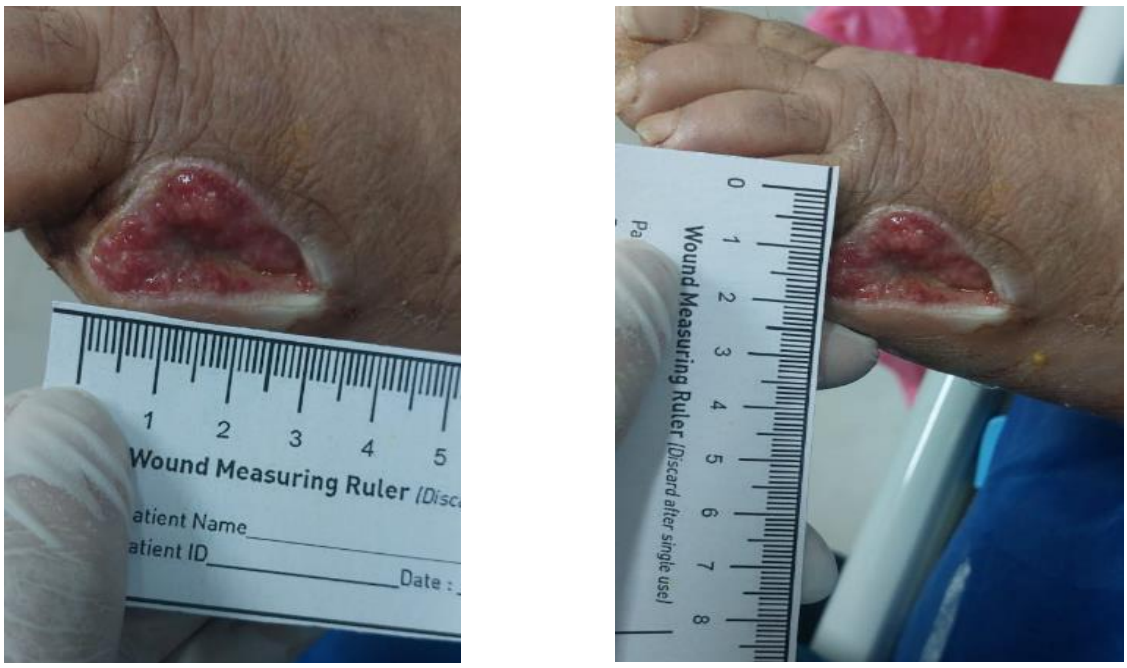
Table (6) : Comparison between the studied groups regarding time of healing

	Insulin group Median (range)	**Saline group Median (range)**	**Z**	**p**
Time of healing	40(30 – 90)	66(42 – 75)	-2.951	0.003*
30 – 40	13 (61.9%)	0 (0%)	χ^2	
>40 – 50	4 (19%)	4 (19%)		
>50 – 60	0 (0%)	9 (42.9%)		
>60 – 70	0 (0%)	4 (19%)	5.809	0.016*
>70 – 80	0 (0%)	4 (19%)		
>80 – 90	4 (19%)	0 (0%)		

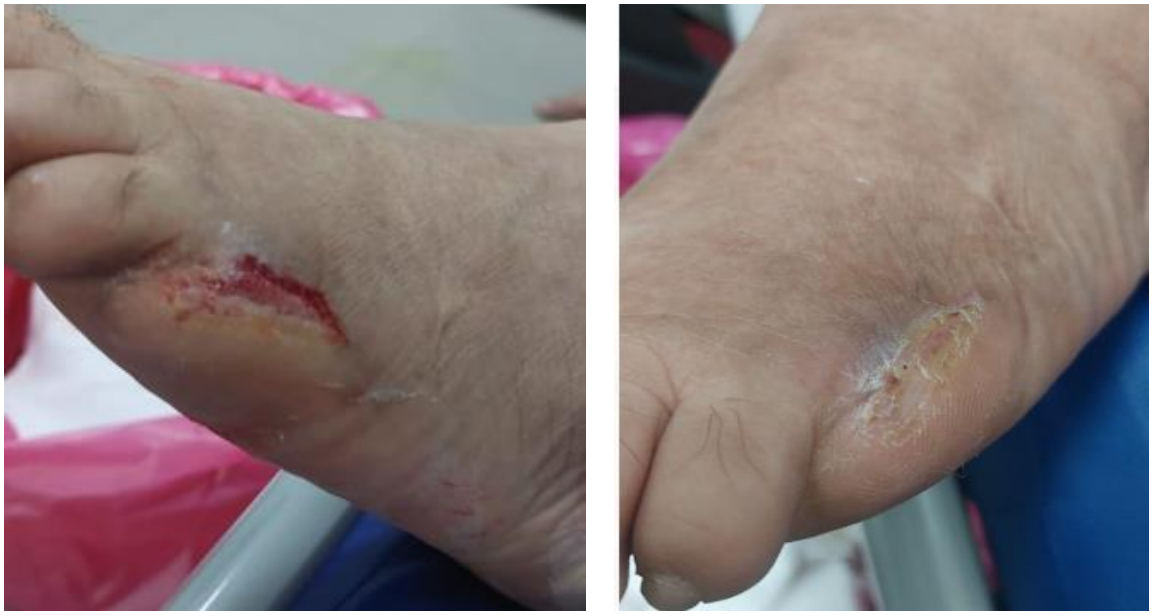
Z Mann Whitney test χ^2Chi square for trend test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant



Before treatment



Diabetic foot ulcer measurement



After treatment

Case 1; The ulcer's initial measurements were 3.2cm × 2.1cm × 1.2cm. When topical insulin was used for a week, the ulcer's size shrank to 3.0cm by 2.0cm by 0.4cm. By the conclusion of the fourth week, the dimensions had shrunk to 1.8 cm by 0.5 cm. By the sixth week, the ulcer was barely 0.7 cm × 0.3 cm and had healed considerably. At the start of the seventh week, full recovery was attained.

DISCUSSION

Although systemic insulin treatment improves pressure ulcer healing and lowers surgical site infections in diabetic patients, it has the disadvantage of causing hypoglycemia and hypokalemia. On the other hand, topical insulin helps both diabetic and non-diabetic people heal wounds without altering blood glucose levels [6].

The demographic profiles of the two groups in this study insulin (n=21) and saline (n=21) were comparable. With no discernible gender difference, the insulin group comprised 57.6% men and 42.9% females (22), whereas the saline group had 52.4% males (23) and 47.6% females (24). In terms of age, the saline group averaged 52.05±4.99 years, while the insulin group averaged 52.29±3.02 years. There was no significant

difference between the two groups (t = 0.187, p = 0.853), suggesting that their demographics were similar.

When comparing the insulin and saline groups' comorbidities and duration of diabetes, the saline group had 38.1% (25) absent and 61.9% present hypertension, whereas the insulin group had 61.9% absent and 38.1% present. However, there was no significant difference between the two groups (χ^2 = 2.381, p = 0.123). The insulin group's median duration of diabetes was 13 years (range: 8–20), whereas the saline group's was 10 years (range: 7–25). There was no significant difference in the groups' profiles (Z = 0.187, p = 0.853) [7].

Clinical studies comparing the insulin and saline groups revealed no significant difference, with the insulin group's mean ABPI of 1.1±0.09 compared to the saline group's 1.06±0.05 (t = 1.46, p = 0.155). There was no significant difference in the HbA1c levels between the insulin and saline groups, which were 7.44± 0.32% and 7.32 ± 0.4%, respectively (t = 1.065, p = 0.293). The insulin group's baseline random blood sugar (RBS) was 185.71 ± 10.28 mg/dl, while the saline group's was 193.81±18.57 mg/dl (p = 0.02). This difference was significant. The insulin group's RBS at the last follow-up was 181.67 ± 5.32 mg/dl, while the saline group's was 183.1±16.01 mg/dl (t = -0.388, p = 0.701), indicating no discernible difference.

It appears that topical insulin largely affects local wound healing rather than systemic vascular function or long-term glucose management, as seen by the lack of significant variations in ABPI and HbA1c between the insulin and saline groups. Large vessel perfusion is probably unaffected by insulin's localized effects on cellular repair and angiogenesis since ABPI represents macrovascular circulation. Likewise, the lack of increases in HbA1c suggests that topical insulin has no discernible effect on systemic glucose metabolism [8].

When comparing disease-specific data between the insulin and saline groups, the insulin group had ulcers on the left side in 81% of cases and the right side in 19%. In contrast, the saline group had ulcers on the left side in 19% of cases and the right side in 81% of cases. However, there was no significant difference between the two groups (χ^2 = 1.867, p = 0.172). There was no discernible difference between the insulin group's 61.9% first grade and 38.1% (25) second grade ulcers and the saline group's 23.8% (30) first grade and 76.2% (31) second grade ulcers (Fisher > 0.999), according to the Wagner grade distribution. The insulin and saline groups had median ulcer durations of 6 months (range: 4–120) and 7 months (range: 2–120), respectively. These differences were not statistically significant (Z = -1.078, p = 0.281).

