RESEARCH
www.commprac.com
ISSN 1462 2815

EFFECT OF LOCAL INSULIN INJECTION ON WOUND VASCULARISATION IN PATIENTS WITH DIABETIC FOOT ULCER DISEASE

Dr. V. Manohar Reddy [1], Dr. J. Sridhar [2], Dr. Nikhil Reddy [3] and Dr. Krithika Kiruba [4]*

[1,3] Post Graduate, Department of General Surgery,
Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem.
[2] Professor and HOD, Department of General Surgery,
Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem.
[4] Assistant Professor, Department of General Surgery,
Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem. Corresponding Author

DOI: 10.5281/zenodo.11066233

Abstract

Background and Objectives- Diabetic foot is a common complication of diabetes. The aim of the present study was to investigate the effect of local insulin injection on granulation tissue formation in the wounds of patients with diabetic foot ulcer **Methods-** It was a Prospective comparative study done between May 2023 to July 2023 (3 months). In Patients with Diabetic foot ulcer admitted in the department of General surgery in VMKVMCH. A total of 50 patients were studied. 50 patients enrolled in study were allocated by lot method to either in insulin group (n=25) and control group (n=25). **Results-** Mean age group was 56.05 years. 30 males - 60% and mean age group is 57.76 years. 20 females - 40% and mean age group is 56.05 years. Mean duration of illness was 6.8 years. With maximum being 20 years and Minimum being 6 months. Fasting blood glucose in the two groups were maintained around 100-200 mg/dl. Local injection showed a marked effect on systemic blood glucose level 1-2 hrs of injection then gradually returned to pre injection level by 4 hrs of injection. No significant difference in blood glucose was found between two groups before injection or upto 4hrs after injection. **Conclusion-** Local insulin injection is noted to be effective for treating refractory diabetic wounds. Local injection of insulin reduced the body blood glucose level. Regular insulin with dose of 1U/cm2 was found to be safe, without hypoglycaemic episodes.

Keywords: Diabetic Foot, İnsulin, Granulation Tissue, Ulcers

INTRODUCTION

One typical complication of diabetes is diabetic foot. Many variables, including elevated blood glucose levels (both locally and systemically), ineffective wound angiogenesis, and fibrous tissue deposition, can contribute to the delayed growth of the local wound granulation tissue in individuals with diabetic foot ulcers.[1,2] Insulin therapy administered locally may promote wound healing in diabetics, according to data from clinical and animal studies.[3] Insulin has been shown in an earlier animal study to expedite the healing of burn wounds by decreasing inflammation and increasing collagen deposition. Furthermore, a diffuse injection of insulin into the wound can hasten the process of wound re-epithelialization.[4,5] This implies that insulin may be involved in the process of wound healing and could be the result of insulin stimulating protein synthesis. Although the local application of insulin in the management of refractory wounds has been extensively researched, the safe dosage and effective concentration of insulin remain unclear.[6]

Poor wound healing in diabetic ulcer wounds is thought to be primarily caused by angiogenesis dysfunction and disorder.[6,7,8] The main issues that need to be resolved right now for patients to heal from wounds are enhancing angiogenesis and regaining

the structure and function of the vasculature. The aim of the study is to compare the effect of local insulin injection on wound vascularization in patients with diabetic foot syndromes and to assess the effects of local insulin injection on ulcer healing clinically in terms of changes seen in ulcer size and granulation and radiologically by Ankle peak systolic velocity.

MATERIALS AND METHODS

It was a Prospective comparative study done between May 2023 to July 2023 (3 months). In Patients with Diabetic foot ulcer admitted in the department of General surgery in VMKVMCH. A total of 50 patients were studied.

Inclusion Criteria-

- Age > 20
- Size >1cm to <10 cm on dorsum of foot/plantar surface/toes/around medial/lateral malleolus.
- Patients with HbA1c < 9
- Haemoglobin > 9 gm

Exclusion Criteria-

- Infected diabetic ulcers extending deep upto level of tendons and bone.
- Uncontrolled diabetes HbA1c > 9
- Severe Anaemia
- Other causes of foot ulcer
- Patients not willing for treatment

METHODOLOGY

50 patients enrolled in study were allocated by lot method to either in insulin group (n=25) and control group (n=25). In the insulin group, 1 ml of physiological saline was used to dilute half of the calculated dose of isophane protamine biosynthetic human insulin (premixed 30:70; Novo Nordisk Pharmaceutical Industries, Inc., Clayton, NC, USA), which was then injected diffusely into the diabetic foot ulcer's base. The abdomen wall was subcutaneously injected with the remaining half of the insulin dose. Two shots of insulin were given each day.

