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Original Research Article

A study of effectiveness of topical insulin on healing of diabetic ulcers at tertiary health care centre: a cross sectional study from Puducherry

Paritoshsingh B. Thakur[1], T. Ramachandrudu[1]*, Anant A. Takalkar[2]

[1]Department of General Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry, India
[2]Department of Community Medicine, MIMSR Medical College and YCRH, Latur, Maharashtra, India

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***Correspondence:**
Dr. T. Ramachandrudu,
E-mail: ram080761@gmail.com

ABSTRACT

Background: Insulin being a growth factor was proved to stimulate angiogenesis, collagen formation, matrix formation and granulation tissue proliferation in several preclinical studies. The objective was to study effectiveness of topical insulin on healing of diabetic ulcers at tertiary health care centre.
Methods: This was a cross sectional study carried out in the Department of surgery of a tertiary health care centre during August 2018 to August 2019 so during this period there were 60 patients. Group A was given topical insulin application. Group B was given saline application. The statistical analysis was done by using SPSS 24.0 version and un-paired t-test and chi-square tests are applied as test of significance.
Results: Average time required for granulation tissue to appear (mean±SD) was significantly less in group A as compared to Group B ($p<0.001$, df=58, t=5.87); Average surface area of wound (mm^2) at day 6th day was significantly less in group A ($p<0.05$, df=58,t=3.98); average depth of the wounds (mm) at day 6th day was significantly less in Group A as compared to in Group B ($p<0.001$, df=58, t=4.92).
Conclusions: The topical application of insulin is significantly associated with fastening of wound healing in the diabetic ulcer.

Keywords: Topical insulin effect, Diabetic ulcers, Chronic ulcers

INTRODUCTION

Chronic wounds or ulcers are the wounds that have failed to progress through the orderly process that produces satisfactory anatomic and functional integrity or that have proceeded through the repair process without producing an adequate anatomic and functional result. The majority of wounds that usually don't heal in 3 months are considered as chronic.[1,2] The unique feature of a chronic wound is their inability to heal despite the best management which would be undertaken, especially the diabetic ulcer, pressure ulcers or bed sores. Current estimates indicate that nearly 6 million people suffer from chronic wounds worldwide. The prevalence of chronic wounds in India has been reported as 4.5 per 1000 population, whereas that of acute wounds is nearly double, at 10.5 per 1000 population. The poor hygienic condition in some third world countries has been attributed as the main cause.[3-5]

With this background we conducted this study in order to assess whether the topical application of the insulin useful or not as compared to conventional treatment.

METHODS

This was a cross sectional study carried out in the Department of surgery of a tertiary health care centre during the one year period i.e. August 2018 to August 2019 so during this period there were 60 patients with

chronic non-healing diabetic ulcers were enrolled into the study by taking written and explained consent out of these 30 were enrolled to group A which was given topical insulin application with routine conventional management of wound and remaining into group B was given saline application to wounds as placebo with routine conventional management of wound all the patients treated with standard treatment protocol and with all aseptic precaution. All the patients treated with the anti-diabetic drugs either oral hypoglycemic drugs or injectable insulin depending upon the glycemic control of the patients and prescribed by the physician. The ulcer healing properties of the patients like appearance of granulation tissue and dimensions of the ulcer at the various stage of the treatment were noted by Vernier calipers. The statistical analysis was done by un-paired t-test and chi-square test.

Statistical analysis and methods

Data was collected by using a structure proforma. Data thus was entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of percentages and proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square test. Comparison of mean and SD within same groups was done by using unpaired t test to assess whether the mean difference between groups is significant or not. Descriptive statistics of each variable was presented in terms of Mean, standard deviation, standard error of mean. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

RESULTS

Table 1 shows distribution according to age and gender in our study. The average age in both the groups was comparable i.e. 39.58±4.32 years. and 40.18±3.29 years (p>0.05; t=1.038, df=58). The male female composition was also comparable i.e. 2. 75:1 and 2: 1 respectively in group A and group B. (p>0.05, X^2=0.576, df=1).

Table 2 depicts ulcer healing properties and its comparison between both groups. It shows the average time required for granulation tissue to appear (mean±SD) was significantly less in group A as compared to group B i.e. 5.68±2.45 and 11.24±3.29 (p<0.001, df=58, t=5.87).

Table 1: Distribution as per the age and sex.

Variable	Group A (n=30)	Group B (n=30)	P value
Age (in years)	39.58±4.32	40.18±3.29	P>0.05; t=1.038, df=58
Sex			
Male	22	20	P>0.05, X^2=0.576, df=1
Female	8	10	

Table 2: Distribution of the patients as per the ulcer healing properties.

