

A Comparative Study between Conventional Betadine Dressing Vs Phenytoin Dressing in the management of Diabetic Ulcers

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Abstract:

Background: Diabetic ulcer is the most frequent reason for hospitalization in patients with diabetes. It has increased the cost of treatment and hospitalization of these patients. Currently a lot of attention is being placed on the development of expensive topical growth factors for wound healing. Thus there remains a quest for better wound healing agents. One such agent is phenytoin which is cheap, easy to use and readily available for medical practice. Phenytoin was initially introduced into therapy for the effective control for convulsive disorder. A common side effect with systemic phenytoin treatment is fibrous overgrowth of gingiva. This apparent stimulatory effect of phenytoin on connective tissue suggested an encouraging possibility for its wound healing.

Materials and Methods: This prospective randomized comparative study included 100 patients with diabetic ulcers. The main inclusion criteria were 1) grade I and II foot ulcers according to Meggitt-Wagner clinical classification 2) control of diabetes mellitus with oral hypoglycemic agents or insulin.

Results: The 100 patients admitted for the study were divided into two equal and comparable groups. Patients subjected to topical phenytoin dressings were classified under study and those who underwent conventional moist wound dressing were classified as control. All patients belonged to middle and low socio economic groups. There were 42 males and 8 females in the study group and 37 males and 13 females in the control group. The mean rate of granulation tissue formation in study group is $95.93\text{cm}^2 \pm 5.7(\text{SD})$ of total ulcer surface area and in control group is $98.09\text{cm}^2 \pm 2.6(\text{SD})$ of total ulcer surface area.

Conclusion: Phenytoin is a cheap, readily available and easy to use alternative in the treatment of diabetic ulcers.

Key Word: Diabetic ulcers, phenytoin dressing, betadine dressing, granulation tissue, graft uptake, graft bed, bacterial overgrowth, hospital stay and phenytoin side effects.

Date of Submission: 12-06-2020

Date of Acceptance: 29-06-2020

I. Introduction

People have tried various non-conventional topical therapies in wound healing, such as aloe vera, collagen, gentian violet, benzoyl peroxide, impregnated gauze, insulin, mercurochrome, oxygen therapy, sugar and vinegar. Studies have also shown that topical phenytoin promotes healing of decubitus ulcer, venous ulcer, pressure ulcer & leprosy ulcer and was found to be of superior in the management of diabetic ulcers.

The present study was conducted to assess the efficacy of topical phenytoin dressing as compared to conventional moist wound dressing in healing process in diabetic ulcers, also to assess the percentage of graft uptake of phenytoin treated wounds and to document any local or systemic side effects of topical phenytoin applications.

II. Material And Methods

This prospective randomized comparative study included 100 patients with diabetic ulcers admitted in SVRRGGH FROM AUGUST 2018 TO AUGUST 2019 satisfying all the inclusion criteria mentioned below after the clearance from the ethical committee was obtained.

Study Design: Prospective randomized comparative study.

Study Location: This was a tertiary care teaching hospital based study done in Department of General surgery, SVRRGGH

Study Duration: AUGUST 2018 TO AUGUST 2019

Sample size: 100 patients.

Sample size calculation: The results obtained were statistically evaluated and the main parameter which were analysed were 1) Rate of granulation tissue formation as percentage of ulcer surface area. 2) graft survival and take up 3) duration of hospital stay.

The variables were compared using paired and unpaired student's t-test and P value of <0.05 was considered significant.

Subjects & selection method: The whole sample population was divided into two equal and comparable groups based on willingness for undergoing topical phenytoin therapy for the wound. Those who were not willing were subjected to conventional wound care forming the control group. Selection of patients was done by purposive sampling method. All patients underwent general physical and clinical examination for peripheral vascular status and peripheral neuropathic changes in lower extremities. Routine hematological, biochemical, urine microscopic investigations were done for each patient. The wounds were thoroughly debrided when necessary.

Inclusion criteria:

1. grade I and II foot ulcers according to Meggitt-Wagner clinical classification
2. control of diabetes mellitus with oral hypoglycemic agents or insulin

Exclusion criteria:

1. grade III,IV,V foot ulcers according to Meggitt-Wagner clinical classification
2. chronic ulcer of other etiology
3. other co morbid conditions like renal failure, generalized debility which adversely affect woundhealing
4. Patients with allergy to phenytoin

Procedure methodology

After written informed consent was obtained, a single 100mg phenytoin sodium capsule was opened and placed in 5ml of sterile normal saline to form a suspension. Sterile gauze was soaked in the suspension and placed over the wound at 20mg/cm² TBSA. Conventional dressing was done with 5% w/v povidone-iodine solution. Dressings were done on twice daily basis. The patients were followed up on a daily basis for 14 days in both study and control groups. Wound culture was obtained at the start of the treatment and on the 14th day of treatment. At the end of 14 days the wounds in both the groups were inspected and compared based on the following parameters

