

Effect of Topical Insulin Versus Normal Saline Dressing on Diabetic Wound Healing: An Experimental Comparative Study

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ABSTRACT

Introduction: Diabetic foot ulcer is one of the most significant and devastating complications and a major cause of hospitalization among patients with diabetes. It leads to severe economic and social burdens. The management of Diabetic foot ulcers remains a major therapeutic challenge. Hence, the present study was conducted to compare the topical insulin and normal saline dressing on wound healing among patients with a diabetic foot ulcers. **Methods:** An experimental research design was adopted to conduct the study with 60 samples matched with the inclusion criteria in Saveetha Medical College and Hospital. Samples were allocated into experimental group I (n=30) and experimental group II (n=30) by simple random sampling. The baseline outcomes were measured at the beginning of the study. Pre-assessment was done using the Bates-Jensen wound assessment tool in experimental I & II. Experimental group I received topical insulin dressing, and experimental group II received normal saline dressing daily for 14 days. Post-assessment was done on the seventh and fourteenth days using the same tool for both groups. Data were analyzed using SPSS. **Results:** A significant improvement in the level of wound healing was observed at the level of $p < 0.001$ within and between a group of pretest, post-test I, and Post-test II by repeated measures ANOVA. The overall comparison of wound healing between experimental groups I & II revealed that the calculated F value of $F=12.679$ shows a statistically ($p < 0.001$) significant difference in the level of wound healing at all lev-

els. **Conclusion:** It is concluded that topical insulin and normal saline dressing effectively improve wound healing of diabetic foot ulcers. Nevertheless, the topical insulin was more effective than the normal saline dressing, proving that topical insulin significantly impacts the wound healing process. However, further study may be conducted to design the intervention protocol and better understand the role of insulin in healing.

Keywords

Diabetic foot ulcer, Topical insulin dressing, Normal saline dressing, Wound healing, Diabetes mellitus

Imprint

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INTRODUCTION

Diabetes mellitus (DM) is a major public health concern and challenging the world in the 21st century. The National Diabetes Statistics Report 2022 by the Centers for Disease Control and Prevention (CDC) stated that 1.4 million new cases of diabetes were diagnosed among people ages 18 and older in 2019 [1]. The prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030, with a maximum increase of 79.4 million individuals in India [2, 3]. Uncontrollable diabetes with improper treatment may lead to long-term complications of microvascular disorders, macrovascular disorders, peripheral neuropathy, diabetic foot ulcer (DFU), and coma or death. DFU is one of the most significant and devastating complications of diabetes. Risk factors associated with diabetic foot ulcers include peripheral neuropathy, peripheral vascular disease, weak immune system, and foot trauma were also reported risk factors in the pathophysiology of foot ulcers. The burden of DFU is expansive, leading to economic, social, and pressure on public health workers globally [4]. The prevalence of DFU was 6.3% in the year 2018 globally and commonly occurred in older adults [5], and it is estimated that 15% of patients with diabetes will suffer from DFU during their lifetime [6]. The major cause of hospitalization in patients with di-

abetes is DFU which is also considered a significant source of morbidity [7-10]. DFU results in approximately 20% of hospital admissions among patients with DM due to infection, gangrene, amputation, and even death if left untreated properly [11]. The length of hospital stay was longer than the inflammation severity [12]. The management of DFU remains a major therapeutic challenge which implies an urgent need to review strategies and treatments to remove foreign material, reduce bacterial contamination, and remove cellular debris or exudate from the wound's surface. However, numerous studies have shown that proper management of DFU can significantly reduce, delay, or prevent complications such as infection, gangrene, amputation, and even death [13-15]. Wound dressing stimulates neovascularization and healthy cell proliferation. Standard solutions for wound irrigation are normal saline, sterile water, or potable water when normal saline or sterile water is unavailable [16]. Different strategies, including honey dressings, medicated dressings, povidone iodine dressings, platelet-rich plasma dressings, saline dressings, vacuum dressings, papaya dressings, karaya powder dressing, and topical insulin dressings, are available in the management of DFU. It is known that normal saline wound irrigation is the conventional practice of wound management and has been followed for many decades. Topical insulin is the newer strategy in treating DFU, as insulin is a peptide hormone and growth factor that can restore damaged skin and accelerate healing [17-19]. Topical insulin also improves the formation of new blood vessels and increases fibrosis [20] without changing blood glucose levels in diabetic and non-diabetic patients [21], such as burn wounds [22]. Considering the health care needs and reviews, the investigators observed the hypothesis of the difference in the level of wound healing after administration of topical insulin and normal saline dressing between the experimental group I & II patients with DFU.

