



Research Article

A COMPARATIVE STUDY OF DIABETIC ULCER DRESSING WITH NORMAL SALINE VERSUS SALINE AND PHENYTOIN SODIUM

Dilip Punnam, Chintham Sravani and Afsha Shireen\*

Prathima Institute of Medical Sciences. Karimnagar, Telangana

ARTICLE INFO

Article History:

Received 10<sup>th</sup> April, 2023

Received in revised form 2<sup>nd</sup>

May, 2023

Accepted 26<sup>th</sup> May, 2023

Published online 28<sup>th</sup> July, 2023

Key words:

Diabetic ulcers, phenytoin with saline dressing, normal saline dressing, granulation tissue, graft uptake, bacterial growth.

ABSTRACT

Diabetic ulcers are the most frequent reason for hospitalization in patients with diabetes. 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. The aim of the study is to compare the efficacy of topical phenytoin with saline and normal saline in healing of diabetic ulcers, in terms of days required for healing, rate of granulation tissue formation, quality of graft bed, graft uptake, effect on bacterial growth and side effects of topical phenytoin. We carried out our study in 2 groups 50 each, Saline and Phenytoin sodium (SP) group and Normal Saline (NS) in our institute. The number of days was 31.3 in group NS and 27.88 in group SP to heal. Negative bacterial growth in NS group was 37, while 45 in SP group. Graft uptake was seen in 37 cases in NS group, while it was 40 in SP group, which were statistically significant. So, we concluded that saline and phenytoin have a good effect than normal saline in diabetic wound dressing.

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INTRODUCTION

Diabetic ulcer is a significant health care problem with its healing depending on many factors such as glycemic control, nutritional status of the patient, bacterial load, vascularity and location of the wound [1,2,3]. Diabetic foot ulcers precede almost 85% of amputations in India [4,5,6]. Diabetic foot ulcers are extremely debilitating and difficult to treat. Multidisciplinary management which includes patient education, glycemic control, debridement, infection control and adequate perfusion is the mainstay of standard care endorsed by most practice guidelines [7,8]. Many agents have been tried in wound healing and one such agent is phenytoin. Phenytoin (diphenyl hydantoin) was introduced into therapy in 1937 for effective control of convulsive disorders [9,10] with a common side effect being gingival hyperplasia. This stimulatory effect of phenytoin on connective tissue suggests the possibility for its use in wound healing. The beneficial effect of phenytoin has been shown in promoting healing of decubitus ulcers, venous stasis ulcers, traumatic wounds, burns [11]. 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. Hence, the present study was taken up to compare the efficacy of topical phenytoin with saline and normal saline in healing of diabetic

ulcers, in terms of days required for healing, rate of granulation tissue formation, quality of graft bed, graft uptake, effect on bacterial growth and side effects of topical phenytoin.

METHODS

100 patients were included in the comparative study during the period of November 2019 to November 2021 at the Prathima Institute of medical sciences. Ethical clearance was taken from the institutional committee. They were randomly allocated into topical phenytoin with saline (SP) and normal saline (NS) dressing groups (50 each).

Inclusion Criteria

1. Grade I and II foot ulcers according to Meggitt-Wagner clinical classification.
2. Control of DM with oral hypoglycemic agents or insulin.
3. Patients willing to follow up.

Exclusion Criteria

1. Grade III, IV, V foot ulcers according to Meggitt-Wagner clinical classification.
2. Chronic ulcers of other etiology.
3. Other comorbid conditions like renal failure, generalized debility, which affects wound healing.
4. Allergy to phenytoin.

Relevant history, a complete clinical examination was done and laboratory investigations (hemogram, ECG, blood sugar, blood urea, serum creatinine, urine analysis, pus and blood for

\*Corresponding author: Afsha Shireen

Prathima Institute of Medical Sciences. Karimnagar, Telangana

culture and sensitivity arterial doppler) were done. Initial ulcer size and rate of granulation tissue formation was measured. A sterile gauze soaked in a suspension of 100mg phenytoin capsule in 5ml normal saline (20mg/cm<sup>2</sup> TBSA) was placed over the wound. The control group dressing was done with normal saline solution. Twice, daily dressing was done for 14 days for both groups. Wound culture was obtained on day 1 and day 14. The patient was then subjected to skin grafting and the wound was assessed on the fifth post operative day for graft uptake and the number of days of hospitalization was noted and compared the efficacy of topical phenytoin with saline and normal saline in healing of diabetic ulcers under the following heads:

- In terms of days required for healing,
- Rate of granulation tissue formation,
- Quality of graft bed, graft uptake,
- Effect on bacterial growth and
- Side effects of topical phenytoin.

