ORIGINAL RESEARCH

Comparative study between conventional dressing and local insulin application in diabetic foot ulcers

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Abstract
Background: Diabetic foot is one the commonly faced surgical conditions by surgeons. It is one of the major causes for morbidity in diabetic patients. Inspite of various types of dressings available, choosing an appropriate dressing is a challenging aspect in the management of diabetic foot. Topical insulin causes rapid wound remodelling in non healing ulcers and its topical application in wound healing needs further study.
Methodology: Our study is a randomized prospective study was conducted in the Department of Surgery, Teaching Hospital attached to Kodagu Institute of Medical Sciences, Madikeri on 50 patients with non healing chronic diabetic ulcer during the period of November 2022 to October 2023. The patients are randomly divided into two groups study and control group (Study – Insulin; Control – Normal saline). Wound measurement and culture growth was taken on day 1 and end of 14th day. Mean reduction in ulcer area and culture growth at the end of 14 days was noted.
Results: In our study, we have observed that mean reduction in ulcer size in insulin (study) (8643.68±2348.95 mm^2) is statistically significant compared to normal saline group (control) (2067.45±464.88 mm^2) and there is 56.8±2.3% reduction in size in insulin group compared to 17.7±1.4% which is statistically significant.
Conclusions: Tropical insulin has an angiogenic, fibroblast growth favouring and antibacterial property which canbe used in faster healing of chronic diabetic ulcers as topical agent and thereby reducing its systemic side effects.
Keyword: Diabetic ulcers, Normal saline, Topical insulin, Wound area

Introduction

Diabetic foot disease is a major financial burden on healthcare systems worldwide and poses a growing global public health challenge due to its high morbidity. The prevalence of type 2 diabetes mellitus is exploding worldwide and is expected to involve more than 500 million people in the next 10 to 15 years.[1]

Diabetes mellitus is the major cause of foot pathology, causing foot ulcerations from infection, ischemia and neuropathy. Most of the non-traumatic amputations are usually secondary to diabetic foot. Infection occurs in approximately half of diabetic foot ulcers, and most of these require amputation. Diabetic foot ulcers are one of the major causes for hospital admissions and costlier aspects of diabetic treatment. This has led to a growing risk of amputation among diabetic patients, because 85% of patients presenting with a foot ulcer are at risk for a subsequent amputation. Various methods has been proposed by many authors over a period of time for healing and prevention of diabetic ulcer.[1,2]

The ideal topical therapy for diabetic foot ulcer is yet to be defined. Standard method of dressings include povidone iodine and normal saline dressings but their disadvantage is maintaining the moist environment for longer duration.[3,4] To overcome this disadvantage, newer type dressings with various mechanism have been introduced. It includes hydrocolloid wound gels, topical phenytoin dressing, silver nitrate dressing, enzymatic debridement compounds, hyperbaric oxygen therapy, cultured skin substitutes, and other

wound therapies have been advocated. All of these therapies are associated with significant expense and are being utilized in some situations without sufficient scientific evidence in favor of their efficacy.[2]

Topical application of insulin has stimulatory effect on VEGFs and fibroblasts along with it's antibacterial properties. This stimulatory effect may helps in wound healing by faster formation of healthy granulation tissue. Various studies shown the efficacy of topical insulin in faster healing of diabetic foot ulcers.[3,5]

Cost-effective Treatment plan for diabetic foot includes

- Surgical debridement
- Surgery or other therapies to improve circulation
- Special dressing and antibiotics.

Diabetic foot ulcers constitutes for 50% of indication of non-traumatic amputations. Hence there is a need for evaluation of newer methods for treating these ulcers which are economical and more effective in increasing healing rate and decreasing the rate of amputations. Some studies on topical insulin have shown increased healing rate in chronic diabetic foot ulcers than other conventional dressings.[4,5,6] Topical insulin acts by stimulating VEGFs, fibroblasts and enhancing granulation tissue formation, decreasing collagenase activity.[5] Systemic absorption of insulin on topical use in diabetic ulcer was not significant. Other side effects noticed on use of topical insulin in diabetic ulcer were pain during local application initially and hypergranulation and rarely hypoglycemia.[4,5,6]

Though many studies are conducted on using topical insulin in chronic ulcers only few studies are conducted on diabetic ulcers and such studies have not been conducted in our institute.