One milliliter of normal saline was subcutaneously injected into the base of the diabetic foot ulcer and the predicted dose of human insulin was administered subcutaneously to the abdominal wall in the control group. Two injections were given each day. For seven days in a row, injections were given to both groups. Patients regular diabetic correction is adjusted accordingly to capillary blood glucose. Insulin injection was given twice daily in the wound site. Wound is reassessed every 7 days clinically and with doppler after 3 weeks.

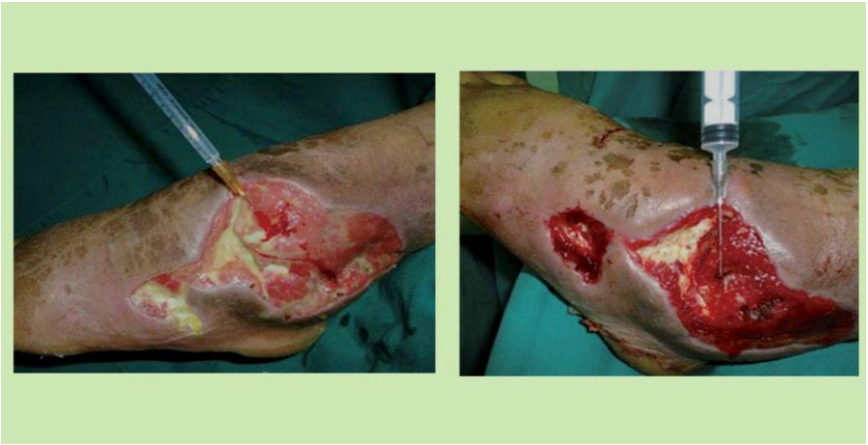

Figure 1: Wound assessment

Following debridement, the fasting fingertip blood glucose levels of the two groups were measured using the blood glucose meter at 0.5, 1.0, 2.0 and 4.0 h after injection each day, the fasting fingertip blood glucose levels of the two groups were also determined, and the measurements and injections were conducted for 21 days. A technique from a prior study (15) was used to assess the extent of granulation tissue expansion. In summary, translucent tracing paper was used to capture the original ulcer wound regions of the two groups before to treatment. After treatment, the wound size was measured using the same technique.

Statistical analysis

The statistical analysis was performed using SPSS for windows version 22.0 software (Mac, and Linux). The findings were present in number and percentage analyzed by frequency, percent, and Chi-square test. Chi-square test was used to find the association among variables. The critical value of *P* indicating the probability of significant difference was taken as <0.05 for comparison.

RESULTS

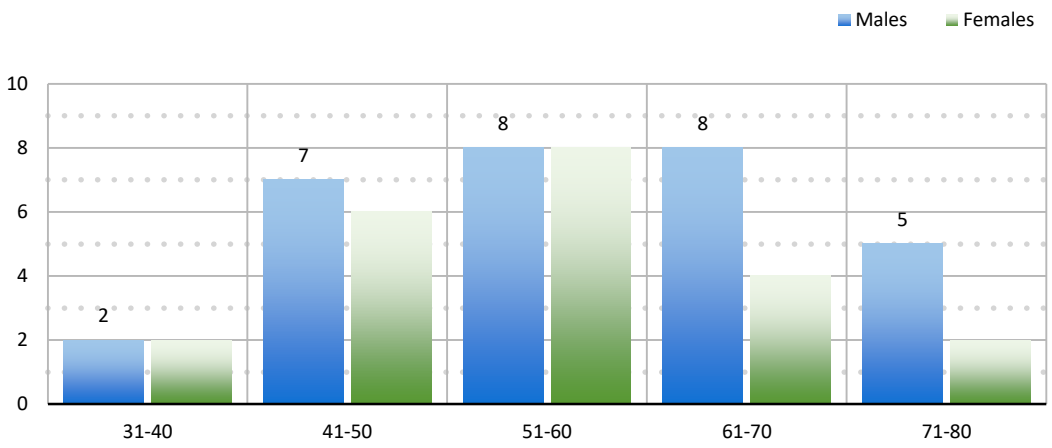

Figure 2: Distribution based on Age and Gender

As per figure 2 Mean age group was 56.05 years. 30 males - 60% and mean age group is 57.76 years. 20 females - 40% and mean age group is 56.05 years. Mean

duration of illness was 6.8 years. With maximum being 20 years and Minimum being 6 months.