- i)Rate of granulation tissue formation as percentage of ulcer surface area
- ii)Quality of ulcer bed
- iii)Present dimensions and surface area of ulcer

Observed or spontaneously reported side effects (local and systemic) were documented. The patients were then subjected to split thickness skin grafting. Both the groups were given the same systemic antibiotics during the post operative period. The wounds were assessed on fifth post operative day for skin graft up take and the total number of days of hospitalization was noted.

The follow up of the patients was done at one month after discharge in outpatient department to assess wound dimensions and post skin grafting complications like contractures, itching, pain and infection.

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

- 1.Rate of granulation tissue formation as percentage of ulcer surface area
- 2.Graft survival and take up
- 3.Duration of hospital stay.

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

Statistical analysis

The results were analysed by unpaired student t-test which showed highly significant difference in the number of days of hospital stay (p <0.0002), highly significant difference in rate of granulation tissue formation (p<0.0002), highly significant difference in graft take up (p of 0.001).

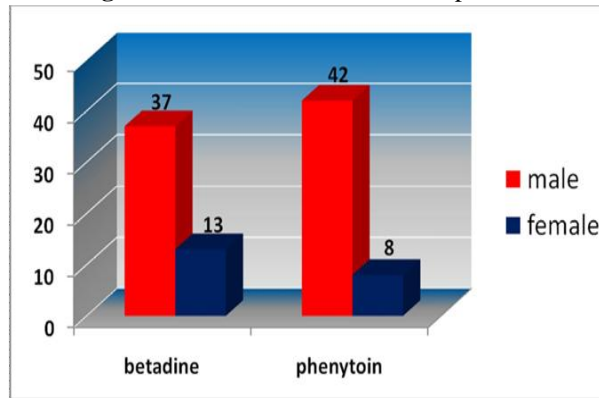
III. Result

The 100 patients admitted for the study were divided into two equal and comparable groups. Patients subjected to topical phenytoin dressings were classified under study and those who underwent conventional moist wound dressing were classified as control.

Table no 1: Sex wise distribution of patients

		Group		Total
		Betadine	Phenytoin	
SEX	F	13	8	21
		26.00%	16.00%	21.00%
	M	37	42	79
		74.00%	84.00%	79.00%
Total		50	50	100
		100.00%	100.00%	100.00%

Fig No. 1: Sex wise distribution of patients

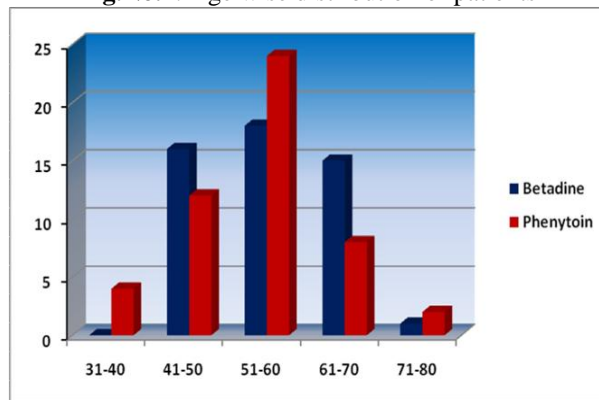


All patients belonged to middle and low socio economic groups. There were 42 males and 8 females in the study group and 37 males and 13 females in the control group.

Table 2: Age wise distribution of patients

Age Group (yrs)	31-40	41-50	51-60	61-70	71-80
Betadine	0	16	18	15	1
Phenytoin	4	12	24	8	2

Fig.No.2: Age wise distribution of patients

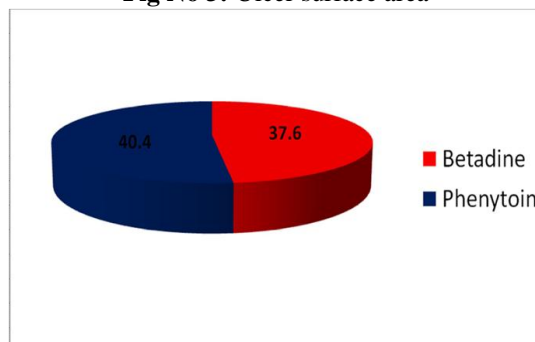


The age wise distribution of patients in this study is as shown above. The mean age in study group was 53.94yrs and mean age in control group was 55.92yrs

Table 3: Ulcer surface area

Group	N	Mean	Std. Deviation	Median	t value	pValue
ULCER AREA	Betadine	50	37.609	7.22872	38.61	2.548
	Phenytoin	50	40.4076	2.84107	40.22	
Total	100	39.0083	5.64235	39.71		Sig0.012

Fig No 3: Ulcer surface area



The mean ulcer surface area in control group is 37.6cm² and in the study group is 40.4cm². The ulcer surface area is measured twice using butter paper.