Properties	Group A (n=30)	Group B (n=30)	P value
Average time required for granulation tissue to appear (mean±SD)	5.68±2.45	11.24±3.29	P<0.001, df=58, t=5.87
Average surface area of wound (mm^2) at day 0	4.13±2.87	3.98±3.82	P>0.05, df=58, t=1.056
Average depth of the wounds (mm) at day 0	7.87±2.19	8.15±4.16	P>0.05, df=58, t=0.98
Average surface area of wound (mm^2) at day 6^{th} day	1.97±1.65	2.98±1.78	P<0.05, df=58, t=3.98
Average depth of the wounds (mm) at day 6^{th} day	3.23±2.11	5.17±4.21	P<0.001, df=58, t=4.92

Average surface area of wound (mm^2) at day 0 was 4.13±2.87 and 3.98±3.82 was comparable (p>0.05, df=58, t=1.056). Average depth of the wounds (mm) at day 0 was 7.87±2.19 and 8.15±4.16 was comparable (p>0.05, df=58, t=0.98). Average surface area of wound (mm^2) at day 6^{th} day was significantly less in group A i.e. 1.97±1.65 and 2.98±1.78 (p<0.05, df=58, t=3.98). Average depth of the wounds (mm) at day 6^{th} day was significantly less in group A i.e. 3.23±2.11 as compared to in group B i.e. 5.17±4.21 (p<0.001, df=58, t=4.92).

DISCUSSION

Foot ulcers are common in diabetics due to angiopathy and neuropathy.[6] They respond poorly and slowly to conventional dressings, thus increasing hospital stay of the patient and putting him out of work for prolonged period. Loss of quality working days is an economic burden to the patient. Additionally, this delay in wound healing has been associated with increased morbidity and mortality. Insulin being a growth factor was proved to stimulate angiogenesis, collagen formation, matrix

formation and granulation tissue proliferation in several preclinical studies.[7-9]

It is well known that the basic cellular and molecular mechanisms that result in wound healing involve cell adhesion, migration, proliferation, differentiation, and apoptosis.[10] Abnormalities of distinct factors contribute to defective wound healing in diabetes, including decreased growth factor production, angiogenic response, macrophage function, collagen accumulation, epidermal barrier function, and keratinocyte and fibroblast migration and proliferation.[10-13] Wound dressings represent a part of the management of diabetic foot ulceration. Conventional dressings were found ineffective in management of these ulcers as they respond poorly thereby increasing hospital stay of the patient. Previous data showed that topical insulin dressing accelerates wound healing in the skin of diabetic rats and humans.[14-17] Insulin stimulates the growth and development of different cell types and affects proliferation, migration, and secretion by keratinocytes, endothelial cells, and fibroblasts.[17]

In our study we have seen that the average age in both the groups was comparable i.e. 39.58±4.32 yrs. and 40.18±3.29 ($p>0.05$; $t=1.038$, $df=58$) the male female composition was also comparable i.e. 2.75:1 and 2:1 ($p>0.05$, $X^2=0.576$, $df=1$).

Average time required for granulation tissue to appear (mean±SD) was significantly less in group A as compared to group B i.e. 5.68±2.45 and 11.24±3.29 ($p<0.001$, $df=58$,$t=5.87$); Average surface area of wound (mm^2) at day 0 was 4.13±2.87 and 3.98±3.82 was comparable ($p>0.05$,$df=58$,$t=1.056$); average depth of the wounds (mm) at day 0 was 7.87±2.19 and 8.15±4.16 was comparable ($p>0.05$, $df=58$, $t=0.98$); Average surface area of wound (mm^2) at day 6^{th} day was significantly less in group A i.e. 1.97±1.65 and 2.98±1.78 ($p<0.05$, $df=58$, $t=3.98$); Average depth of the wounds (mm) at day 6^{th} day was significantly less in group A i.e. 3.23±2.11 as compared to in group B i.e. 5.17±4.21 ($p<0.001$, $df=58$, $t=4.92$).

These findings are similar to Pandey et al, they found topical application of insulin in diabetic patients with ulcers has a significant improvement in healing of the ulcer.[18]

Reddy et al they found improvement of the wound in the form of diameter and depth is seen.[19] Significantly increased proliferation of granulation tissue is noticed in most of the patients belonging to group A, that is who received local insulin therapy.

CONCLUSION

It can be concluded from our study that topical application of insulin was superior to conventional treatments with respect to average time required for granulation tissue to appear (mean±SD) was significantly less in group A as compared to group B ($p<0.001$, $df=58$, $t=5.87$); Average surface area of wound (mm^2) at day 6^{th} day Was significantly less in group A ($p<0.05$, $df=58$, $t=3.98$) ; Average depth of the wounds (mm) at day 6^{th} day was significantly less in group A as compared to in group B ($p<0.001$, $df=58$, $t=4.92$).

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