Original Research Paper

Volume - 13 | Issue - 05 | May - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Surgery

A COMPARATIVE STUDY OF TOPICAL PHENYTOIN VERSUS CONVENTIONAL DRESSING (5% W/V POVIDONE-IODINE) IN THE MANAGEMENT OF DIABETIC ULCER

Dr. Vivek Kumar — PG-JR 3rd year, Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad Uttar Pradesh

Dr. Nitin K Rastogi* — Professor, Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad Uttar Pradesh*Corresponding Author

Dr. Utkarsh Mittal — PG-JR 3rd year, Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad Uttar Pradesh

ABSTRACT **Introduction:** Diabetic Foot Ulcer (DFU) is a prevalent cause of morbidity in India, affecting around fifteen percent of diabetics in their lifetime. Though numerous dressing modalities have been described with variable degrees of effectiveness, we conducted a comparative study to determine the efficacy of topical phenytoin and conventional dressing in managing diabetic ulcers. Methodology: A prospective randomized controlled trial was done on 54 patients with diabetic ulcers who were randomly divided into two groups. In group P, the dressing was done with topical phenytoin. In group B, the dressing was done by conventional dressing (5% w/v povidone-iodine). Both the groups were compared on various parameters like ulcer area reduction, granulation tissue colour and hospital stays were recorded, and the results were statically evaluated. **Objective:** To compare the effectiveness of topical phenytoin versus conventional dressing (5% w/v povidone iodine) in the management of diabetic ulcers. **Results:** Among the enrolled patients, most of them had grade II DFU in both groups. The mean duration of hospital stays was longer in group B [15.79±1.90] compared to group P [14.56±1.06]. A significant reduction in ulcers was noted in group P compared to group B (p=0.0049*). On contrasting the effect on bacterial load in topical phenytoin dressing with conventional betadine dressing, the former yielded better results. **Conclusion:** Phenytoin is an effective alternative to conventional treatment for DFU. It is inexpensive, readily available, simple to apply, and safe.

KEYWORDS : Diabetic foot ulcers, Topical Phenytoin, Wound dressing, Granulation tissue colour.

INTRODUCTION

As reported by recent data, 69.2 million Indians are afflicted by diabetes. Diabetes mellitus (DM) is a foremost people health concern with a rising incidence worldwide. [1] Diabetic foot ulcers (DFU) are a frequent consequence of diabetes. It affects 15 per cent of all people with diabetes throughout their lives and 15 to 20 per cent of cases resulting in amputation. [2] In India, diabetes imposes a significant socioeconomic burden, the majority of which is attributable to complications related to diabetic feet. [3] Expensive topical molecular factors for wound healing are currently attracting a lot of attention. These factors include epidermal growth factors, vacuum-assisted dressing, tissue-stimulating factors, and hyperbaric oxygen dressing. Consideration should be given to such agents' uncertain efficacy and expense. Improved wound-healing agents are still being sought. One such agent is phenytoin, which is inexpensive, user-friendly, and widely available for medical practice. [4] Phenytoin (Diphenylhydantoin), well recognized for its medical usage in epileptic disorders, was initially described to promote wound healing by Shapiro in 1931. Topical phenytoin has been studied extensively for healing wounds, and its application has been extended to cover skin ulcers of diverse origins. [5] Gingival fibrous overgrowth is a typical complication of phenytoin therapy. This stimulative phenytoin effect over connective tissue hints at a potential utility in wound healing. Phenytoin promotes good granulation tissue development, enhancing graft bed quality and uptake. This offers more effective wound care for the patient. [3] In macrophages as well as monocytes, phenytoin upsurges the role of platelet-derived beta chain genes of growth factor. Phenytoin, due to its positive benefits on ulcer healing, has been used. It includes increased fibroblast proliferation and collagen deposition, neovascularization, enhanced granulation tissue formation, and reduced collagenase activity and bacterial contamination. The major objective of this study was to assess the effectiveness of topical phenytoin and standard dressing in treating diabetic ulcers.

MATERIALAND METHODS

Source of data: Patients with Type I and Type II Diabetic ulcer presented in general surgery department, Teerthanker Mahaveer Medical College & Research Centre, Moradabad as per inclusion and exclusion criteria.

Study type: Randomized Controlled Trial
Period of study: 18 months
Total number of participants: 54

INCLUSION CRITERIA:

- Patients with grade I and grade II Diabetic ulcers according to Wagner's classification.
- Control of the diabetes mellitus with oral hypoglycemic agents or insulin.
- Patients with age between 18-75 years

EXCLUSION CRITERIA:

- Patients having non-healing ulcers of other etiologies.
- Patients have other comorbid conditions like generalized debility, that can adversely affect ulcer healing.
- Patients who have allergy to phenytoin sodium or povidone iodine.
- Patients who do not want to complete 14 days treatment course.
- Pregnant females.