Table1: Changes in the capillary blood glucose level

Group	Blood glucose before insulin	0.5h	1.0h	2.0h	4.0h
Insulin (n=25)	180.84 ± 17.28	170.08±11.7	168.68±10.26	119.7±3.24	178.18±4.80
Control n=25)	185.08±10.98	168.12±3.42	167.04±4.86	119.88±5.5	180.82±5.76

As per table 1 Fasting blood glucose in the two groups were maintained around 100-200 mg/dl. Local injection showed a marked effect on systemic blood glucose level 1-2 hrs of injection then gradually returned to pre injection level by 4 hrs of injection. No significant difference in blood glucose was found between two groups before injection or upto 4hrs after injection.

Table 2: Clinical Assessment

	0 days	7 days	14 days	21 days
Insulin	7.09±0.18	24.87±0.24	45.06±1.58	60.25±1.24
Control	7.28±0.28	18.66±0.45	23.06±1.57	44.36±1.45

As per table 2 Granulation tissue clinically denotes angiogenesis. After 3 weeks of injection Granulation tissue in the insulin group was more marked 60.25% ± 1.24%. The Control group at this time-point has granulation of 44.36% ±1.45%.

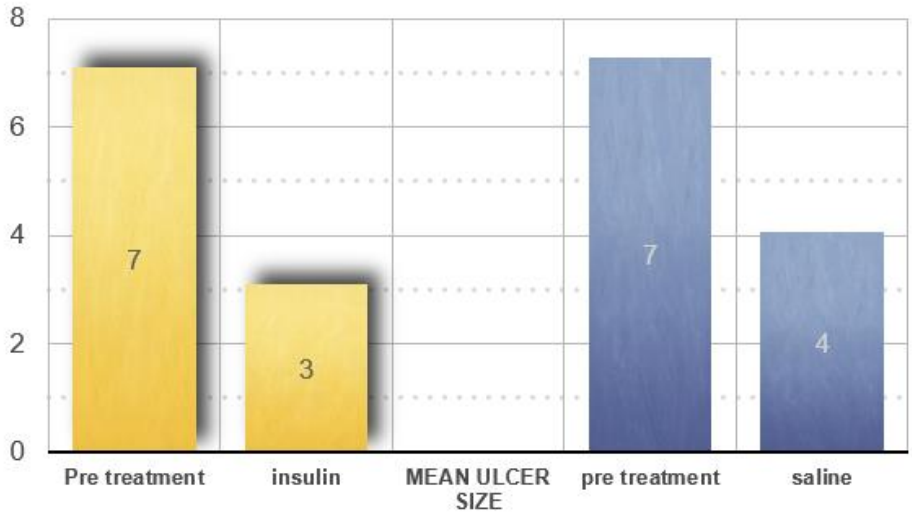

Figure 3: Changes in Ulcer size

As per figure 3 Mean ulcer size in the intervention group was reduced from7.099cm2 to 3.112 cm2. Mean ulcer size of 7.281 cm2 is reduced to 4.068 cm2 in control group.