Area, length, width, and depth of ulcers compared to the saline and insulin groups throughout time revealed initial similarities but notable differences favoring insulin as therapy advanced. Starting at 9 cm² (insulin) versus 8.7 cm² (saline) (p = 0.281), the ulcer area decreased significantly from week three (p = 0.029) to 0.15 cm² versus 0.54 cm² by week twelve (p = 0.074). The difference in length between 4 and 3 cm (p = 0.133) decreased to 0.5 and 0.9 cm (p = 0.101), reaching significance at week eight (p = 0.036). The width decreased from 2.1 cm to 2.9 cm at the beginning (p = 0.797) to 0.25 cm to 0.4 cm (p = 0.042), which was significant from week two (p = 0.041). With highly significant differences from week two (p<0.001), depth began at 1 cm versus 1.9 cm (p = 0.077) and reached 0.1 cm compared 0.2 cm (p = 0.504). Insulin's better efficacy in lowering ulcer size across all dimensions was demonstrated by Wilcoxon tests, which indicated substantial overall reductions (p < 0.001).

Topical insulin's better ability to reduce ulcer size is probably caused by its ability to promote collagen deposition, angiogenesis, and cellular proliferation. Insulin promotes fibroblast and keratinocyte activity, which speeds up the production of extracellular matrix and re-epithelialization [9]. It also promotes the production of vascular endothelial growth factor (vascular epidermal growth factor), which improves blood flow and oxygen delivery to the area[10]. Furthermore, insulin regulates inflammation by lowering oxidative stress and excessive cytokine activity, this facilitates

the transition of the wound from the inflammatory to the proliferative stages [11]. Faster healing without systemic glucose changes is further supported by its localized immunomodulatory and antibacterial actions [12]. Together, these processes account for the notable decrease in ulcer size seen with insulin therapy.

There was a significant difference in the median healing time between the insulin and saline groups (Z = -2.951, p = 0.003), with the insulin group taking 40 days (range: 30–90) and the saline group taking 66 days (range: 42–75). A significant trend favoring faster healing with insulin was indicated by the distribution of healing times, which showed that 61.9% (26) of the insulin group healed within 30–40 days and 19% within both >40–50 and >80–90 days, while the saline group had 19% in >40–50, 42.9% (22) in >50–60, and 19% in both >60–70 and >70–80 days. No cases healed within 40 days. These results demonstrate how well insulin works to speed up the healing process.

Uddin, Hasina, and Kumar Shill's study [13] Between July 2017 and June 2019, 60 diabetic foot ulcer patients were evaluated at Rajshahi Medical College Hospital and divided equally into two groups: Group A received topical insulin, and Group B received saline. Most patients were male, with male-to-female ratios of 2.7:1 in Group A and 4:1 in Group B. The mean ages were similar (P=1.00). Group A showed a significantly greater reduction in ulcer area (314.30±171.26 mm²) and percentage reduction (15.30±3.28%) compared to Group B (110.5±56.23 mm² and 6.35±2.03%, respectively; P<0.001).

Stephen, **Agnihotri, and Kaur [14]** conducted a study to compare the effects of topical insulin versus normal saline dressing on pressure ulcer healing. Fifty patients were randomized equally into two groups, receiving either insulin dressing (1 U/cm² twice daily) or saline dressing for seven days. Ulcer dimensions and healing progression were assessed using the Pressure Ulcer Scale for Healing (PUSH) at baseline, day 4, and day 7. Blood glucose levels were monitored in the insulin group to ensure safety. By day 7, the insulin group showed a significant reduction in mean wound area compared to the saline group (P<0.05). The study concluded that topical insulin is a safe and effective option for promoting pressure ulcer healing.

A prospective study by **Nagaraj and Subbiah** [15] About 60 diabetic foot ulcer patients who sought outpatient treatment at the Perambalur tertiary care hospital's Department of General Surgery between September 2021 and August 2022. They comprised all patients with ulcers ranging from grade 1 to 2 who gave written informed permission. Patients with foot ulcers brought on by other causes, such as osteomyelitis or renal insufficiency, were not included. They used the number lot method (randomization) to split the chosen study participants into three groups. Each of the three groups (groups 1, 2, and 3) consisted of twenty study participants. Local insulin was administered to group 1, topical phenytoin was administered to group 2, and a standard saline dressing was administered to group 3. Before the trial started, they measured the size and depth of the wound, and for a month, they checked in every seven days. IBM Corp., Armonk, NY's SPSS, version 21, was used to analyze the data. The study participants in the three groups had nearly identical mean fasting blood sugar levels, mean age, and mean duration of diabetes. For the insulin, normal saline, and phenytoin groups, the mean difference in wound size before and after treatment was 4.98, 3.74, and 3.805 square centimeters, respectively. The three previously mentioned groups' mean differences were statistically significant (P < 0.001). For the insulin, normal saline, and phenytoin groups, the mean difference in wound depth before and after treatment was 47.005, 4.945, and 4.820 square centimeters, respectively. The three previously mentioned groups' mean differences were statistically significant (P < 0.001).