This prospective randomized controlled trial was conducted in the Department of General Surgery in collaboration with the Department of Pharmacology at Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh. After obtaining ethical approval and informed consent, 54 patients aged 18-75 years with grade I and grade II diabetic ulcers based on Wagner's classification were included in the study. While patients with non-healing ulcers of other aetiologies, those with comorbid conditions such as generalized debility that can negatively affect ulcer healing, those who were allergic to phenytoin sodium or povidone-iodine, those unwilling to complete the 14-day treatment course, and pregnant women were excluded from the study. All patients were randomly (lottery method) divided into two groups: Group P (n=29; topical phenytoin dressing) and Group B (n=25; conventional dressing; 5% w/v povidone-iodine) dressing. Every patient underwent a general physical and clinical examination. Topical phenytoin dressing was done by 2% w/v suspension. To make a phenytoin sodium suspension, one 100 mg tablet was pulverized and dissolved in 5 ml of sterile normal saline. A gauze made of sterile material was soaked in the suspension, which was then put over the wound at a concentration of 20mg/cm2 TBSA. The conventional dressing was done by 5% w/v povidone-iodine solution. Each patient had a single ulcer selected, and surgical debridement was performed if necessary. After the slough was scraped away, the area was measured by tracing its outline on a plastic sheet. Eventually, a variation of this outline on graph paper was created. Every time, the surface area of the ulcer was measured twice. The dressing was done daily or two times a day. Patients were observed for fourteen days. At the beginning of treatment and on day 14 of

treatment, cultures were taken from the wounds. Any drug-related adverse effects (both local and systemic) were recorded. Additionally, the colour of granulation tissue was recorded and compared.

Statistical Analysis:
SPSS (SPSS Inc., Chicago, Illinois, USA) for Windows was used for the statistical analysis (26.0 version). The continuous variables were assessed by mean (standard deviation) or range value when essential. Chi-square analysis was performed on the numerical/frequency displays of the dichotomous variables. Student t-test, Spearman correlation, and ROC analysis with a 95% confidence interval were performed to compare the means of the two groups. It was considered statistically significant when the p-value was less than 0.05 or 0.001.

RESULTS

Among the enrolled patients, most were aged 44-51 years in both group B 6(24.00%) and group P 8(27.59%). The mean age was [49.76±11.34] in group P and [48.20±13.01] in group B. Male dominancy was noted in group B 17(68.00%), while female dominancy was noted in group P 15(51.72%). Most patients in group B 20(80.00%) and group P 18(62.07%) had grade II diabetic ulcers. [Figure-1-3] The mean duration of hospital stays was significantly longer in group B [15.79±1.90 days] compared to group P [14.56±1.06 days]. The mean value of ulcer area reduction (%) was substantially higher in group P [24.58±4.43%] compared to group B [21.00±4.49%]. Vivid red was the prominent granulation tissue colour in the majority of the group B patients (60.00%). On the contrary, light red was the most prominent granulation tissue colour in most group P patients (58.62%). This shows better healing in group P. Further, we assessed the culture sensitivity (CS) and found that 60.00% of the group B patients had positive CS, while in group P, 75.86% had negative culture sensitivity. Statistically, a significant difference was observed in culture sensitivity among groups [p=0.0075*]. The majority of the patients had no systemic examination in both group. [Table-1]

TABLE-1: Comparison of various parameters of enrolled patients in both groups

		GROUP-B		GROUP-P		P-VALUE
		N/MEAN	%/SD	N/MEAN	%/SD	
Hospital Stays (Days)		15.79	1.90	14.56	1.06	t=2.991 p=0.0042*
Ulcer Area Reduction (%)		21.00	4.49	24.58	4.43	t=2.943 p=0.0049*
Granulation Tissue Color	Light Red	8	32.00 %	17	58.62 %	X=6.644 p=0.0361*
	Red With Yellow Spots	2	8.00 %	3	10.34 %	
	Vivid Red	15	60.00 %	9	31.03 %	
Culture Sensitivity	Negative	10	40.00 %	22	75.86 %	X=7.152 p=0.0075*
	Positive	15	60.00 %	7	24.14 %	