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

**RESULTS**

**Age Distribution**

Among the study population, in normal saline group (NS), 6% belonged to the age group of 40-49 years, 28% belonged to the age group of 50-59 years, 26% belonged to the age group of 60-69 years and 40% belonged to age group of 70 and above. Among Saline and Phenytoin sodium group (SP), 4% belonged to the age group of 30-39 years, 6% belonged to the age group of 40-49 years, 24% belonged to the age group of 50-59 years, 20% belonged to the age group of 60-69 years and 46% belonged to the age group of 70 and above. (Table 1. Age-wise distribution in the study.)

**Table 1** Age-wise distribution in the study.

Age group	normal saline (NS)	%	phenytoin with saline (SP)	%
30-39 years	0	0	2	4
40-49 years	3	6	3	6
50-59 years	14	28	12	24
60-69 years	13	26	10	20
70 years and above	20	40	23	46
Grand Total	50	1.00	50	100

**Gender Distribution**

Among the study population, in group NS, 28% were females and 72% were males.

In group SP, 16% were females and 84% were males.(Table 2: gender distribution in study).

**Table 2** Gender Distribution in Study

Gender	NS	%	SP	%
Female	14	28	8	16
Male	36	72	42	84
Grand Total	50	100	50	100

**The Days of Hospitalization**

Among the study population, regarding hospital stay, it was 31.3 in group NS and 27.88 in group SP. The difference between the two groups was statistically significant with a P

value of 0.000002. The mean duration of hospital stay was significantly less in the SP group.

(Table 3: the days of hospitalization.)

**Table 3** The days of hospitalization

Hospitalization days	NS	%	SP	%
23	0	0	3	6
25	2	4	5	10
26	3	6	8	16
27	0	0	2	4
28	10	20	17	34
29	3	6	0	0
30	10	20	9	18
31	1	2	0	0
32	9	18	6	12
34	1	2	0	0
35	3	6	0	0
36	1	2	0	0
38	4	8	0	0
40	1	2	0	0
42	2	4	0	0
Grand Total	50	100	50	100

**The Culture Findings**

In group NS, 26% were positive for culture. In group SP, 10% were positive for cultures. There were significantly lower rates of infections in the SP group, when compared with the NS group. P=0.02 (Significant) (Table 4: the culture findings.) Parameters

**Table 4** the culture findings

Culture	NS	%	SP	%
Positive	13	26	5	10
Negative	37	74	45	90
Grand Total	50	100	50	100

**Other Parameters**

Among the study population, regarding ulcer area, it was 37.609 in group NS and 40.40 in group SP. The difference between the two groups was statistically significant with a P value of 0.01. The mean ulcer area was significantly higher in the SP group.

Among the study population, regarding granulation tissue, it was 36.07 in group NS and 39.63 in group SP. The difference between the two groups was statistically significant with a P value of 0.0001. The mean granulation tissue was significantly higher in the SP group.

Among the study population, regarding STSG uptake, it was 370.8 in group NS and 40.01 in group SP. The difference between the two groups was statistically significant with a P value of 0.0009. The mean STSG uptake was significantly higher in the SP group.

**Table 5** the means of various parameters

Parameter	NS	SP	P value
Ulcer area	37.609±7.22	40.40±2.84	0.01
Granulation tissue	36.07±5.71	39.63±2.67	0.0001
STSG uptake	37.08±5.45	40.01±2.68	0.0009
Hospital stay	31.3±4.2	27.88±2.41	0.000002

**DISCUSSION**

The present study was taken up to compare the efficacy of topical phenytoin with saline, normal saline wound dressings in healing of diabetic ulcers. It was conducted in the General Surgery Department at Prathima Institute of Medical Sciences,

Karimanagar, for a duration of 18 months, with a total study sample of 100.

