ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 07 | July - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARATIVE ANALYSIS OF THE EFFICACY OF TOPICAL PHENYTOIN WITH CONVENTIONAL WOUND DRESSING IN HEALING OF DIABETIC FOOT ULCERS

General Surgery

Dr. Eedara Sri Kousalya* Junior Resident Department of General Surgery Sree mookambika institute of medical sciences*Corresponding Author

Dr. Renukadevi Vadivelu Junior Resident Department of General Surgery Sree Mookambika Institute of Medical Sciences

Dr. P. Maharaja Associate Professor Department of general surgery

ABSTRACT

Background: Foot ulcers caused by diabetes mellitus are extremely difficult to treat. Different agents have been employed to treat them, with differing degrees of effectiveness. One of the most crucial aspects of managing chronic ulcers is wound care and dressing changes. Recently, phenytoin has been utilized to treat these ulcers. By stimulating fibroblast proliferation, enhancing the creation of granulation tissue, and inhibiting collagenase activity, phenytoin improves wound healing. **Aim:** To compare the efficacy of topical phenytoin with conventional wound dressings in healing of diabetic foot ulcers. **Materials and Method:** The present study was a prospective study conducted for a period of 10 months. The purposive sampling technique was used to choose a sample of sixty patients who had diabetic ulcers. Two groups of patients were created: Group A (phenytoin group) (n= 30) and Group B (conventional group) (n=30) The patient was dressed with phenytoin in Group A and normal saline in Group B. For a period of 14 days, patients in both groups were monitored. Rate of granulation tissue production, decrease in wound surface area, culture and sensitivity, and length of hospital stay were taken into consideration while evaluating the wound. Results were analyzed using SPSS 20.0 version and the association was tested using student t test and Chi square test. **Results:** The groups with phenytoin and conventional groups had mean ages of 56.7±10.24 and 54.3±8.76, respectively. Diabetic foot ulcers were most commonly found on the dorsum (35%), soles (15%), legs (25%), toes (11.67%), and around the ankle joint (8.33%). The mean surface area of ulcer for the phenytoin group was 875.6±486.7 mm2 and for the conventional group it was 2032.8±1156.4 mm2. Patients in the topical phenytoin dressing-based treatment group had healthier granulation tissue appearance and a shorter hospital stay ($p<0.05$) than those in the conventional saline dressing-based treatment group. Reflecting the antibacterial activity of phenytoin, the conversion of a negative culture was 60% in the phenytoin group and only 30% in the conventional group. **Conclusion:** Topical phenytoin dressings provide a cheap, widely accessible, and efficient treatment option for wound healing in patients with persistent diabetic ulcers. In comparison to conventional dressing, it not only speeds up the granulation tissue but also reduces the bacterial load because of its inherent antibacterial activity and its indirect effects on neovascularization and anti-inflammatory cells.

KEYWORDS

Diabetic foot ulcers, Phenytoin, Topical, Wound dressing.

INTRODUCTION:

Diabetes is a category of metabolic disorders characterized by hyperglycemia. One of the most prevalent complications associated with diabetes mellitus is diabetic foot ulcers.[1] Individuals who have diabetic ulcers frequently experience poor wound healing and infections, which can ultimately result in lower limb amputation.[2] It has become a substantial health-care problem, affecting 15% of all diabetics over the course of their lives, with 15%-20% of cases requiring amputation. In India, 2.4% of people with diabetes live in rural areas and 12–17% in urban areas. Diabetic foot infections account for up to 10% of diabetes-related hospital admissions. Every year, nearly 40,000 legs are amputated in India, with 75% of them being neuropathic with subsequent infection that could have been avoided.[3]

A cost-effective treatment plan for diabetic foot involves antibiotics, specific dressing, surgical wound debridement, and improved circulation through surgery or therapy. Many gels and topical medications are advertised for ulcer healing. Compared to saline wet to dry dressings, relatively few have shown to be more effective. Topical antiseptics like povidine-iodine are typically thought to be harmful to the healing process of wounds.[4]