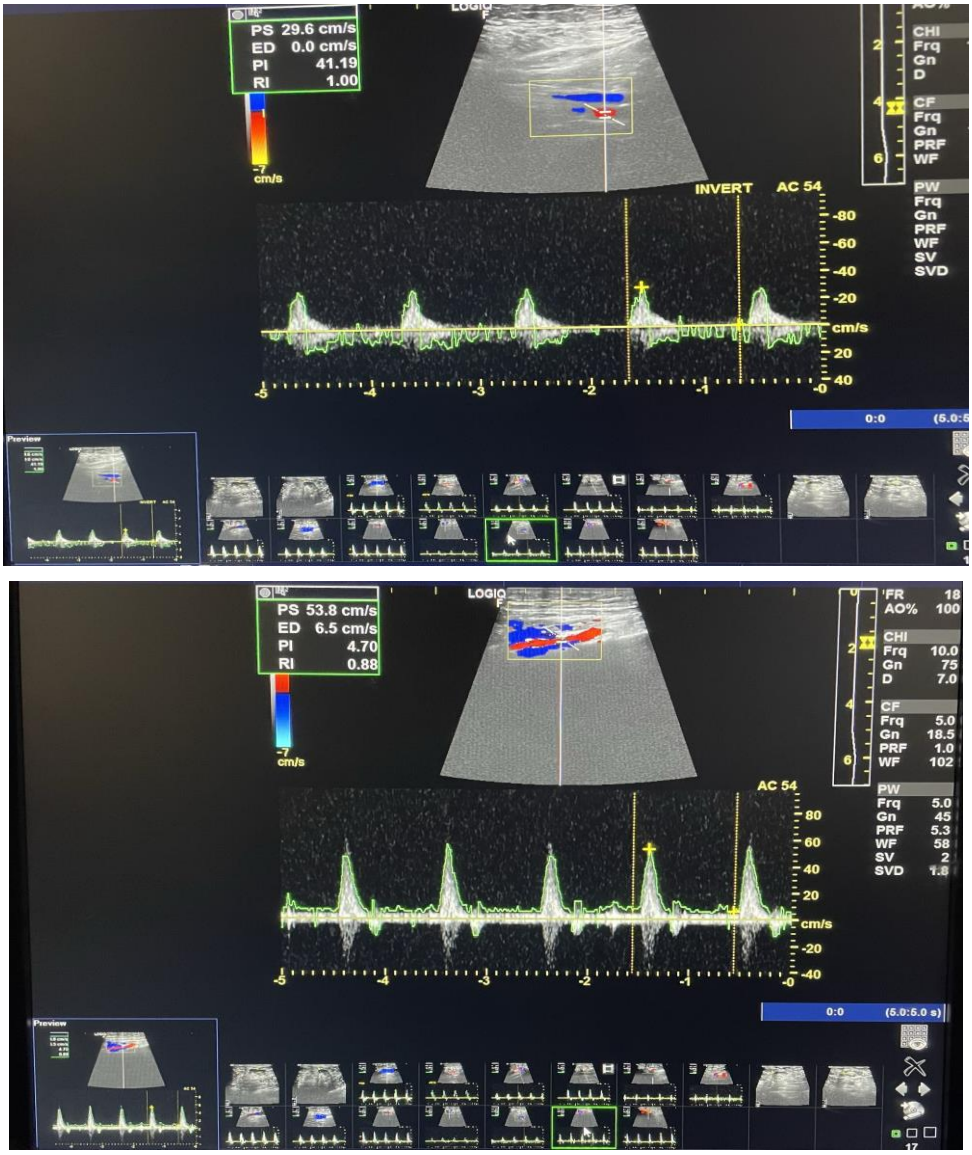

Figure 4: Radiological Assessment (A & B)

As per figure A and B Mean Ankle peak systolic velocity of 29.52cm/s in the intervention group was increased to 46.8 cm/s by 3 weeks. In control group mean APSV is increased from 30.04 cm/s to 41 cm/s.

DISCUSSION

Insulin performs a variety of tasks, including vascular endothelium protection, vascular dilatation, cardiac protection, and actions against platelet aggregation and atherosclerosis.[8] It is reported that treating refractory diabetic wounds locally with insulin (local wet dressing or injection) is successful[9]; however, the results have been achieved in animal tests, and the insulin doses utilized lack a theoretical basis.[10] Therefore, it is unclear if local insulin usage in people is safe. Insulin wet packing struggles to produce the desired result because of obstructive variables like tissue necrosis, exudation from the wound surface, and low insulin permeability. A systematic review and meta-analysis as part of a comprehensive compilation of the body of research on the effectiveness and safety of topical insulin delivery for wound healing. After obtaining seven relevant research, the quantitative synthesis produced a

noteworthy outcome for topical insulin in the decrease of wound area alone. The following outcomes were not shown to be significantly impacted by topical insulin use: microvessel density, granulation tissue growth percentage, and wound healing rate.[11]

A randomized and controlled trial was conducted to evaluate the impact of topical insulin in comparison to normal saline on the healing of pressure ulcers. In comparison to ordinary saline, they discovered that their research indicated that topical insulin dramatically accelerates the rate of pressure ulcer healing.[12] Ucciolo and colleagues conducted a study whereby they examined the effects of local application of low-dose insulin, high-dose insulin, and normal saline on wound healing following deep burn surgery. In wound healing, they discovered that insulin worked better than regular saline.[13] The outcomes of this investigation were discovered to differ from those of earlier, comparable investigations. This may be related to the complicated and multifaceted wound healing process. Adequate debridement, pressure offloading, moist wound care, infection management, and revascularization of an ischemic limb are all necessary for the treatment of a diabetic foot ulcer.[14] The rate at which a wound heals is impacted when necrotic tissue is present over it. Wagner's Grade 3 or higher ulcers were not included in this study; nonetheless, multiple patients with Grade 2 ulcers needed surgical serial debridement.[15]