Among the study population, in group NS, 28% were females and 72% were males. In group SP, 16% were females and 84% were males. In group NS, 6% belonged to the age group of 40-49 years, 28% belonged to the age group of 50-59 years, 26% belonged to the age group of 60-69 years and 40% belonged to the age group of 70 and above. Among group SP, 4% belonged to the age group of 30-39 years, 6% belonged to the age group of 40-49 years, 24% belonged to the age group of 50-59 years, 20% belonged to the age group of 60-69 years and 46% belonged to the age group of 70 and above. Regarding ulcer area, it was 37.609 in group NS and 40.40 in group the SP. The difference between the two groups was statistically significant with a P value of 0.01[12]. The mean ulcer area was significantly higher in the SP group. Regarding granulation tissue, it was 36.07 in group NS and 39.63 in group the SP. The difference between the two groups was statistically significant with a P value of 0.0001[13,14]. The mean granulation tissue was significantly higher in the SP group. Regarding STSG uptake, it was 370.8 in group NS and 40.01 in group SP. The difference between the two groups was statistically significant with P value of 0.0009[15]. The mean STSG uptake was significantly higher in the SP group. Regarding hospital stay, it was 31.3 in group NS and 27.88 in group SP. The difference between the two groups was statistically significant with a P value of 0.000002. The mean duration of hospital stay was significantly less in the SP group. In group NS, 26% were positive for culture. In group SP, 10% were positive for cultures. There were significantly lower rates of infections in the SP group, when compared with the NS group. No side effects were noted among phenytoin with the saline group[16]. Follow-up observations revealed that the topical SP dressing group suffered lesser post- skin grafting complications like wound contracture, residual raw area and pain compared to the NS group compared with few clinical experiences study groups like War and non-war wounds[17,18], burns [19,20], abscess cavities[21], diabetic foot ulcers[22,23], trophic leprosy ulcers[24,25,26], chronic skin ulcers [27, 28,29,30], Stage II Decubitus Ulcers in the elderly [31,32].

## CONCLUSIONS

The present study concludes that the mean days required for healing was significantly lesser among the Saline and Phenytoin sodium (SP) group. The rate of granulation tissue formation, rate of granulation tissue formation, quality of graft bed and graft uptake were significantly higher in the SP group. There were significantly lower rates of infections in the SP group, when compared with the NS group. Therefore, phenytoin with saline is the safe and effective alternative for dressing of diabetic ulcers.

Funding: "This research received no external funding".

Informed Consent Statement: "Informed consent was obtained from all subjects involved in the study." "Written informed consent has been obtained from the patient(s) to publish this paper" Conflicts of Interest "The authors declare no conflict of interest."

## References

1. Calhoun, J., Overgaard, K., Stevens, C., Dowling, J. and Mader, J. (2002). Diabetic Foot Ulcers and Infections Current Concepts. *Advances in Skin & Wound Care*, 15(1), pp.31-42.
2. Younes N, Albsoul A, Badran D, and Obedi. Wound bed preparation with 10 percent phenytoin ointment increases the take of split-thickness skin graft in large diabetic ulcers. *Dermatol Online* 2006; 12(6): 5.
3. Frykberg RG. An evidence-based approach to diabetic foot infections. *Am J Surg* 186:44S-54S, 2003.
4. Pendsey, S. Understanding diabetic foot. *International Journal of Diabetic in developing countries*. 2010; 30(2): 75.
5. American Diabetes Association. Implications of the Diabetes Control and Complications Trial. *Diabetes Care* 23(Suppl 1): S24-S26, 2000.
6. Van Gils CC, Wheeler LA, Mellstrom M, Brinton EA, Mason S, Wheeler CG. Amputation prevention by vascular surgery and podiatry collaboration in high-risk diabetic and nondiabetic patients. The Operation Desert Foot experience. *Diabetes Care* 22:678-683, 1999.
7. Caputo GM, Cavanagh PR, Ulbrecht JS, Gibbons GW, Karchmer AW. Assessment and management of foot disease in patients with diabetes. *N Engl J Med* 331:854-860, 1994.
8. Eneroth M, Larsson J, Apelqvist J. Deep foot infections in patients with diabetes and foot ulcer: an entity with different characteristics, treatments, and prognosis. *J Diabetes Complications* 13:254-263, 1999.
9. Meritt HH, and Putnam TJ. Sodium diphenylhydantoinate in the treatment of convulsive disorders. *JAMA*. 1938;111: 1068-1073
10. Silverman AK, Fairley J, and Wongs RC. Cutaneous and Immunologic reactions to phenytoin. *J. Am. Acad. Dermatol.* 1988;18: 721-741.
11. Bethesda MD. ASHP drug information. American Society of Health System Pharmacists. 2001; P2081.
12. Reddy MS, Madinur CRJ. Effect of topical phenytoin with normal saline dressing in patients of diabetic foot ulcers. *Int Surg J* 2021;8: 1754-8.
13. Anusha, Reddy MV, Vijayendra P. A comparative study of efficacy of topical phenytoin versus conventional wound care in diabetic ulcers. *IJAR* 2018;8(10)
14. Silodia A, Narnoli S, Damde HK. Prospective Comparative Study of Topical Phenytoin v/s Normal saline for Diabetic Foot Ulcers. *JMSCR*.2018;6(3);328-332
15. Kumar MN, Pawan BM, Arava S. A Comparative Study of Topical Phenytoin Vs Conventional Wound Care in Diabetic Ulcer. *IOSR Journal of Dental and Medical Sciences*2015;14(4)6-11Meritt HH, and Putnam TJ. Sodium diphenylhydantoinate in the treatment of convulsive disorders. *JAMA*. 1938;111: 1068-1073
16. Delbridge L, Perry P, Marr S, Arnold N, Yue DK, Turtle JR, Reeve TS. Limited joint mobility in the diabetic foot: relationship to neuropathic ulceration. *Diabet Med* 5:333-337, 1988.
17. Lavery LA, Armstrong DG, Wunderlich RP, Tredwell JL, Boulton AJM. Predictive value of foot pressure