Methodology

This prospective randomized comparative study included 50 patients with diabetic ulcers admitted in Teaching Hospital of Kodagu Institute of Medical Sciences, Madikeri from November 2022 to October 2023 satisfying all the inclusion criteria mentioned below after obtaining consent and clearance from the ethical committee.

Inclusion Criteria

Patients with chronic ulcers (ulcers of 4 weeks duration) with diabetes mellitus. Wound size <5% Total body surface area.

Exclusion Criteria

Chronic non-healing wounds of other etiology Diabetes mellitus with gangrenous changes.

Wounds with osteomyelitis

Other co-morbid conditions like generalized debility and other factors, which adversely affect wound healing

The data was collected from 50 patients who are having diabetic ulcers satisfying the inclusion criteria mentioned above. The whole sample population was divided into group A and group B randomly. Group A contain 25 patients and Group B contain 25 patients.

Eleven patients underwent detailed clinical examination and relevant investigations and the wounds were thoroughly debrided and the ulcer dimensions as well as the surface area assessed using measuring tape, before both types of dressings were applied. The control group and study group were subjected to daily dressing. Discharge is sent for culture and sensitivity. Empirical antibiotics are started withciprofloxacin and metronidazole changed to sensitive antibiotics after sensitivity report. The patients were followed up for 2 weeks in both study and control groups.

Application of Dressing

Group A is dressed with topical insulin (study group) and group B with normal saline (control group).

Topical insulin

Regular insulin was diluted with normal saline to form a suspension. Sterile gauze was soaked in the suspension and spread evenly over the ulcer and also injected to edges of wound subcutaneously and left for 24 hours till the next dressing.

Dosage of regular insulin depend on the surface area of ulcer

- 0 to 5 cm2 - 5U
- 5.1 to 9cm2 -10U
- 9.1 to 15cm2 -15U
- >15cm2 - 20U

Control group dressing was done with normal saline once a day.

Before applying both dressing daily wound is cleaned with normal saline and debridement is done if necessary. Ulcer size is measured initially and at the end of 14 days, size is recorded. Size is measured twice and mean of two is taken. Wound is also observed for granulation tissue, discharge at the end of 14 days are recorded, wound discharge is sent for culture and sensitivity on 14th day of treatment.

Statistical analysis

Analysis was done by using Cramer's V test, Independent-Samples t-test, repeat measure ANOVA and level of significance chosen at $p<0.05$.

Results

Table 1: Age-wise distribution

Age groups (years)		Groups		Total
		Control	Study	
40-45	Number	5	3	8
	Percentage	62.5%	37.5%	100.0%
45-50	Number	5	4	9
	Percentage	55.6%	44.4%	100.0%
50-55	Number	4	4	8
	Percentage	50.0%	50.0%	100.0%
55-60	Number	4	2	6
	Percentage	66.7%	33.3%	100.0%
60-65	Number	6	7	13
	Percentage	46.2%	53.8%	100.0%
65 and above	Number	1	5	6
	Percentage	16.7%	83.3%	100.0%
Total	Number	25	25	50
	Percentage	50.0%	50.0%	100.0%
Significance		0.546		

Table 2: Gender-wise distribution

			Groups		Total
			Control	Study	
Gender	Male	Number	19	20	39
		Percentage	48.7%	51.3%	100.0%
	Female	Number	6	5	11
		Percentage	54.5%	45.5%	100.0%
Total		Number	25	25	50
		Percentage	50.0%	50.0%	100.0%
Significance			0.733		

In the STUDY group total number of males and females were 20(80%) and 5(20%) respectively. In the CONTROL group total number of males and females were 19(76%) and 6(24%) respectively. Statistically in this study, there was no significant difference in sex distribution between interventional and control group.

Table 3: Culture growth on day 1 in two groups

			Groups		Total
			Control	Study	
Culture (Day 1)	Positive	Number	20	21	41
		Percentage	48.8%	51.2%	100.0%
	Negative	Number	5	4	9
		Percentage	55.6%	44.4%	100.0%
Total		Number	25	25	50
		Percentage	50.0%	50.0%	100.0%
Significance			0.713		

In our study on day one, 21(84%) patients in study group showed growth on culture and 4(16%) patients showed no bacterial growth. In control group 21(84%) patients showed growth on culture media and remaining 4(16%) showed no growth.