The development of costly topical molecules for wound healing, such as tissue stimulating factor, vacuum-assisted dressings, dressings with hyperbaric oxygen, and epidermal growth factors, is currently receiving a lot of interest.[5] It is important to consider the cost element and the uncertain effectiveness of these drugs. The search continues for more effective wound-healing substances. Phenytoin is one such medication that is inexpensive, simple to use, and widely accessible for usage in medical settings. In 1937, phenytoin (diphenylhydantoin) was first made available to treat convulsive disorders. The development of fibrous gingiva overgrowth is a typical adverse effect associated with systemic phenytoin treatment. Phenytoin is one such medication that has been investigated for the purpose of wound repair.[6]

Due to its beneficial effects on ulcer healing, including increased fibroblast proliferation and collagen deposition, neovascularization, improved granulation tissue formation, decreased collagenase activity, and reduced bacterial contamination, phenytoin has been employed by numerous workers.[7,8] When applied topically to ulcers, phenytoin has been shown to have anti-microbial activity and aid in the management or prevention of microbial infections caused by S. aureus, Escherichia coli, Klebsiella species, and Pseudomonas. As a result, phenytoin is beneficial in the healing of chronic ulcers. This results in improved wound treatment for the patient.[9]

Recent research has demonstrated that topical phenytoin is superior in the treatment of diabetic ulcers and enhances the healing of decubitus, venous, pressure, and leprosy ulcers. Few studies have been done on diabetic ulcers, despite the fact that topical phenytoin is frequently used to treat chronic leg ulcers. For this reason, the current study was designed to determine whether topical phenytoin dressing is a better option for managing diabetic ulcers and to evaluate its effectiveness in promoting wound healing in diabetic ulcers when compared to traditional moist wound dressings (saline).

AIMS AND OBJECTIVES:

To assess the efficacy of topical phenytoin dressing as compared to conventional wound dressing in diabetic ulcers.

MATERIALS AND METHODS:

Present study was a prospective study conducted in patients with diabetic ulcers attending as outpatient or inpatient under Department of General surgery, Sree Mookambika Institute of Medical Sciences, Kulasekharam. Patients with blood glucose levels between 110 and 130 gm/dl, grades one and two of Wagener's categorization and who were willing to participate in the study were included in the study. Patients with grade 3, grade 4, and grade 5 ulcers according to Wagener's classification, patients with a bent peripheral pulse-dorsalis pedis, anterior tibial, and posterior tibial artery, patients who are not on regular follow-up and unwilling to enroll in the study, patients with other co-morbid conditions such as renal failure, generalized debility, and other factors that adversely affect wound healing were excluded.

Purposive sampling was used to choose a sample of sixty patients. Group A (the Phenytoin group) consisted of thirty patients, whereas Group B (the Conventional group) also had thirty patients. Phenytoin was used for patient dressing in Group A, while regular saline was used in Group B. Informed written consent was received at the time of enrollment.

All patients underwent a full clinical examination, pertinent investigations, and a thorough debridement of their wounds before applying either type of bandage. The dimensions and surface area of ulcers were measured using a measuring tape. Both the study group and the control group had to dress every day.

Topical phenytoin dressing was the basis of treatment for Group A. If there was a lot of slough, debridement was performed after the wound had been cleansed with saline. Under aseptic circumstances, a 100 mg tablet of phenytoin sodium was suspended in 5 ml of sterile saline solution. After soaking in the aforementioned suspension, sterile gauze was applied to the ulcer at a concentration of roughly 20 mg/cm2 of TBSA. Finally, the surrounding area was cleaned with povidone iodine and a dry, sterile surgical pad was placed. The surface area of the ulcer determined the phenytoin dosage, which ranged from 0 to 5 cm2-100 mg, 5.1 to 9 cm2-150 mg, 9.1 to 15 cm2-200 mg, and >15 cm2-300 mg. Regular saline was applied to the group once a day for conventional dressing. If there was a lot of slough, debridement was performed after cleaning the ulcer with saline. The surrounding skin was cleaned with povidone iodine and the wound covered with sterile surgical pads.

Patients underwent 14 days of follow-up in both groups. After 14 days, the wounds in both groups were examined and compared based on the following factors: the size and surface area of the ulcer, the wound's culture and sensitivity, the length of the hospital stay, and the rate of granulation tissue formation as a percentage of the ulcer surface area.

