EFFICIENCY OF TOPICAL PHENYTOIN ON HEALING IN DIABETIC ULCER: A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Diabetic foot ulcers are the major complication of diabetes mellitus; 15% of diabetic people suffer from foot ulcers. Phenytoin is used as a topical application in many studies on diabetic foot ulcers and it is found to stimulate the formation of granulation tissue as early as 2-7 days.[1]

OBJECTIVE

The objective of this study was to compare the efficiency of topical phenytoin application on healing in diabetic foot ulcer with control group using conventional wound dressing.

METHOD

Totally, 100 patients with diabetic foot ulcer attending Thanjavur Government Medical College Hospital are randomized into two groups, assigned regular saline and betadine dressing for the control group.[2] and phenytoin powder application for the study group. Patient with vascular impairment or uncontrolled diabetes are not included. Both study and control group are compared in terms of number of days required for healing, rate of granulations tissue formation. Rate of reduction in mean ulcer surface area. Quality of graft bed. Skin graft take up and serial culture and sensitivity of wound swabs to assess the effect of topical phenytoin on bacterial load.

RESULTS

The rate of granulation tissue formation was assessed at the end of 2 weeks; 81 to 90% granulation was seen in study group. In study group, 84% cases graft take up was good and 70% in the control group. Graft take up was 72.4% and 58.43% respectively. Hospital stay 21 days in study group and 45 days in control group.

CONCLUSION

In our present study it was concluded that the rate of granulation tissue formation, overall graft survival and patient compliance was better in topical phenytoin dressing group.[3] as compared to conventional dressing group.[4]

KEYWORDS

Diabetic Foot, Granulation Tissue, Graft Uptake, Hospital Stay, Topical Phenytoin, Wound Healthy.

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INTRODUCTION

Diabetes mellitus is a common metabolic disorder that share the phenotype of hyperglycaemia. Diabetic foot ulcers are the major complication of diabetes mellitus; 15% of diabetic people suffer from foot ulcers.[5] The major increase in mortality is due to microvascular, macrovascular complications and poor wound healing.[6] Poor wound healing is due to prolonged inflammatory phase, which leads to poor granulation tissue formation. The peculiarity of a chronic wound is that whatever management you give they refuse to heal, especially pressure ulcers or bed sores.[7] The notion that wounds should be kept dry.[8] although still held by a considerable number of clinicians is steadily losing ground. We now know that wounds re-epithelial much faster or develop granulation tissue faster when treated with dressings, which allow moist wound healing.

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We recognize that occluding wounds does not lead to infection. Even though many modalities of wound care have come up to assist a surgeon, for example the use of compression bandages to treat venous ulcers.[9] the problem of chronic wound still remains. A wound care revolution is currently in the making. Many techniques have been tried over the centuries to heal chronic leg ulcers.[7] Although wound dressing have been used for at least two millennia, there exists no ideal dressing. Surgical dressing of both open and closed wound is based mainly on tradition, training and surgeon's own philosophy. This study is done to prove the efficiency of phenytoin, a much easily available drug with property of wound healing in diabetic individual.

MATERIAL AND METHODS

This study was conducted as randomized case control study in Department of General Surgery, Thanjavur Medical College Hospital, from January 2014 to December 2014. Totally 100 patients were studied for more than 4 weeks' duration without any comorbid conditions. The main inclusion criteria were patients with age between 25-75 years. Patients with chronic ulcers with diabetic mellitus. Wound size <5% TBSA patients giving consent for topical phenytoin therapy.

The main exclusion criteria for the study included chronic non-healing wounds of other aetiology. Diabetes mellitus with gangrenous changes.

Other comorbid condition like renal failure, generalized debility and other factors, which adversely affect wound healing.[10]

PROCEDURE

A single 100 mg phenytoin sodium capsule.[11] was opened and placed in 5 mL of sterile normal saline to form a suspension. Sterile gauze was soaked in the suspension.[12] and placed over the wound at 20 mg/cm2 TBSA.

Conventional dressing was done with 5% w/v povidone-iodine solution. Before applying both dressing, daily wound is cleaned with normal saline.[13] At the end of 14 days, the wounds in both the groups were inspected and the wounds were compared based on the following parameters.

They are,

- Rate of granulation tissue formation as percentage of the ulcer surface.
- Quality of the ulcer bed.
- Present dimensions and surface area of the ulcer.

Once these parameters were assessed, both the groups were subjected to split thickness skin grafting. Both groups were given the same systemic antibiotics during the postoperative period.[14] The wounds were reassessed at the end of the fifth postoperative day and the following parameters were accounted for. They were skin graft take up.[15] as a percentage of ulcer surface area number of days of hospitalization.

- After discharge, patients were followed up in the outpatient department.

After one month to assess post skin grafting complications like contractures.[16] itching, pain and infection.

The results obtained were statistically evaluated and the main parameters which were analysed,

- Rate of granulation tissue formation.
- Graft survival and take up.
- Duration of hospital stay.