MATERIALS AND METHODS

An experimental comparative study was conducted among patients with diabetic foot ulcers to compare the impact of normal saline and topical insulin dressing on the level of wound healing. It was conducted at Saveetha Medical College and Hospital Chennai after obtaining formal permission from the hospital authority and concerned department. The samples included in the study were patients of the age group

between 20 to 60 years of both the sex, meeting Wagner's ulcer grade II and III, both conscious and unconscious, and willing to participate in the study. Patients who had been operated on for Diabetic foot infections earlier (in the same foot), ulcers of Wagner's grade III with osteomyelitis, grade IV which requires amputation (major) and grade V, X-rays showing features of osteomyelitis, Doppler show in gross atherosclerotic arterial changes and venous abnormalities like varicosities of lower limbs, uncontrolled diabetes with HbA1C Levels >8 were excluded from the study. Sixty patients with diabetic foot ulcers were selected for the study using simple random sampling. Experimental group I (n=30) was selected from the I unit of male & female surgical wards, and Experimental group II (n=30) was selected from the II unit of male & female surgical wards. The investigators explained the study's purpose and obtained consent from the participants. The demographic variables and clinical variables were collected by using a structured questionnaire. The pre-test assessment was done using the Bates-Jensen wound assessment tool for both groups. Bates – Jensen wound assessment Tool (BWAT) is a standardized tool for assessing diabetic foot ulcers developed by Barbara Bates-Jensen; it evaluates 13 wound characteristics with a numerical rating scale and rates from best (1) to worst (5). It is interpreted as 1 to 13 – Healthy tissue; 13 to 60 – Tissue regeneration; 60 to 65 – Tissue degeneration; and 65 and above – Gangrene. The participants in the experimental group I received topical insulin dressing. This dressing was done by covering the wound with long acting insulin sprinkled over the gauze piece after cleaning the wound aseptically daily for 14 days. Experimental group II received normal saline dressing applied on the wound after cleaning the wound aseptically daily for 14 days. The post-assessment I was done on the seventh day, and post-assessment II was done on the fourteenth day by using Bates-Jensen wound assessment tool for both experimental group I and experimental group II. Data were tabulated and analyzed by the descriptive and inferential using SPSS statistical package, and the probability of 0.05 or less was taken as statistically significant.

RESULTS

Out of 30 participants in each group, more than 50% were aged 50 years and above, 80-90% were male and had ulcer in the fore foot, not adhered to the diabetic diet and had, 70% were undergone till school ed-

ucation, 70-80% were residing in rural area, 90% had type II DM, 50-60% had DM for more than 5 years, all 100% were not following the foot care practices, 50-70 were on the treatment of both insulin and oral hypoglycemic agent, and were hospitalized with the duration of 1- 2 weeks and had hypertension. 70-90% had grade II under Wagners grading of ulcer scale in both experimental group I & experimental group as represents in Table 1.

Table 1
Baseline outcome measures

Baseline outcome mea- sures	Experimental GroupI		Experimental GroupII	
	No	%	No	%
Age				
40–45years	2	6.7	0	0
46–50years	7	23.3	0	0
51–55years	5	16.7	7	23.3
56–60years	16	53.3	23	76.7
Gender				
Male	27	90.0	25	83.3
Female	3	10.0	5	16.7
Educational Status				
Illiterate	4	13.3	0	0
School education	23	76.7	22	73.3
Diploma	1	3.3	1	3.3
Graduate	2	6.7	7	23.3
Income				
5000–9000	9	30.0	1	3.3
10, 000–15, 000	17	56.7	22	73.4
15, 000and above	4	13.3	7	23.3
Residence				
Urban	6	20.0	9	30.0
Rural	24	80.0	21	70.0
Dietary Practices				
Normal diet	28	93.3	25	83.3
Diabetic diet	2	6.7	5	16.7
Type of DM				

Baseline outcome mea- sures	Experimental GroupI		Experimental GroupII	
	No	%	No	%
Type I	3	10	2	7
Type II	27	90	28	93
Duration of DM				
5-10 Years	12	40	14	47
More than 10 Years	18	60	16	53
Regular Foot care practices				
Yes	-	-	-	-
No	30	100	30	100
Site of DFU				
Forefoot	24	80	25	83
Hind foot	6	20	5	7
Method of treatment				
Oral hypoglycemic agents	8	26.7	4	13.3
Insulin	0	0	10	33.3
Both	22	73.3	16	53.4
Duration of hospitalization				
One week	23	76.7	8	26.7
Two week	4	13.3	16	53.3
Three weeks	1	3.3	5	16.7
Four weeks and above	2	6.7	1	3.3
Presence of HT				
Yes	18	60	17	57
No	12	40	13	43
Wagners grading				
Grade II	21	70.0	29	96.6
Grade III	9	30.0	1	3.4

Out of 30 participants in each group, all 30(100%) were in the stage of tissue regeneration in the pretest, post-test 1 and post-test 2 in both Experimental group I and Experimental group II as depicts in Table 2.