Statistical Analysis was carried out using SPSS 20.0 version. The means were compared using paired and unpaired student's t-test, while number comparisons between the groups for various grading was done using chi-square test and p-value of <0.05 was considered significant.

OBSERVATION AND RESULTS:

Among the 60 diabetic patients included in the present study, most of the diabetic foot patients were in the age group of 50 to 60 years in 26(43.33%) followed by 60 to 70 years in 13(21.67%), more than 70 years in 12(20%) and 40 to 50 years in 9(15%) patients. The most common site of diabetic foot ulcers was in dorsum in 21(35%), sole in 9(15%), leg in 15(25%), toes in 7(11.67%) and around Ankle joint in 8(13.33%). The mean age in Phenytoin group and conventional group were 56.7±10.24 and 54.3±8.76, respectively. Statistically there was no significant difference in mean age between interventional and control groups.

There were a total of 24 (80%) males and 6 (20%) females in the phenytoin group. The ratio of men to women was 4:1. There were a total of 25 (83.33%) males and 5 (16.67%) girls in the traditional group. There were five men for every woman. According to statistics, gender distributions in the interventional and control groups did not differ significantly.

The mean ulcer area at the beginning of the study was 2763.5±1256.7 mm^2 in the phenytoin group and 3186.5±1532.4 mm^2 in the conventional group. The initial mean area did not significantly differ between the two groups (p=0.27). The mean area on follow-up day 14 was 2032.8±1156.4 mm^2 in the group treated with conventional saline dressings and 875.6±486.7 mm^2 in the group treated with topical phenytoin dressings. There was a significant difference (p<0.001) in the final wound area between the two groups. Comparison of size of ulcer with duration of treatment in both group was given in table 1.

Table 1: Comparison of size of ulcer

Group		Size of Ulcer			p value
		<5cm	610 cm	>10 cm	
Phenytoin group (n=30)	Day 0	7 (23.33%)	12 (40%)	11 (36.67%)	0.003
	Day 7	16 (53.33%)	8 (26.67%)	6 (20%)	
	Day 14	24 (80%)	5 (16.67%)	1 (3.33%)	
Conventional group (n=30)	Day 0	5 (16.67%)	16 (53.33%)	9 (30%)	0.072
	Day 7	8 (26.67%)	15 (50%)	7 (23.33%)	
	Day 14	12 (40%)	13 (43.33%)	5 (16.67%)	

Following two weeks of treatment, it was shown that patients in the topical phenytoin dressing-based treatment group had higher appearance of healthy granulation tissue than those in the conventional saline dressing-based treatment group. The rate of granulation tissue formation on days 0 and 14 of both the groups has been compared in tables 2. This rate was significantly higher in patients who were treated with phenytoin dressing.

Table 2: Comparison of rate of granulation tissue formation on day 0 and 14 as percentage of ulcer surface area in both groups.

Group	Rate of granulation tissue formation	
	Day 0	Day 14
Phenytoin group	37.13±3.67	43.35±5.08
Conventional group	34.89±5.12	36.44±4.77
p value	0.001	0.003

The antibacterial activity of phenytoin was demonstrated by the observation that a negative culture was converted 60% in the phenytoin group compared to 30% in the conventional group. The bacterial burden is reduced more in the phenytoin group than in the conventional group. (Table 3)

Table 3: Comparison of culture growth between groups at day 0 and 14.

Group		Culture		p value
		Positive	Negative	
Phenytoin group (n=30)	Day 0	25(83.33%)	5(16.67%)	0.004
	Day 14	12(40%)	18(60%)	
Conventional group (n=30)	Day 0	26(86.67%)	4(13.33%)	0.057
	Day 14	21(70%)	9(30%)	

In the conventional saline dressing-based treatment group, 6 (20%) of 30 patients stayed in the hospital for less than 15 days, whereas 24 (80%) stayed for more than 15 days. Out of the 30 patients in the topical phenytoin dressing therapy group, 19 (63.33%) stayed in the hospital for less than 15 days, whereas the remaining 11 (36.67%) stayed for more than 15 days. Patients in both groups spent a total of nine to twenty-seven days in the hospital. Compared to patients in the topical phenytoin dressing-based treatment group, it was shown that patients in the conventional saline dressing-based therapy group had a noticeably longer hospital stay.