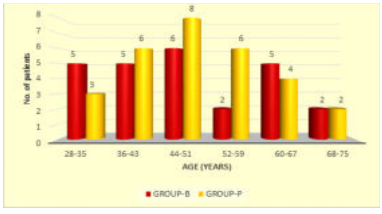

FIGURE-1: Age-wise distribution of patients in both groups

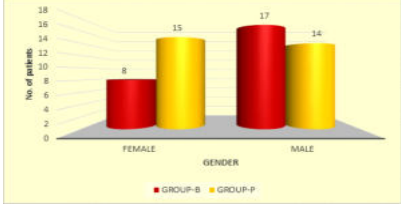

FIGURE-2: Gender of patients in both groups

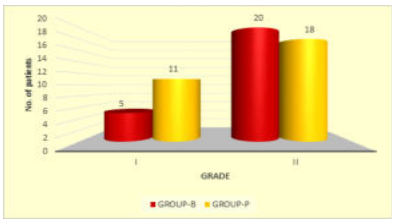

FIGURE-3: Grade of diabetic ulcer in patients in both groups

DISCUSSION

In our study, the majority in group B 20(80.00%) and group P 18(62.07%) had grade II diabetic ulcers, followed by grade I ulcers in group B 5(20.00%) and group P 11(37.93%). Statistically, a non-significant difference was observed in the grade of diabetic ulcer among groups [p=0.1502]. In contrast, Patil V et al. [6] and Prasad S et al. [7] noted an equal number of grades I and II patients. In the present study, the mean duration of hospital stays was higher in group B [15.79±1.90] compared to group P [14.56±1.06]. Statistically, a significant difference was observed in the duration of hospital stays among groups [p=0.0042*]. Similarly, Prasad S et al. [7] noted a shorter mean hospital stays in the phenytoin group (17.64 days) compared to the conventional group (20.04 days). Likewise, Tauro L et al. [8] observed a mean hospital stay was 32.26 days in the phenytoin group. In contrast, the mean hospital days for the conventional group were 40.97 days. Another study by, Jayalal et al. [9] noted the mean duration of hospitalization was significantly reduced in the phenytoin group. Muthukumarasamy MG et al. [10] observed shorter mean hospital stays of 21 days in the phenytoin group and longer mean stays of 45 days in the conventional group. We noted that the mean value of ulcer area reduction (%) was higher in group P [24.58±4.43] compared to group B [21.00±4.49]. Statistically, a significant difference was observed in ulcer area reduction among groups [p=0.0049*]. Similarly, Patil V et al. [6] and Pai MR et al. [11] observed mean reduction in ulcer area was considerably greater ($p > 0.05$) in the phenytoin group compared to the conventional group. The average difference in ulcer area between pre-treatment and posttreatment values was 6.45±1.53 against 5.44±1.49. As compared to controls, the phenytoin group exhibited a small effect acceleration. Many other researchers also noted a reduction in ulcer area of patients treated with phenytoin compared to the conventional group. [7,10,] Healed wounds have typically been described as shrinking in size over time. While assessing the granulation tissue colour, we noted that most patients had vivid red tissue colour in group B 15(60.00%), followed by light red 8(32.00%). At the same time, in group P, most patients had light red tissue colour 17(58.62%), followed by vivid red 9(31.03%). Red with yellow spots was observed in 2(8.00%) patients in group B and 3(10.34%) patients in group P. Statistically, a significant difference was observed in tissue colour among groups [p=0.0361*]. Similarly, Patil V et al. [6] noted pale granulation in 38 cases (76%) and good granulation was observed in three cases in the phenytoin group. On day 14, 15 cases (30%) showed pale granulation, whereas 31 cases (62%) showed good granulation. Pale granulation was seen in 11 (22%) of the control group's 50 patients, and good granulation did not occur until day 7. [8] Granulation was found successful in 6 cases (12%). The data showed that this difference was substantial. Similarly, Maji A et al. [12] saw that healthy granulation tissue formed in the phenytoin group before it did with conventional dressing. The mainstay of treatment for diabetic ulcers is the removal of all necrotic tissue. [13-15] Diabetic ulcers are susceptible to infection, and wound healing is exceedingly sluggish. The formation of granulation tissue is crucial for the success of skin grafting. Sodium phenytoin promotes the production of granulation tissue. [16] The method by which phenytoin promotes wound healing is complex. They result in the production of granulation tissue, a decrease in slough and bacterial load, and a decrease in wound size. [2] Multiple studies have demonstrated that phenytoin is an effective topical treatment for wound healing in diabetic ulcers. [2,6,13] In the present study, the majority of the patients in group B showed positive culture sensitivity 15(60.00%), while in group P, the majority showed negative culture sensitivity 22(75.86%). Statistically, a significant difference was observed in culture sensitivity among groups [p=0.0075*]. Similarly, Prasad S et al. [7] found higher negative culture sensitivity in the phenytoin group (96%) compared to the conventional group (52%). Likewise, Tauro L et al. [8] also noted maximum negative culture in the phenytoin group (70%) compared to the conventional group (54%).