Table 4: Rate of granulation tissue formation as percentage of ulcer surface area.

Group		N	Mean	Std. Deviation	Median	t value	p Value
GRAN	Betadine	50	36.071	5.7160	37.060	3.996	HS0.00
TISSUE	Phenytoin	50	39.638	2.6753	39.650		
Total		100	37.855	4.7881	38.985		

The efficacy of the dressing was assessed as percentage of ulcer surface area covered by healthy granulation tissue after 14 days.

The mean rate of granulation tissue formation in study group is 95.93cm² ± 5.7(SD) of total ulcer surface area and in control group is 98.09 cm² ± 2.6(SD) of total ulcer surface area.

Table 5: Graft take up as percentage of ulcer surface area

Group		N	Mean	Std. Deviation	Median	t value	p Value
STSG	Betadine	50	37.089	5.4570	37.51	3.399	HS0.001
	Phenytoin	50	40.011	2.6801	39.90		
Total		100	38.55	4.5222	39.35		

The patients in both groups were subjected to split thickness skin grafting as the final treatment modality. The graft take up was then assessed at the end of the 5th post operative day as the percentage of ulcer surface area is given above.

The mean graft take up in the study group is 99.03% ± 2.6(SD) and in the control group is 97.61% ± 5.6(SD).

Table 6: Duration of hospital stay

Group		N	Mean	Std. Deviation	Median	t value	p Value
NO OF DAYS	Betadine	50	31.3	4.2	30	4.992	HS0.00
	Phenytoin	50	27.88	2.413	28		
Total		100	29.59	3.817	28.5		

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

The mean hospital stay in control group was 31.3 ± 4.2(SD) days and that in the study group was 27.8 ± 2.4 (SD) days. P value is <0.0002 which is highly significant.

Table 7: Percentage of negative culture sensitivity at the end of 14 days

		Group		
		Betadine	Phenytoin	Total
C/S	N	37	45	82
		74.00%	90.00%	82.00%
P		13	5	18
		26.00%	10.00%	18.00%
Total		50	50	100
		100.00%	100.00%	100.00%

$\chi^2 = 4.33, p=0.037, sig$

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

90% of the study group showed negative culture sensitivity at the end of 14 days whereas in control group it was 74%. In both groups, no complications occurred during the application of dressings, skin grafting or in the post operative period. The patients were followed up after one month of discharge.

The main post operative parameters noted in both the groups during follow up were:

- 1) wound size
- 2) contracture of graft
- 3) pain
- 4) infection.

IV. Discussion

Phenytoin (diphenylhydantoin) was initially introduced into therapy for the effective control of convulsive disorders. A common side effect with systemic phenytoin treatment is the development of fibrous overgrowth of gingiva. This apparent stimulatory effect of phenytoin on connective tissue suggested an

encouraging possibility for its use in wound healing. In the study, Both groups had comparable age and sex distribution as seen in above depicted graphs. The mean rate of granulation tissue formation in study group is 95.93cm² of total ulcer surface area and in control group is 98.09 cm². The results were analysed by unpaired student t-test which showed highly significant difference in rate of granulation tissue formation (p<0.0002). The mean graft take up in the study group is 99.03cm² and in the control group is 97.61cm. The results were analysed by unpaired student t-test which showed highly significant difference in graft take up (p of 0.001). The total number of days of hospital stay for the patient was also compared. The mean number of days of hospital stay in control group was 31.3 days and that in the study group was 27.8 days. The results were analysed by unpaired student t-test which showed highly significant difference in the number of days of hospital stay (p <0.0002). 45% of the study group showed negative culture sensitivity at the end of 14days whereas in control group it was 37%.

Table 8 : Comparison of present study to study by Muthu kumaraswamy et al shows following similarities.

	MuthukumaraSwamy et al		Present Study	
	Phenytoin	Betadine	Phenytoin	Betadine
Mean age in years	56.4	58.7	53.9	55.9
Rate of granulation tissue	74%	53.30%	98%	95.90%
Graft uptake in percentage	72.40%	58.40%	99.03%	97.61%
Hospital stay in days	21	45	27	31
Negative bacterial culture	82%	54%	90%	74%

Mean age group in Muthu kumaraswamy et al study in study group is 56.4 yrs and in the control group is 58.7yr While In The Present Study It Is 53.94yrs In Study Group and 55.92yrs In Control group.