DISCUSSION:

The role of wound dressings has changed throughout time, moving from only shielding the exposed skin physically, collecting secretions, and using local drugs to manage local infections to the point where they now create an environment that is conducive to wound healing. This has been made possible by contemporary wound dressing techniques that encourage the development of granulation tissue.[10]

One such medication that promotes faster wound healing is phenytoin. Heinrich Biltz, a German chemist, created phenytoin in 1908. Tracy Putnam and H. Houston Meritt identified this to be helpful in managing seizures.[11] One of the adverse effects of phenytoin is gum hyperplasia, which led its evaluation in wound healing. Phenytoin-induced wound healing involves a complex mechanism. They include the development of granulation tissue, slough reduction, and bacterial load/wound size reduction.[12]

Among the 60 diabetes patients that were part of this study, 43.33% of diabetic foot patients were between the ages of 50 and 60. The interventional group had a mean age of 54.8±9.96, whereas the control group had a mean age of 56.9±10.77 and a male preponderance was observed in the study by Reddy MS et al.[13], which was similar to the current study. Similar results were seen in studies conducted by Sandhu DK et al.[14]

The most common site of diabetic foot ulcers was in dorsum in 21(35%) followed by leg in 15(25%) patients. In the study conducted by Gunasekaran V et al.[15] diabetic foot ulcers most frequently

presented in the dorsum (31%), sole (19%), leg (21%), toes (20%), and area surrounding the ankle joint (8%).

In the group treated with phenytoin, the mean wound surface area was 875.6±486.7 mm^2, while in the group treated with standard saline dressings, it was 2032.8±1156.4 mm^2. There was a substantial ($p<0.001$) difference in the wound area between the two groups. Similar to this study, Reddy MS et al.[13] observed that the patients treated with topical phenytoin dressings had an average reduction in wound area of 1856.9±724.9 mm^2, while patients treated with normal saline dressings had an average reduction in wound area of 1066.8±565.3 mm^2, which is statistically significant ($p<0.001$). In the study conducted by Kumar CS et al.[16] the wound surface area, percentage of granulation tissue, and VAS score for the patients were 29.4 ± 29.88 cm2, 92 ± 4.46%, and 2.8 ± 0.94, respectively, while the controls had these values: 38.92 ± 23.24 cm2, 78.56 ± 8.19%, and 4.88 ± 1.17. The rate of granulation tissue formation was higher in cases when compared to controls.

After two weeks of treatment, it was shown that patients in the topical phenytoin dressing-based treatment group had higher appearance of healthy granulation tissue than those in the conventional saline dressing-based treatment group. When compared to a standard group, the phenytoin group reduces the bacterial load more. Phenytoin was found to be more effective in each parameter and was statistically significant with a p value of 0.0001, according to a study conducted by Sudhir S et al.[17] The study evaluated the progress of wounds in each group by comparing the amount of slough, discharge, and time taken for granulation tissue to appear. Reddy et al.[13] also found that, out of the 20 patients in the phenytoin group who tested positive for culture growth on day zero, only 9 showed no growth on day ten. This difference was statistically significant ($p=0.004$). This was similar to the present study.

In the current study, more than 15 days were spent in the hospital by 24 (80%) and 11 (36.67%) patients in the conventional group and the phenytoin group, respectively. This suggests that the conventional group's patients had longer hospital stays. Sandhu DK et al.[14] Sudhir S et al. and Bharadva PB et al.[18] in their study also found that the duration of stay in hospital and number of dressings were significantly lesser in phenytoin dressing over conventional dressing. Selvakumarkothandapani DB et al.[19] found that the average duration of the hospital stay in the control and study groups were 24.66 and 17.4 days, respectively.

CONCLUSION:

Phenytoin dressing stimulates fibroblast proliferation while lowering collagenase activity on the wound surface, which increases the rate of granulation tissue formation. In addition to being more effective than traditional saline-based dressing treatment for chronic non-healing ulcers, the current study found that topical phenytoin administration also inhibits microbial infection and colonization in diabetic ulcers. It is more economical for the patient because the length of stay in the hospital is shortened. With phenytoin dressing, patients can return to their regular activities sooner than they would otherwise be able to if time is of the importance. Thus, topical phenytoin dressing can be considered a better option for diabetic ulcer treatment.

