

A COMPARATIVE STUDY OF EFFICACY OF LOCAL INSULIN VERSUS TOPICAL PHENYTOIN IN DIABETIC FOOT ULCER

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ABSTRACT

BACKGROUND

Diabetic foot ulcer is the common complication and it affects almost 15% of all diabetic patients. Majority of the ulcer can heal. Healing is better in neuropathic ulcer than neuroischaemic ulcer. In India, diabetic foot ulcer is common cause of nontraumatic amputation of limbs, which is preventable.

MATERIALS AND METHODS

It is an open labelled randomised prospective study conducted at Department of General Surgery, Konaseema Institute of Medical Sciences, Amalapuram. Total 90 patients divided randomly into three groups include this study as per exclusion and inclusion criteria. Group A were diabetic foot ulcer belongs to topical insulin dressing group. Group B belongs to topical phenytoin group and group C belongs to conventional wound care group.

RESULTS

In group A, size of the wound reduced from mean value 6.8 cm² to 1.4 cm²; percentage change in the size of the wound was 79.4%. In group B, the size of the wound reduced from 5.9 cm² to 2.4 cm²; percentage reduction in the size of the wound was 59.3%. In group C, the mean size of the wound was reduced from 7.1 cm² to 4.2 cm²; percentage reduction was 40.8%. The depth of the wound also reduced in the entire three groups. Mean reduction in the depth of the wound in group A was 9 mm to 2 mm that is 77.7%. In group B, the percentage mean reduction was 69.0%, and in group C, it was 51.2%.

CONCLUSION

In present study, we have found that percentage change in the mean surface area of wound in insulin group is 79.4%. The percentage change in mean of wound surface area of wound in group B (phenytoin group) was 59.3%, which is less than insulin group. There was significant change in the depth of wound in both the group, but in insulin group, it is better than phenytoin group.

KEYWORDS

Diabetic Foot Ulcer, Insulin, Phenytoin.

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BACKGROUND

Globally, around 422 million adults are living with diabetes in 2014, which was 108 million in 1980. Over the past decade, the prevalence has risen faster in low and middle-income countries.¹ Diabetes mellitus is a group of common metabolic disorder that shares the phenotype of hyperglycaemia. The metabolic dysfunction associated with it causes secondary pathophysiological changes in multiple organ systems that leads to complication in many parts of the body that increases the overall risk of dying prematurely.²

The morbidity associated with long-standing diabetes caused by lesions involving both large and medium-sized muscular arteries (macrovascular diseases) and capillary dysfunction in target organs (microvascular diseases). The macrovascular disease causes accelerated atherosclerosis that along with diabetic neuropathy leads to lower extremity gangrene and non-healing ulcer.³

Diabetic foot ulcer is the common complication and it affects almost 15% of all diabetic patients. Majority of the ulcer can heal. Healing is better in neuropathic ulcer than neuroischaemic ulcer. In India, diabetic foot ulcer is common cause of non-traumatic amputation of limbs, which is preventable.^{4,5,6}

Management of diabetic foot is a big challenge; it is a multisystem approach, which includes the nervous, vascular, skeletal, immune and integumentary system.

Since ancient days, various techniques were used for the dressing of wounds. Sushruta in ancient India has described the procedure and more than 100 plants for treatment of wounds.

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Over 100 known physiological factors contribute to wound healing deficiencies in diabetic patients. These include impaired or decreased growth factor production, angiogenesis response, collagen accumulation, epidermal barrier function, quantity of granulation tissue, keratinocytes and fibroblast migration and proliferation number of epidermal nerves.⁷

From the various studies, it has been found that wound healing in diabetic foot ulcer can be improved by topical insulin, which acts by enhancing AKT (anti-serine-threonine kinase) and ERK (anti-phosphor extra cell signal-regulated protein kinase) pathway.⁸

It has also been found that phenytoin, which is an anti-epileptic drug is associated with increase in neovascularisation, collagen deposition, granulation tissue formation and decrease in collagenase activity.⁹

Present study has been designed to evaluate the efficacy of topical insulin versus topical phenytoin on wound healing.

MATERIALS AND METHODS

Before start of the study, written consent was obtained from the institutional ethics committee. Informed written consent was obtained from patient who has been participated into the study.

It is an open labelled randomised prospective study conducted in the Department of General Surgery, Konaseema Institute of Medical Sciences, Amalapuram. Total 90 patients divided randomly into three groups include this study as per exclusion and inclusion criteria. Group A were diabetic foot ulcer belongs to topical insulin dressing group. Group B belongs to topical phenytoin group and group C belongs to conventional wound care group.

Inclusion Criteria

All the diabetic foot ulcer up to grade 2 as per Wagner-Meggitt classification of diabetic foot.^{10,11}

Exclusion Criteria

Ulcer with other aetiology, osteomyelitis, patient with renal failure and other factor, which effect wound healing.

Before start of the study, details of the patient were recorded that includes, age, sex, duration of diabetes mellitus, treatment, peripheral pulses and neuropathic changes. All the routine investigations of the patient were done. Strict glycaemic control was brought in all patients before study.

Culture and sensitivity of the entire wound was done and proper antibiotic was prescribed. Surgical debridement of wound was done as per the requirement of the wound. Also, before start of the study, wound size and depth of the wound was measured and further during the study, it was measured weekly till 8 weeks.