The mean rate of granulation tissue formation, graft survival and hospital stay was calculated and compared for both groups.[17]

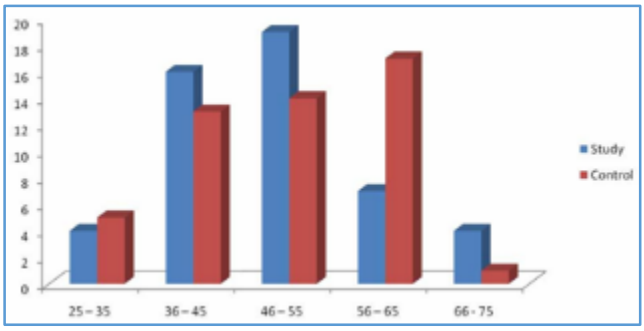
STATISTICAL ANALYSIS

The variables were compared using the Unpaired Student's t-test. A P value <0.05 was considered significant.

RESULTS

The patient's characteristics of the two groups were well matched in the table below.

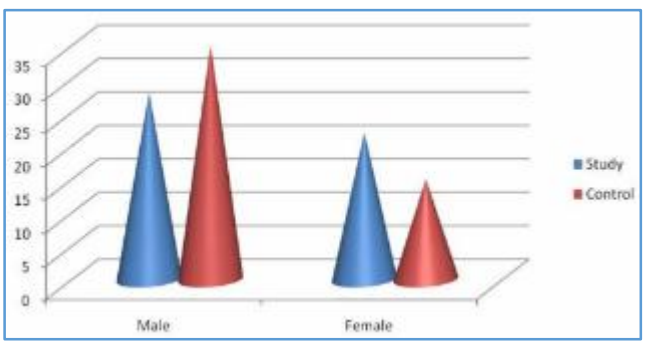
Age of Patients in Years	Study No. of Patients	Control No. of Patients
25 – 35	4	5
36 – 45	16	13
46 – 55	19	14
56 – 65	7	17
66 – 75	4	1



Sex Wise Distribution

	Male	Female
Study	28	22
Control	35	15

In both study and control group, diabetes is more common among males compared to females. Among them 67% of the patients were male and 33% were female.



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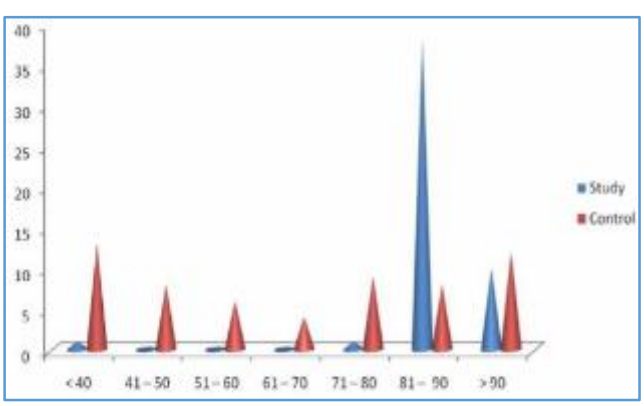
Ulcer Surface Area	Study	Control
<40	1	13
41– 50	0	8
51– 60	0	6
61– 70	0	4
71– 80	1	9
81– 90	38	8
>90	10	12

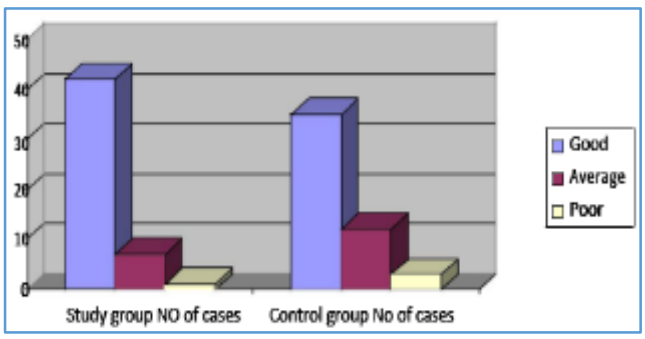


The rate of granulation tissue formation was assessed at the end of 2 weeks; 81 to 90% granulation was seen in study group. The patients in both the groups were subjected to split

thickness skin graft as the final treatment modality. The graft take up was assessed on the fifth postoperative day.

Graft Take Up Percentage of Surface Area

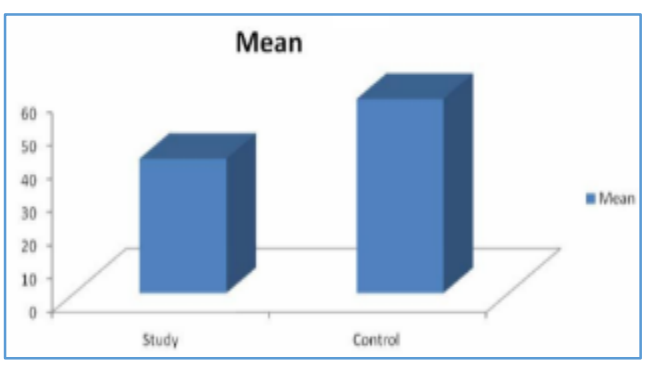
	Study Group No. of Cases	Control Group No. of Cases
Good	42	35
Average	7	12
Poor	1	3



In study group, 84% cases graft take up was good and 70% in the control group.