The table 3 shows the overall comparison of wound healing among patients with diabetic foot ulcer in Experimental group I (Topical Insulin Dressing) and Experimental group II (Normal Saline Dressing) revealed that the calculated “F” value of F=12.679 shows

Table 2
Pre-test and Post-test score on level of wound healing

Level of Wound Healing	Experimental GroupI						Experimental GroupII					
	Pretest		PostTest1		PostTest2		Pretest		PostTest1		PostTest2	
	F	%	F	%	F	%	F	%	F	%	F	%
Healthy tissues	-	-	-	-	-	-	-	-	-	-	-	-
Tissue regeneration	30	100	30	100	30	100	30	100	30	100	30	100
Tissue degeneration	-	-	-	-	-	-	-	-	-	-	-	-
Gangrenes	-	-	-	-	-	-	-	-	-	-	-	-

that there was significant difference in the level of wound healing at the all levels which was found to be statistically significant at $p<0.001$ level.

Table 3

Between and within group analysis of topical insulin and normal saline dressing on Level of wound healing

Study Group	Test	Level of Wound Healing	
		Mean± SD	Within group F-value
Experimental group I	Pre test	43.23±5.24	F=12.679 P<0.001***
	Post-test 1	33.77±4.66	
	Post-test 2	28.67±4.66	
Experimental group II	Pre test	43.07±4.63	
	Post-test 1	39.07±4.03	
	Post-test 2	31.00±3.98	
Pair wise comparison		Mean Diff.	Sig
Experimental group I	Pretest Vs. Post-test 1	9.467	P<0.001***
	Pretest Vs. Post-test 2	14.567	P<0.001***
	Post-test 1 Vs. Post-test 2	5.100	P<0.001***
Experimental group II	Pretest Vs. Post-test 1	4.000	P<0.001***
	Pretest Vs. Post-test 2	12.067	P<0.001***
	Post-test 1 Vs. Post-test 2	8.067	P<0.001***
Between group comparison		Mean Diff.	Sig
Experimental Group I & II	Pretest	0.167	P=0.897
	Post-test 1	5.300	P<0.001***
	Post-test 2	2.333	P=0.042, P<0.05*

The pairwise comparison of wound healing in the Experimental group I shows that the calculated value of mean difference score between pretest Vs. Post- test 1 (9.467), pretest Vs. Post-test 2 (14.567) and post-test 1 Vs. Post-test 2 (5.100) was observed to be statistically significant at $p<0.001$ level. This clearly shows that after the administration of topical Insulin Dressing among the patients with diabetic foot ulcer there was significant improvement in the level of wound healing among them in the Experimental Group I.

The pairwise comparison of wound healing in the Experimental group II shows that the calculated value of mean difference score between pretest Vs. Post test 1 (4.000), pretest Vs. Post test 2 (12.067) and post test 1 Vs. Post test 2 (8.067) was observed to be statistically significant at $p<0.001$ level. This clearly shows that there was significant improvement in the level

of wound healing among them in the Experimental group II who had been administered with normal saline dressing.

From the above table between the groups comparison of Experimental Group I and Experimental group II shows that the mean difference score in Post Test 1 (5.300) and Post-test 2 (2.333) shows that there was significant difference in the level of wound healing which was found to be statistically significant at $p<0.001$ and $p<0.05$ level respectively. This was evident from the post-test 2 mean scores of Experimental Group I (28.67±4.66) and Experimental group II (31.0±3.98) in which the wound healing was improved significantly in the experimental group than the Experimental group II. This infers that Topical Insulin Dressing was found to be effective in improving the level of wound healing among the patients with diabetic foot ulcer than the patients in the Experimental group II who had undergone normal saline dressing. The trends in level of wound healing during the study period is depicted in Figure 1.

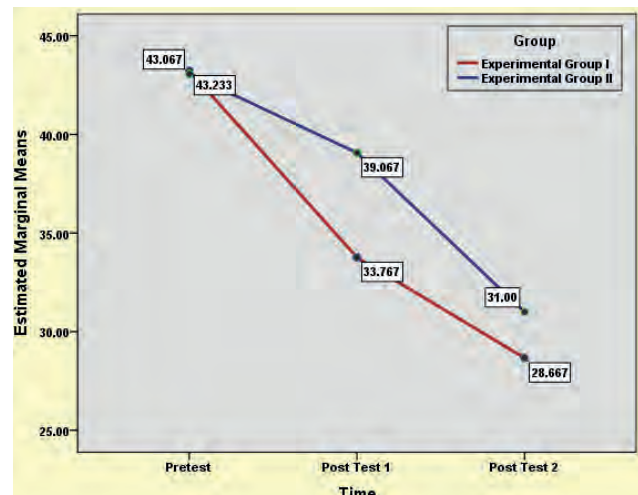


Figure 1. Trend graphs showing the effectiveness of topical insulin and normal saline dressing on wound healing by Repeated Measures ANOVA