There was no significant difference between two groups in positive culture growth on day one.

Table 4: Culture growth on day 14 in two groups

			Groups		Total
			Control	Study	
Culture (Day 14)	Positive	Number	20	13	33
		Percentage	60.6%	39.4%	100.0%
	Negative	Number	5	12	17

		Percentage	29.4%	70.6%	100.0%
Total		Number	25	25	50
		Percentage	50.0%	50.0%	100.0%
Significance			0.037		

Table 5: Mean wound area on day 1 and day 14

Culture	Groups	N	Mean	Std.Deviation	Std. Error Mean
Day 1 area	Control	25	12671.4400	18461.24091	3692.24818
	Study	25	14488.4000	14940.76439	2988.15288
Day 14 area	Control	25	10301.3200	15060.27986	3012.05597
	Study	25	6816.0400	7839.66993	1567.93399

Table 6: t-test for Equality of Means

Culture	t	DF	Sig. (2-tailed)	MeanDifference	Std. ErrorDifference	95% Confidence Interval of theDifference	
						Lower	Upper
Day 1 area	-.383	48	.704	-1816.960	4749.92150	- 11367.31727	7733.39727
Day 14Area	1.026	48	.310	3485.280	3395.71762	-3342.26787	10312.82787

Table 7: Mean and percentage reduction in wound

	Groups	N	Mean	Std.Deviation	Std. Error Mean
Reduction	Control	25	2369.8800	3440.07671	688.01534
	Study	25	7671.5600	7267.81520	1453.56304
Reduction in Percent	Control	25	17.6400	7.52905	1.50581
	Study	25	57.2000	9.63933	1.92787

Table 8: t-test for Equality of Means

	t	DF	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Reduction	-3.297	48	.002	-5301.680	1608.16996	-8535.12242	-2068.23758
Reduction in Percent	-16.172	48	.000	-39.560	2.44625	-44.47851	-34.64149

In our study, we have observed that mean reduction in ulcer size in insulin group (7671.56±1453.56 mm^2) is statistically significant compared to normal saline group (2369.88±688.015 mm^2) and there is 57.2±1.9% reduction in size in insulin group compared to 17.64±1.5% reduction in normal saline group which is statistically significant.

Discussion

An ideal dressing is every surgeon's desire, a dressing that promotes chronic ulcer healing without any complications. Successful wound dressing should keep the wound moist and be devoid of any adverse reactions such as infection, maceration and allergy.[7,8]

Diabetic ulcers are chronic wounds, stuck in inflammation phase and shows cessation of epidermal growth. The present study was conducted at Kodagu Institute of medical sciences, Madikeri to study the effect on diabetic ulcer healing dynamics.

Our study compares the efficacy of topical insulin with conventional normal saline dressing on chronic non-healing diabetic ulcers. In both the groups the base line characteristics were similar. In our study non-healing ulcers of more than 4 weeks were chosen and in this study the treatment period was 2 weeks. In patients treated with topical insulin dressings the mean wound area reduced from 14488.400 to 6816.0400. The percentage of reduction in wound size is 57.2±1.9% compared to the

17.64±1.5% in control group. This study demonstrates that topical insulin dressings results in rapid wound area reduction and reduces wound infection in diabetic foot ulcers.

In the present study it was seen that the incidence of diabetic ulcers were more in males (84%) as compared to females (16%). The second national data source, NHDS documented higher hospital rates in males suffering from diabetic ulcers.

In our study, there is very significant faster reduction in wound size in insulin group compared to normal saline group that is on day 14 (P-0.002) on wound area which is in study group (6816.0400 mm^2) when compared to control group

(10301.3200 mm^2). Overall this study shows that insulin dressing is safe and effective in treating chronic foot ulcers. This study was conducted only for 2 weeks and complete epithelialization and wound reduction was not awaited for.

Conclusion

With the use of topical insulin dressing in comparison with the normal saline dressing for the treatment of diabetic foot ulcers, the following conclusions were derived.

- Compared to study group, topical insulin dressing showed faster and better healing rates.
- Topical insulin group had better wound area and percentage reduction
- There were no adverse reactions on topical application.
- Compared to normal saline group the appearance of granulation tissue was earlier in topical insulin group.
- Topical insulin may also have an anti infective effect.

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