As a result, as compared to the other two groups, the local insulin group's wound healing improved statistically significantly. The average time for wound healing was 20, 26, and 23 days for the insulin, normal saline, and phenytoin groups, respectively. The aforementioned three groups' mean

differences were statistically significant (P < 0.001).

Biradar, Patil [16] conducted a 12-month prospective analytical study on 60 diabetic patients aged 25–70 years with newly diagnosed diabetic foot ulcers. Patients were randomized into two groups: Group A received topical insulin dressings, while Group B received normal saline dressings. Wound areas were measured on days 0, 7, and 15. By day 15, the percentage reduction in wound surface area was significantly greater in the insulin group (67.8±11.45%) compared to the saline group (49.51±18.21%; p<0.001). Additionally, granulation tissue appeared earlier in the insulin group (6.08±2.15 days) than in the saline group (9.48±4.21 days), indicating a statistically significant difference

Prasad, Thomas and Mahadevan [17] 70 patients with diabetic foot who met the inclusion criteria were chosen, and they were divided into two groups: one for insulin (test n = 35) and another for saline (control n = 35). Following initial wound debridement, the wound was routinely examined for the presence of granulation tissue, necrotic tissue, and slough. The ulcer's initial and final sizes were noted, and the % decrease in wound surface area was calculated. They found that the mean ultimate ulcer diameters in the saline and insulin groups differed significantly. The student independent t-test shows that this difference is highly significant with a p-value of less than 0.01. The student independent t-test revealed a statistically significant difference in the presence of granulation tissue between the insulin and saline groups, with a p-value of less than 0.01.

In a different trial, **Katiar and Shanker [18]** evaluated the effectiveness of traditional saline dressings, platelet-rich plasma (PRP), and topical insulin in treating diabetic foot ulcers. After meeting all inclusion and exclusion criteria and gaining the required written and informed consent from patients and their families, 60 patients were randomized to one of three dressing groups: normal saline dressing, topical insulin dressing, or PRP dressing. This study was a duration-based prospective comparative analysis. At days 0, 7, and 14, the ulcers' size, depth, and % reduction in wound area were assessed. At day 14, the normal saline group's average ulcer size was 4.19±0.95, the insulin group's was 2.64±0.83, and the PRP group's was 2.08±0.47. On day 14, the average ulcer depth was 2.35±1.42 (mm) in the PRP group, 5.35±1.18 in normal saline, and 4.30±1.38 in insulin. The mean ulcer size decreased by 27.02±4.46, 50.31±7.53 in the insulin group, and 63.80±5.75% in the PRP group.

A study by **Lyba Ghayour and Baseerullah [19]** carried out a randomized control trial in the South Surgical Ward's Emergency and Outdoor Department at Mayo Hospital in Lahore. The six-month study period ran from September 2022 until March 2023. Following an explanation of the technique, 86 patients who fit into Wagner's classification I and II and who were admitted to the general surgery department's outdoor/emergency department at Mayo Hospital in Lahore after giving their informed consent were included in the study. Patients were then chosen at random (by lottery) to be in Group A (Topical insulin dressing) or Group B (Normal saline soaked dressing). The ulcer area decrease rate was expressed in days. The label "yes" indicated that the patient required re-debridement, and "no" indicated that they did not. Groups A and B had baseline mean wound areas of 34.87±29.23 cm2 and 27.45±24.00 cm2, respectively. The area of the wound decreased to 9.35±10.75 cm2 and 7.33±9.29 cm2 after two weeks. Patients in Group A saw a substantially lower mean number of days for the rate of ulcer area reduction compared to those in Group B (p-value<0.001). Patients in Group B experienced a considerably higher rate of re-debridement than those in Group A (18.6% vs. 46.5%, p-value = 0.006). Reduced need for minor to major foot amputations and redebridement will result from improved wound healing.

Mahmoud Elrefaey and El-Deeb's study [20] evaluated how topical insulin affected the healing of diabetic wounds in patients with diabetic foot ulcers. After two and three weeks of daily topical insulin treatment, the insulin-treated group showed a statistically significant improvement in all aspects of foot ulcer assessment when compared to the

control group. Additionally, the study demonstrated that the insulin group's diabetic foot ulcers healed faster than the control group's.

CONCLUSION

When compared to conventional saline dressings, topical insulin dressings dramatically improve the healing of diabetic foot ulcers, lowering lesion dimensions and healing time. It is a safe, efficient, and useful therapeutic approach that could enhance clinical results and lessen the financial strain on healthcare systems brought on by complications from diabetic foot.

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