The mean rate of granulation tissue formation in Muthu Kumaraswamy et al study in study group was 74% and in control group was 53.3%.

The mean rate of granulation tissue formation in study group is 95.93cm² of total ulcer surface area and in control group is 98.09 cm².

The percentage of graft take up in Muthu kumaraswamy et al study in the study group is 72.4% and in the control group is 58.4% while the percentage of graft take up in the study group is 99.03% and in the control group is 97.61%

The duration of hospital stay in Muthu kumaraswamy et al study in control group was 45days and that in the study group was 21 days while in the present study the mean hospital stay in control group was 31days and that in the study group was 27days.

The negative wound culture sensitivity at the end of 14days in Muthu kumaraswamy et al study was 82% in study group and 54% in control group.

Whereas in the present study the negative culture sensitivity at the end of 14days was 90% of the study group and in control group it was 74%.

Important difference between present study and Muthu kumaraswamy et al study in that in the latter a thin layer of phenytoin powder is laid over the wound and covered with a dry gauge as the method of application.

V. Conclusion

Phenytoin is a cheap ,readily available and easy to use alternative in the treatment of diabetic ulcers.

References

- [1]. Madden JW. Wound healing: the biological basis of hand surgery. ClinPlastSurg.1976;3(1):3-11
- [2]. JeterKF,TintleTE.Wounddressingsofthenineties:indicationsandcontraindications. ClinPlast Surg. 1991Oct;8(4):799-816.
- [3]. Cohen IK. Lessons from the history of wound healing. ClinDermatol. 2007 Jan- Feb;25(1):3-8.
- [4]. Helling TS, Daon E. In Flanders fields: the Great War, Antoine Depage, and the resurgence of débridement Ann Surg.1998;228(2):173-81.
- [5]. Cohen IK et al. Interleukin-1alpha and collagenase activity are elevated in chronic wounds. PlastReconstrSurg1998;102(4):1023-9
- [6]. Winter GD. Formation of the Scab and the rate of epithelialization of superficial wounds on the skin of young domestic pig.1962. J Wound Care.1995;4(8):368-71.
- [7]. Hernandez AM. Pathology of Wounds. 3rd ed. Philadelphia: Lipincott Raven Publ; 1999:p.76-102.
- [8]. Singer AJ, Clark RA. Cutaneous Wound Healing. N Engl J Med. 1999;341(10):738- 46.
- [9]. Chiang TM. The role of protein phosphatases 1 and 2A in collagen-platelet interactions. Arch BiochemBiophys1993;302(1):56-63.
- [10]. Banson BB, Llacy PE. Diabetic microangiopathy in human toes with emphasis on the ultrastructural change in dermal capillaries. Am J Pathol1964;45:41-58.
- [11]. Steed DT, Donahoe D, Webster MW, Linsley L. Diabetic ulcer study Group : Effect of extensive debridement and treatment on the healing of diabetic foot ulcers. J Am CollSurg1996;183:61-4.

- [12]. Gentzkow GD, Jensen JL, Pollak RA. Improved healing of diabetic foot ulcers after grafting with a living human dermal replacement. *Adv Wound Care*1999;11(3):77.
- [13]. Eaglstein WH, Falanga V. Tissue engineering and the development of Apligraf, a human skin equivalent. *Chin Therapeut*1997;19(5):894-905.
- [14]. Donaghue VM, Chazan JS, Rosenblum BI. Evaluation of a collagen alginate wound dressing in the management of diabetic foot ulcers. *Adv Wound Care* 1998; 11(3):114-9.
- [15]. Demling RH, De Santi L. Involuntary weight loss and the non healing wound -the role of anabolic agents. *Adv Wound Care* 1999;12(Suppl1):1-15.
- [16]. Argenta LC, Morykwas MI. Vacuum assisted closure: a new method for wound control and treatment- a clinical experience. *Ann Plat Surg* 1997Jun;38(6):563-76.
- [17]. Santilli SM, Valusek PA, Robinson C. Use of non contact radiant heat bandage for the treatment of chronic venous stasis ulcers. *Adv Wound Care*1999;12(2):89-93.
- [18]. Landau Z. Topical hyperbaric oxygen and low energy laser for the treatmentof diabetic foot ulcers. *Arch Orthop Trauma Surg*1998;117:156-8.

Dr.M.A.Haribabu, et. al. "A Comparative Study between Conventional Betadine Dressing Vs Phenytoin Dressing in the management of Diabetic Ulcers." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(6), 2020, pp. 31-36.