FINANCIAL SUPPORT AND SPONSORSHIP:

Nil.

CONFLICTS OF INTEREST:

There are no conflicts of interest

REFERENCES:

1. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna journal of medicine. 2020 Oct;10(04):174-88.
2. Burgess JL, Wyant WA, Abdo Abujamra B, Kirsner RS, Jozic I. Diabetic wound-healing science. Medicina. 2021 Oct 8;57(10):1072.
3. Akinlotan MA, Primm K, Bolin JN, Ferdinand Cheres AL, Lee J, Callaghan T, Ferdinand AO. Racial, rural, and regional disparities in diabetes-related lower-extremity amputation rates, 2009–2017. Diabetes Care. 2021 Sep 1;44(9):2053-60.
4. Boulton AJ, Armstrong DG, Hardman MJ, Malone M, Embil JM, Attinger CE et al. Diagnosis and management of diabetic foot infections. 2020.
5. Oliveira A, Simões S, Ascenso A, Reis CP. Therapeutic advances in wound healing. Journal of Dermatological Treatment. 2022 Jan 2;33(1):2-2.
6. Löscher W. Anticonvulsant Agents: Pharmacology and Biochemistry. Neuro Psycho pharmaco therapy. 2020:1-27.
7. van de Vyver M, Idensohn PJ, Niesler CU. A regenerative approach to the pharmacological management of hard-to-heal wounds. Biochimie. 2022 May 1;196:131-42.
8. Hassan KM, Hamdi AA, Alhamad SA, Alanzi RQ, Aleid YA, Aldarwish AS et al. Healing the chronic wounds in diabetes using old drugs. International Journal of Community Medicine and Public Health. 2020 Oct;7(10):4185.
9. Spampinato SF, Caruso GI, De Pasquale R, Sortino MA, Merlo S. The treatment of impaired wound healing in diabetes: looking among old drugs. Pharmaceuticals. 2020 Apr 1;13(4):60.
10. Rezvani Ghomi E, Niazi M, Ramakrishna S. The evolution of wound dressings: From traditional to smart dressings. Polymers for Advanced Technologies. 2023 Feb;34(2):520-30.
11. Meijer JW, Meinardi H, Binnie CD. The development of antiepileptic drugs. Discoveries in Pharmacology-Volume 1-Nervous System and Hormones. 2022 Sep 9:247.
12. Patocka J, Wu Q, Nepovimova E, Kuca K. Phenytoin–An anti-seizure drug: Overview of its chemistry, pharmacology and toxicology. Food and chemical toxicology. 2020 Aug 1;142:111393.
13. Reddy MS, Madinur CR. Effect of topical phenytoin with normal saline dressing in patients of diabetic foot ulcers. International Surgery Journal. 2021 May 28;8(6):1754-8.
14. Sandhu DK, Singh DK, Banga DR, Sandhu DK, Samria DJ. Role of topical phenytoin (Diphenylhydantoin) dressing in diabetic ulcers: A comparative study with conventional dressing. Int. J. Orthop. Sci. 2018;4:239-42.
15. Gunasekaran V, Subbaraj S, Aroul T. The efficacy of phenytoin dressing in healing of diabetic ulcer: a randomized control study. International Surgery Journal. 2017 Sep 27;4(10):3311-6.
16. Kumar CS, Vasudeva N, Rao DV, Naidu CR. Outcomes of topical phenytoin in the management of traumatic wounds. Journal of Clinical Orthopaedics and Trauma. 2021 Feb 1;13:116-21.
17. Sudhir S, Ganashree MH, Naik D, Dilip DK. To compare the efficacy of topical phenytoin over conventional wound care (5% povidone-iodine) in diabetic ulcer. Int J Surg Sci. 2020;4(1):122-8.
18. Bharadva PB, Choksi DB, Damor S, Shah J. Topical phenytoin dressing versus conventional dressing in diabetic ulcers. IntSurg J. 2017; 4(5):1682-6.
19. Selvakumarkothandapani DB, Kaveri M, Kandasamy S. Efficiency of topical phenytoin in diabetic foot ulcer care: A randomized control trial. International Journal of Surgery. 2022;6(1):165-7.