DISCUSSION

DFU lowers the quality of life due to emotional and physical distress, productivity, and financial losses. Furthermore, it may lead to amputation due to an increased risk of ulcer progression. Overall, the lower limb amputation rate is 15 times higher in patients with DM when compared to those without DM, which is approximately 50%-70% of all lower limb amputations due to DFU [23]. In addition, every 30 s, one leg is amputated due to DFU globally [24]. The primary goal in managing DFU is to assess the wound and provide ad-

equate care to avoid amputations and promote well-being. Hence the study intensively analyzed the wound level and compared the level of wound healing on topical insulin dressing with conventional normal dressing. The present study reported the pre-test and post-test & II shows that all participants in both groups had tissue regeneration. Though they were in tissue regeneration before and after the intervention, the mean difference was higher in topic insulin dressing than in normal saline dressing. It shows that topical insulin dressing is more effective in wound healing than normal saline dressing. Topical insulin improves wound healing by decreasing the levels of reactive oxygen species, which can induce effects on lipids, proteins, and DNA in burn wounds in rats [25]. In addition, topical insulin acts as an anti-inflammatory effect in wounds by increasing the number of M2 macrophages and IL-10 levels to eliminate dead tissues [26] and increases the number of newly formed blood vessels in healing tissues [25]. The present study finding is supported by a review of animal and human evidence by Jiao Wang et al., which reported that topical insulin improves wound healing through several mechanisms without causing side effects [27]. Another study by Radwa M Ali et al. demonstrated topical short and long-acting insulin in diabetic wound healing. It was found that both topical insulin treatments resulted in an acceleration of the wound healing process with no significant difference between short and long-acting preparations of insulin [28]. In contrast, a study by Vikash Katiar et al. compared the topical application of insulin versus platelet-rich plasma versus regular normal saline dressing to heal DFU. The result reported that platelet-rich plasma is a promising agent for faster wound healing and a more significant reduction in the size of DFU compared to topical insulin and other conventional dressings. However, topical insulin dressing is more effective than conventional dressing [29]. K Ramarao et al. stated that topical insulin dressing provided favorable outcomes in patients with DFU by significantly reducing wound area compared to normal saline dressing and positively reducing wound infection [30]. Vijay V Kamat et al. also reported a significant reduction in ulcers after 15 administrations of topical insulin and safe and efficacious treatment of diabetic foot ulcers [31]. Similarly, Md Abbas Uddin et al. proved that topical insulin dressing provided better outcomes in patients with DFU by significantly reducing wound area compared to normal saline dressing [32]. Paritoshsingh B. Thakur

et al. concluded that the topical application of insulin is significantly associated with the fastening of wound healing in diabetic ulcer [33]. Regarding baseline outcomes, 80-90% were male, and 10-20% only had completed till graduation. Some studies have shown that foot ulceration is more common in men with diabetes than in women [34]. Poverty and illiteracy are the risk factors for DFU due to the usage of inappropriate footwear and the late presentation of foot lesions [35]. Wagner's Grade II of DFU had shown a statistically significant association with the experimental group I post-test level of wound healing. This finding is in line with the study by Maryam Mohammad Zadeh et al. revealed that the only predictor significantly associated with time to healing was the University of Texas classification grade II [36]. The measurement of the wound culture is limited to the present study. Despite this, based on the current study finding with the support of similar findings, we may recommend utilizing the topical insulin dressing in today's clinical practice to complement the conventional dressing method. Continuous practicing topical insulin dressing improves wound healing, reduces the patient's burden by cost, and prolongs hospitalization. However, further study could be done with a large sample and grade II & grade IV DFU and comparing short- and long-acting insulin dressing to design the intervention protocol and better understand the role of insulin in healing.

CONCLUSION

The present study's findings conclude that topical insulin and normal saline dressing effectively improve wound healing of diabetic foot ulcers. Nevertheless, the topical insulin was more effective than the normal saline dressing, proving that topical insulin significantly impacts the wound healing process. Therefore, topical insulin can be included in DFU management strategies to decrease the disease burden and improve the quality of life. However, further study may be conducted with a large sample and grade II & grade IV DFU and a comparison of short and long-term insulin dressing to design the intervention protocol and better understanding of the role of insulin in healing.

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CONFLICT OF INTEREST

Authors declare no conflict of Interest.

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