CONCLUSION

According to the results, we can deduce that by lowering bacterial burden and promoting the formation of healthy granulation tissue, topical phenytoin promotes healing of Diabetic ulcers than standard dressing. In the phenytoin group, overall hospital stays and post-operative problems were reduced due to improved healing. Thus, moist wound dressing containing topical phenytoin might be the optimal treatment for diabetic ulcers. It is safe, accessible, and inexpensive. In addition, randomized, large-scale clinical trials are required before topical phenytoin dressing might be added to the extensive diversity of therapies already available for treating diabetes and other ulcers.

Summary: Foot ulcers with diabetes are a frequent consequence of diabetes mellitus. The development of pricey topical molecular factors for wound healing in such cases is currently receiving considerable interest. One of them medication is phenytoin. conventional dressing with povidone iodine is also in use. Phenytoin promotes good granulation tissue development, enhancing graft bed quality and uptake. This offers more effective wound care for the patient. improved formation of granulation tissue was observed in dressing with topical phenytoin when compared to dressing with conventional dressing. Less hospital stay time was seen in the topical phenytoin dressing group. Topical phenytoin dressing seems to be an effective, cheap and easily available agent which therapeutically improve wound healing.

REFERENCES

1. Vibha SP, Kulkarni MM, Ballala AK, Kamath A, Maiya GA. Community based study to assess the prevalence of diabetic foot syndrome and associated risk factors among people with diabetes mellitus. BMC endocrine disorders. 2018 Dec;18(1):43.
2. Sudhir S, Ganashree MH, Naik D, et al. To compare the efficacy of topical phenytoin over conventional wound care (5 % povidone-iodine) in diabetic ulcer. International Journal of Surgery Science 2020;4(1):122-128.
3. Viswanathan M. The Diabetic Foot Worldwide: India. The Foot in Diabetes. 2020 Apr 24:43-5.
4. Sandhu KS, Singh K, Banga RK, Sandhu KS, Samria J. Role of topical phenytoin (Diphenylhydantoin) dressing in diabetic ulcers: A comparative study with conventional dressing. Int J Orthop Sci. 2018;4(1d):239–42.
5. Yadav JK, Singhvi AM, Kumar N, Garg S. Topical phenytoin in the treatment of split-thickness skin autograft donor sites: a comparative study with polyurethane membrane drape and conventional dressing. Burns. 1993 Aug 1;19(4):306-10.
6. Patil V, Patil R, Kariholu PL, Patil LS, Shahapur P. Topical phenytoin application in grade i and ii diabetic foot ulcers: a prospective study. Journal of clinical and diagnostic research: JCDR. 2013 Oct;7(10):2238.
7. Prasad S, Prakash A, Patel S, Lunawat A, Mahore D. A comparative analysis of the efficacy of topical phenytoin with conventional wound dressing in healing of diabetic foot ulcers. International Surgery Journal. 2017 Mar 25;4(4):1389-93.
8. Tauro LF, Shetty P, Dsouza NT, Mohammed S, Sucharitha S. A comparative study of efficacy of topical phenytoin vs conventional wound care in diabetic ulcers. Int J Molecul Med Sci 2013;3.
9. Jayalal JA, Kumar SJ, Dhinesh, Thambithurai D, Kadar JMA. Efficiency of topical phenytoin on healing in diabetic foot ulcer: a randomized controlled trial. Int J Sci Stud. 2015;3(3):84-89.
10. Muthukumarasamy MG, Sivakumar G, Manoharan G. Topical phenytoin in diabetic foot ulcers. Diabetes Care. 1991;14:909-11.
11. Pai MR, Sitaraman N, Kotian MS. Topical phenytoin in diadetic ulcers: a double blind controlled trail. Indian J Med Sci. 2001;55:593–9.
12. Maji A, Sultan P, Mukhopadhyay M. Comparison of Efficacy-Phenytoin Vs. Conventional Dressing (Povidone Iodine) Vs. Local Sucralfate Vs. L-Lysine as Wound Dressing Following Surgical Debridement of Diabetic Foot Gangrene.
13. Silodia A, Narnoli S, Damde HK. A Prospective Comparative Study of Topical Phenytoin v/s Conventional Dressing for Diabetic Foot Ulcers. infection. 2018;6:8.
14. American Diabetes Association. Consensus Development Conference on Diabetic Foot Wound Care: 7-8 April 1999, Boston, Massachusetts. American Diabetes Association. Diabetes care. 1999 Aug 1;22(8):1354-60.
15. Armstrong DG, Lavery LA. Diabetic foot ulcers: prevention, diagnosis and classification. American family physician. 1998 Mar 15;57(6):1325.
16. Bansal NK. Comparison of topical phenytoin with normal saline in the treatment of chronic trophic ulcers in leprosy. International journal of dermatology. 1993 Mar;32(3):210-3.