www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i3.55

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Thesis Paper

A Prospective Comparative Study of Topical Phenytoin v/s Conventional Dressing for Diabetic Foot Ulcers

Authors
A. Silodia[1], Saket Narnoli[2], H.K Damde[3]
[1]Associate Professor, [2]Resident, [3]Assistant Professor

Abstract

Introduction: *Diabetic Foot Ulcer (DFU) is a common cause of morbidity in India and is estimated to affect 15% of all diabetic individuals during their life time. Its prevalence in clinical population is 3.61% and precedes almost 85% of amputation. Though many modalities of dressing have been described for such patients but they are quite costly for patients coming to our setup.*

Aims & Objectives

- *To evaluate the effectiveness of phenytoin as methods of dressing in treatment of Diabetic Foot Ulcer.*
- *To compare the results of topical phenytoin dressing v/s conventional dressing using Eusol & Betadine (povidone iodine)*

Material & Methodology: *50 patients were taken in study & randomly divided into two groups of equal size with ulcer size (<5% TBSA) and depth (TEXAS grade 1) as the only selection criteria. Group I was treated with topical phenytoin 20mg/cm^2 and Group II with conventional dressing of eusol and povidone iodine.*

Daily dressing with oral antibiotics was given in both groups.

Parameters studies were:

a) Presence of Healthy Granulation Tissue (HGT) on Day14.

b) Mean Reduction in Percentage of Ulcer Area on Day 7 & Day 14.

c) > 50% reduction of ulcer area on Day 14.

Observation: *In our study we found that there was a significant difference between the two groups in all three parameters we studies in favor of study group.*

Presence of HGT on Day14: 86.95 % v/s 48% (p= 0.004)

Mean Reduction in ulcer area on day 7 &14: 41.38 & 68.17 v/s 24.56 & 47.85 (p < 0.001)

>50% reduction in ulcer area on Day 14: 62% v/s 38% (p= 0.004).

Conclusion: *It can be concluded that Phenytoin for healing of DFU is an acceptable alternative to conventional method. It is safe, easily available, easy to apply and in expensive.*

Introduction

Foot complications are a major cause of hospitalization in patients with diabetes mellitus (DM), which consumes a high number of hospital days because of multiple surgical procedures and prolonged length of stay[1]. Patients with DM have

up to a 25% lifetime risk of developing a foot ulcer[2], which precedes amputation in up to 85% of cases[3]. A mainstay of diabetic foot ulcer (DFU) therapy is debridement of all necrotic, callus, and fibrous tissue[4,5], with a primary goal to obtain wound closure. The management of the DFU is largely determined by its severity (grade), vascularity of the limb, and the presence of infection[6–8].

In India habits like walking barefooted, lack of knowledge regarding diabetic foot, hot climate leading to increased perspiration, poor hygiene, poor sanitation, diet poor in proteins, general poverty, lack of basic medical infrastructure, etc have worsened the problem.

Over the years the life expectancy of diabetic patient with gangrene of foot has not changed much. Advances in treatment of diabetes have caused increase in life span of diabetic patient which has resulted in an increase in

Complications of Diabetes Mellitus like vasculopathy, neuropathy and nephropathy. This in return has increased the prevalence and incidence of diabetic foot.

The optimal topical therapy for DFU remains ill-defined. Betadine (povidone iodine) dressing or moist saline gauze dressing has been standard method; however, it has been difficult to continuously maintain a moist wound environment with these dressings.

Subsequently, various hydrocolloid wound gels, growth factors, enzymatic debridement compounds, hyperbaric oxygen therapy, cultured skin substitutes, and other wound therapies have been advocated. All of these therapies are associated with significant expense and are being utilized in some situations without sufficient scientific evidence in favor of their efficacy[9].

Phenytoin (diphenylhydantoin) was introduced into therapy in 1937 for effective control of convulsive disorders with a common side effect being gingival hyperplasia. This stimulatory effect of phenytoin on connective tissue suggested 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, leprosy trophic ulcers [10].

Aim

The present study was conducted to assess the efficacy of topical phenytoin dressing as compared to conventional moist wound dressing in the healing process of diabetic ulcers and to check whether it is a better alternative in the management of diabetic ulcers.

Materials and Methods

A randomized control trial was conducted including 50 patients with diabetic ulcers admitted in the department of Surgery of a tertiary care hospital of Jabalpur, India. All diabetic ulcers where conventional dressings are indicated were included in the study.

The inclusion criteria were:

(1) Patients with chronic ulcers (ulcers of 8 weeks duration) with diabetes mellitus.

(2) Wound size <5% of TBSA

The exclusion criteria were:

(1) Chronic non-healing wounds of other etiology

(2) Diabetes mellitus with gangrenous changes

(3) Wounds with osteomyelitis.

(4) Wounds with poor vascularity determined by arterial Doppler study.

(5) Other co-morbid conditions like renal failure, generalized debility and other factors, which adversely affect wound healing.

All 50 patients were randomly divided into two groups of 25 each.

All patients underwent detailed clinical examination and relevant investigations. The wounds were thoroughly debrided (surgically under anesthesia) and the ulcer dimensions as well as the surface area were assessed using vernier calipers, immediately after debridement and reassessed after 7 days and 14 days in either type of dressings. Both the groups underwent wound dressings twice a day. The patients were followed up on a daily basis for 14 days in both the study and the control groups. A single 100 mg

phenytoin sodium capsule was opened and placed in 5 ml of sterile normal saline to form a suspension. Sterile gauze was soaked in the suspension and placed over the wound at 20 mg/cm^2 TBSA. Conventional Dressing was done with 5% w/v povidone – iodine solution. Before applying the dressing, the wound was cleaned with normal saline and hydrogen peroxide.