The total 90 patients included in this study divided into three groups. Group A were given insulin dressing, half of the calculated insulin requirement of the patient was diluted upto 1 mL and injected into base of the wound and remaining half of the requirement was injected on abdominal wall.¹² In another group B, all the insulin required by the

patient was injected on the abdominal wall and wound dressing was done with topical phenytoin. Dose of the phenytoin was as per the size of the wound 0-5 cm² 100 mg, 5-10 cm² 150 mg, 10-15 cm² 200 mg and >15 cm² 300 mg.¹³ Third group were treated with abdominal insulin and conventional wound dressing.

Various parameters like size and depth of wound, granulation tissue status in the form of absent pink and good vascularity were observed weekly up to eight weeks. Fasting and postprandial blood sugar was measured everyday average blood sugar were calculated for each group.



Figure 1. Diabetic Foot Ulcer Wound

RESULTS

	Age Mean	Sex		Duration of DM (Mean)	FBS (Mean) mg/dL
		M	F		
Group A insulin	58 yrs.	19	11	10.2 yrs.	90.2
Group B phenytoin	60 yrs.	20	10	11.4 yrs.	88.4
Group C control	56 yrs.	21	9	12.1 yrs.	92.0

Table 1. Demography of Patient

	Size of the Wound (Mean) Cm ²	Depth of the Wound
Group A	6.8	9 mm
Group B	5.9	8.4 mm
Group C	7.1	8.6 mm

Table 2. Size and Depth of Wound Before Treatment

	Size of the Wound Mean	Percentage Reduction	(After Treatment) (8 weeks) Depth of Wound	Percentage Decrease in Depth
Group A	1.4 cm ²	79.7	2 mm	77.7
Group B	2.4 cm ²	59.3	2.6 mm	69.0%
Group C	4.2 cm ²	40.84	4.2 mm	51.2%

Table 3. Size and Depth of Wound After Treatment

	Group A		
	Poor	Pink	Sound Heart
1 st week	30	0	0
2 nd week	5	22	3
4 th week	0	0	29

Table 4. Development of Granulation Tissue in Group A

	Group B		
	Poor	Pink	Sound Heart
1 st week	30	0	0
2 nd week	9	19	2
4 th week	0	2	28

Table 5. Development of Granulation Tissue in Group B

	Group C		
	Poor	Pink	Sound Heart
1 st week	30	0	0
2 nd week	16	12	2
4 th week	-	10	20

Table 6. Development of Granulation Tissue in Group C

Total 90 patients having diabetic foot ulcer were included in this study and were divided into three groups. In group A, mean age of the patient were 58 yrs. and out of 30 patients 19 were males and 11 were females. Mean duration of diabetes was 10.2 yrs. and mean fasting blood sugar was 90.12 mg/dL. In group B, there was 30 patients with mean age 60 yrs. Out of thirty, 20 were males and 10 patients were females. Duration of diabetes was 11.4 yrs. (mean) and mean fasting blood sugar was 88.4 mg/dL. Third group C that is control group, men age was 56 yrs. and 21 were males and 9 were females, mean duration of diabetes mellitus was 12.1 yrs. Mean fasting blood sugar was 92.0 mg/dL.

As per table 2 in the start of the study in group A, mean size of the wound was 6.8 cm² and mean depth of the wound was 9 mm. Group B patient having mean size of wound 5.9 cm² and depth 8.4 mm.

Patients in group C have mean size of wound 7.1 cm² and depth of wound 8.6 mm.

From table 3, it is clear that in group A, size of the wound reduced from mean value 6.8 cm² to 1.4 cm², percentage change in the size of the wound was 79.4%. In group B, the size of the wound reduced from 5.9 cm² to 2.4 cm² percentage reduction in the size of the wound was 59.3%.

In group C, the mean size of the wound was reduced from 7.1 cm² to 4.2 cm² percentage reduction was 40.8%.

The depth of the wound also reduced in the entire three groups. Mean reduction in the depth of the wound in group A was 9 mm to 2 mm that is 77.7%. In group B, the percentage mean reduction was 69.0%, and in group C, it was 51.2%.

From table-4, granulation tissue formation in group A at the wound of second week, 5 patients has poor granulation tissue, group B has 9 patients with poor granulation tissue and group C has 10 patients with poor granulation tissue.

At the end of second week, 22 patients has pink granulation tissue in Group A 19 patients with same in group B and 12 patients with pink granulation in group C.

At the end of fourth week, all patients has healthy wound in group A, group B 28 patients has healthy wound and in group C 20 patients healthy wound.

DISCUSSION

The present study is a hospital-based study conducted in the Department of General Surgery, Konaseema Institute of Medical Sciences from June 2015 to December 2017.

In present study, we have found that percentage change in the mean surface area of wound in insulin group is 79.4%, which similar to the work of Greenway SE et al and Swaminathan et al.^{14,15} The percentage change in mean of wound surface area of wound in group B (phenytoin group) was 59.3%, which is less than insulin group similar to the

study of Kato Tokahahi¹⁶ and Moy LS et al.¹⁷ There was significant change in the depth of wound in both the group, but in insulin group is better than phenytoin group, which is similar to the study of Goenka et al.¹⁸

In our study, we have found the patient in group A that is insulin group has early growth of granulation tissue than the phenytoin group. In second week, the insulin group has very good response than control group.^{8,19} Both the drugs work by different mechanism from, but local injection of insulin has better response in wound heading than other methods.^{7,19}

CONCLUSION

In our two year hospital-based study of diabetic foot ulcer healing, we have found that local installation of insulin in the diabetic foot ulcer is better than topical phenytoin and phenytoin is effective than convention wound dressings.

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