Duration of Hospital Stay

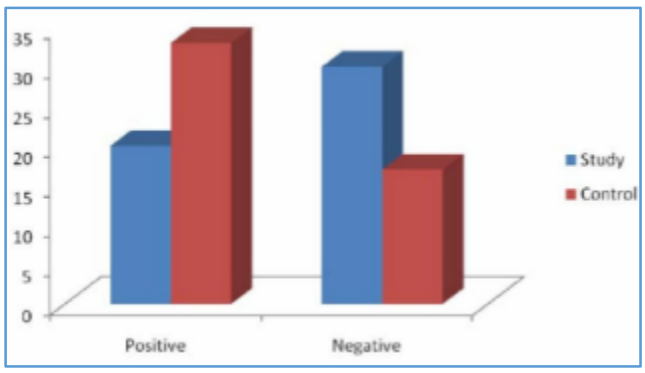
	Mean Number of Days In Hospital	SD Standard Deviation
Study	40.50	5.70
Control	58.52	9.99



The quality of life of the patients in both the groups was assessed by the assessment of total hospital stay as number of days of admission in the hospital is as above.

Percentage of Negative Culture Sensitivity at the end of 14 days

	Positive	Negative
Study	20	30
Control	33	17



Patient in both the groups were assessed for effect of topical agents on the bacterial load as percentage of people who are culture sensitivity negative at 14 days.

The mean hospital stay in study group was 40.50±5.70 (sd) days and that in control was 58.52±9.9 (sd) days. In both the groups, no complications occurred during the application of dressing, skin grafting or in the postoperative period.[18] The patients were followed up after one month of discharge. The main postoperative parameters were,

- Wound size
- Contractures
- Pain
- Infection

All the parameters were less in study as compared to control.

DISCUSSION

Wound dressings have evolved from the status of providing physical protection to the raw surface.[19] absorbing exudates and controlling local infections by local medications to the level of providing adequate environment promoting wound healing. This has been achieved by modern wound dressing equines promoting granulation tissue formation.

The concept of moist wound dressings, which came into vogue in 1960 which revolutionized wound care. This led to further research in this direction leading to influx of many products. People have tried various non-conventional topical agents in wound healing.[18] such as aloe vera, antacids, benzoyl peroxide, collagen, gentian violet, impregnated gauze, insulin, mercurochrome oxygen therapy, sugar and vinegar. Each claiming a better wound healing rate than the others. As the concept of outcome based medicine evolved, the need for better wound dressing modality became more acute. Now wound dressing systems were compared not only on the basis of the rate of granulation tissue formed or the rate of wound healing, but also on the cost and duration of hospital stay of the patient which was considered as a measure of the morbidity of the patient.

Future Trends

The important areas where significant advances have occurred in chronic wound care.[20] are the development of wound dressing systems, which stimulate wound healing process by improved granulation tissue formation and the development of permanent composite skin replacement.[21] in the form of genetically engineered keratinocyte culture techniques and growth factors. The main problem of the latter technique is that it is still in the experimental phase and will not be available to common man in the near future. Extensive research is going on in the development of artificial skin

substitutes by combining cultured keratinocytes with artificially formed dermal analogues namely Integra, AlloDerm, polyglactin mesh, human allogeneic dermis, etc., which has immense potential. It is only a matter of time before a successful approach to the management of chronic wounds is devised. The study is similar to the study conducted by Muthukumarswamy MG, et al.

The difference between the present study and the one done by Muthu was he used a thin layer of phenytoin powder over the wound. The study's sample size was 100, fifty in each group, mean age in study group was 56.4 yrs. and 58.7 yrs. in control. Graft take up was 72.4% and 58.43% respectively. Hospital stay, 21 days in study group and 45 days in control group. In study made by me, the mean age group – in study group is 48 yrs. and 49 yrs. in control group. Graft take up was 84% and 74% respectively. Hospital stays, 40.5 days in study group and 58 days in control group. His study was done as a prospective randomized controlled comparative study.[22] to compare the efficacy of topical phenytoin moist dressing to conventional most wound dressing in management of diabetic ulcer.[23]

The quantitative assessment of the postoperative parameters like wound contraction, pain and residual raw ulcer area was also not included in the present study, which if included might have given a much better analysis of the efficacy of topical phenytoin moist dressings as compared to conventional moist dressings.

CONCLUSION

In our present study it was concluded that the rate of granulation tissue formation, overall graft survival and patient compliance was better in topical phenytoin dressing group as compared to conventional dressing group. It was also seen that the overall hospital stay and postoperative complications were less in the topical phenytoin dressing group. Thus, topical phenytoin moist wound dressing can be considered as a superior option in the management of diabetic ulcers. But further studies with larger population will be needed in the future before topical phenytoin dressing.[24] can be added to the wide spectrum of treatment modalities available in the management of diabetic ulcers and ulcers of other aetiology.

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