- assessment as part of a population-based diabetes disease management program. *Diabetes Care* 26:1069-1073, 2003
18. Pham H, Armstrong DG, Harvey C, Harkless LB, Giurini JM, Veves Screening techniques to identify people at high risk for diabetic foot ulceration: a prospective multicenter trial. *Diabetes Care* 23:606-611, 2000.
  19. Armstrong DG, Peters EJ, Athanasiou KA, Lavery LA. Is there a critical level of plantar foot pressure to identify patients at risk for neuropathic foot ulceration? *J Foot Ankle Surg* 37:303-307, 1998
  20. Shah BR, Hux JE. Quantifying the risk of infectious diseases for people with diabetes. *Diabetes Care* 26:510-513, 2003.
  21. Eneroth M, Larsson J, Apelqvist J. Deep foot infections in patients with diabetes and foot ulcer: an entity with different characteristics, treatments, and prognosis. *J Diabetes Complications* 13:254-263, 1999.
  22. Jeffcoate WJ, van Houtum WH. Amputation as a marker of the quality of foot care in diabetes. *Diabetologia* 47:2051-2058, 2004.
  23. Moulik PK, Mtonga R, Gill GV. Amputation and mortality in new-onset diabetic foot ulcers stratified by etiology. *Diabetes Care* 26:491-494, 2003.
  24. LoGerfo FW, Gibbons GW, Pomposelli FB, Jr., Campbell DR, Miller A, Freeman DV, Quist WC. Trends in the care of the diabetic foot. Expanded role of arterial reconstruction. *Arch Surg* 127:617-621, discussion 620-621, 1992
  25. Frykberg RG. An evidence-based approach to diabetic foot infections. *Am J Surg* 186:44S-54S, 2003.
  26. UK Prospective Diabetes Study Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 352:854-865, 1998.
  27. American Diabetes Association. Implications of the Diabetes Control and Complications Trial. *Diabetes Care* 23(Suppl 1): S24-S26, 2000.
  28. Reiber GE, Pecoraro RE, Koepsell TD. Risk factors for amputation in patients with diabetes mellitus: a case control study. *Ann Intern Med* 117:97-105, 1992.
  29. Nelson RG, Gohdes DM, Everhart JE, Hartner JA, Zwemmer FL, Pettitt DJ, Knowler WC. Lower extremity amputations in NIDDM: 12-year follow-up study in Pima Indians. *Diabetes Care* 11:8-16, 1988.
  30. Larsson J, Apelqvist J, Agardh CD, Stenstrom A. Decreasing incidence of major amputation in diabetic patients: a consequence of a multidisciplinary foot care team approach? *Diabet Med* 12:770-776, 1995.
  31. Ebskov LB. Diabetic amputation and long-term survival. *Int J Rehabil Res* 21:403-408, 1998
  32. Van Gils CC, Wheeler LA, Mellstrom M, Brinton EA, Mason S, Wheeler CG. Amputation prevention by vascular surgery and podiatry collaboration in high-risk diabetic and nondiabetic patients. The Operation Desert Foot experience. *Diabetes Care* 22:678-683, 1999.

**How to cite this article:**

Dilip Punnam, Chintham Sravani and Afsha Shireen (2023) 'A Comparative Study of Diabetic Ulcer Dressing With Normal Saline versus Saline and Phenytoin Sodium', *International Journal of Current Advanced Research*, 12(07), pp. 2194-2197. DOI: <http://dx.doi.org/10.24327/ijcar.2023.2197.1480>

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