In a prospective study by Reiber et al discovered that the APSV demonstrated 92.9% (95% confidence interval [CI] 82–97%) sensitivity, 90.6% (95% CI 76–96%) specificity, 92.9% positive predictive value, and 90.6% negative predictive value in predicting non-healing of diabetic foot lesions at a cutoff value of 35 cm/s.[16] The primary constraint of this research was a comparatively reduced sample size.

CONCLUSION

Local insulin injection is noted to be effective for treating refractory diabetic wounds. Local injection of insulin reduced the body blood glucose level. Regular insulin with dose of 1U/cm2 was found to be safe, without hypoglycaemic episodes. In terms of wound healing, insulin treated wounds have faster rate healing than normal saline wounds. Growth of granulation tissue and decrease in ulcer size in the insulin group was more marked than saline group. Radiologically it is evident that insulin promotes angiogenesis more than in the saline group.

Conflict of Interest- None declared

References

1) Wild S, Roglic G, Green A, Sicree R, King H: Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. Diabetes Care 2014, 27:1047–1053.

2) Heidari SH, NooriTajer M, Shirazi F, Sanjari M, Shoghi M, Salemi S: The relationship between Family support and diabetes control in type 2 diabetic patients. Iranian Journal of Diabetes and Lipid Disorders 2018, 8(2):93–102

3) American Diabetes Association: Economic Costs of Diabetes in the U.S. in 2007. Diabetes Care 2008, 31:596–615.

4) Holzemer LW: Improving Health through nursing research. International Council of Nurses: Wiley-Blackwell; 2010.

5) Singh D: Diabetic foot: It's time to share the burden. Calicut Med J 2016, 4(3):e4.

6) Zgonis T, Stapleton J, Girard-Powell V, Hagino R: Surgical management of diabetic foot infections and amputations. AORN J 2018, 87(5):935–950.

7) Fryberg RG, Armstrong DG, Giurini J, Edwards A, Kravatte M, Kravitz S, et al: Diabetic foot disorders, a clinical practice guideline. American College of Foot and Ankle Surgeons and the American College of foot and Ankle Orthopedics and Medicine 2000, 1–48.

8) Reiber GE, Lipsky BA, Gibbons GW: The burden of diabetic foot ulcers. Am J Surg 2018, 176(2A Suppl):S5–S10.

9) Jude EB, Boulton AJM: The diabetic foot. In Diabetes: current Perspectives. 11th edition. Edited by Betteridge DJ.: Martin Dunitz Ltd; 2021:179–196.

10) Ramachandran A, Snehalatha C, Mukesh B, Bhaskar AD, Vijay V: The Indian Diabetes Prevention programme shows that lifestyle modification and metformin Prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 2016, 49(2):289–297.

11) Akhbar DH, Mira SA, Zawawi TH, Malibary HM: Subclinical diabetic Neuropathy: a common complication in Saudi diabetics. Saudi Med J 2000, 21(5):433–437.

12) Tabatabaei-Malazy O, Mohajeri-Tehrani MR, Pajouhi M, Shojaei Fard A, Amini MR, Larijani B: Iranian diabetic foot research network. Adv Skin Wound Care 2010, 23(10):450–454.

13) Ucciolo L, Faglia E, Monticone G, Favales F, Durola L, Aldeghi A, et al: Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes Care 2015, 18:1376–1377.

14) Chantelau E, Kushner T, Spraul M: How effective is cushioned therapeutic footwear in protecting diabetic feet?aclinical study. Diabet Med 2010, 7:355–359.

15) Boulton AJM: The pathway to ulceration: aetiopathogenesis. In The foot in diabetes. Edited by Boulton AJM, Connor H, Cavanagh PR: John Wiley and Sonms; 2019:19–31.

16) Reiber GE, Vileikyte L, Boyko EJ, et al: Causal pathways for incident lower extremity ulcers in patients with diabetes from two settings. Diabetes Care 2019, 22:157–162.