Result

Of the 50 DFU patients, the majority of the patients belong to 51-60 years of age and the next common presentation was between 61 and 70 years (Table 1). Of the 50 patients, 33 patients were male and 17 were female. Of the patients having DFU majority of them had diabetes for 5-10 years. All the 50 patients had strict glycemic control with insulin.

All the 50 patients were of TEXAS GRADE 1.

The wound swab from DFU showed that most common organism isolated from

The wound was Staph aureus (Table 2).

At the end of 2 weeks of monitoring of topical phenytoin these were the end results; group 1 v/s group 2: unhealthy wound-03 v/s 13, healthy granulating tissue-20 v/s 12,

Ascending infection-Bk amputation-0, and complete wound healing – 02 v/s 00.

The following parameters were observed on day 7 and day 14.

Presence of HGT on Day14: 86.95 % v/s 48% (p= 0.004) (Table 3)

Mean Reduction in ulcer area on day 7 &14: 41.38 & 68.17 v/s 24.56 & 47.85

($p < 0.001$) (Table 4)

>50% reduction in ulcer area on Day 14: 62% v/s 38% (p= 0.004). (Table 5)

Table: 1 Showing age Incidence of DFU in Both Group

S No.	AGE GROUPS (YEARS)	GROUP I No. / %	GROUP II No. / %	TOTAL No. /%
01.	40 -50	04 /16	00/00	04/08
02.	51 – 60	13/52	13/52	26/52
03.	61 – 70	06/24	11/44	17/34
04.	71 - 80	02/08	01/04	03/06
	TOTAL	25/100	25/100	50/100

Though this table shows that maximum number of patients with DFU belongs to 51 – 60 years of age group. But age is not the criteria for development of DFU and other age is groups are not immune to development of DFU.

Table: 2 Showing Pattern of Organisms Grown in Wound Culture in Both Group

S No.	ORGANISM GROWN	GROUP I No./%	GROUP II No./%	TOTAL No./%
01.	Staph aureus	10/40	09/26	19/38
02.	Staph albus	03/12	00/00	03/06
03.	Pseudomonas	02/08	06/24	08/16
04.	Streptococcus	03/12	02/08	05/10
05.	E. coli	03/12	02/08	05/10
06.	Klebsiella	01/04	01/04	02/04
07.	Sterile	04/16	04/16	08/16
	TOTAL	25/100	25/100	50/100

Table: 3 Showing Presences or Absence of Healthy Granulation Tissue (HGT) in Both Groups on D14.

S No.	PARAMETER	GROUP I No./%	GROUP II No./%	TOTAL No./%
01.	HGT PRESENT	20/86.95	12/48	32/66.66
02.	HGT ABSENT	03/13.05	13/52	16/33.33
	TOTAL	23/100	25/100	48/100

In our study 20 out of 23 patients developed healthy granulation tissue (2 had 100 % wound healing) i.e, 86.95% in group I, whereas 12 out of 25 patients, i.e., 48 % in Group II.

Table: 4 Showing Comparision in Mean Reduction (MR) in Percentage of Ulcer Area on Day 7 & Day 14 in Both Group

S No.	PARAMETER	GROUP I %	GROUP II %	P	LEVEL OF SIGNIFI
01.	MEAN RED. ON DAY 07	41.38	24.56	<0.001	Highly significant
02.	MEAN RED. ON DAY 14	68.17	47.85	<0.001	Highly significant

Table: 5 Showing Comparision of Efficiency as more than 50% Reduction in Ulcer Area On Day 14 in Both Groups

S No.	Gp.	FREQ.	>50% REDC. IN SURFACE AREA OF ULCER (n)	t	LEVEL OF SIGNIFICANCE
01.	I	25	22	<0.001	Highly significant
02.	II	25	09		

Discussion

Phenytoin has been investigated as a treatment for more than 100 diseases. Numerous allergy and proliferative, idiosyncratic cutaneous side effects have been reported with its use.[13] A frequent observed and unwanted side effect of phenytoin, an anticonvulsant medication, is gingival hyperplasia, especially in children.[14] This side effect suggested that phenytoin can induce the growth of connective tissue, and may have the ability to promote wound healing. In 1939, Kimball and Horan first observed that gingival hyperplasia occurred in some patients treated with phenytoin. This stimulated the first controlled clinical trial in 1958, which found that the periodontal patients with surgical wounds who were pretreated with oral phenytoin had less inflammation, less pain, and accelerated healing when compared with controls.[15] Phenytoin promotes wound healing by following mechanisms: Stimulation of fibroblast proliferation, enhancing the formation of granulation tissue, decreasing collagenase activity, inhibition of glucocorticoid activity, direct or indirect antibacterial activity by affecting inflammatory cells, neovascularization and phenytoin increase gene expression of the platelet-derived growth factor β chain in macrophage and monocytes. It is not known if phenytoin has intrinsic antibacterial activity, or whether the effect of phenytoin on the bacterial load of wounds is mediated indirectly by effects on inflammatory cells and neovascularization[16-19]

Conclusion

Finally we conclude that use of phenytoin for healing of DFU is an acceptable alternative to conventional method. We recommend its use in wound healing. It is also safe, easily available, easy to apply and in-expensive.

Topical Phenytoin has following mechanism of action:

- Increased fibroblast proliferation
- Inhibition of collagenase activity
- Enhances granulation tissue formation

- Probably decreases bacterial contamination
- Reduces wound exudate formation.

Further recommendations: There are several issues which needs further evaluations like:-

1) Possible use of different delivery mode.
2) Combination with other methods of therapy.
3) Systemic absorption with different wound types.
4) Other additional mechanism by which phenytoin acts.

References

1. Ahmed AM. History of diabetes mellitus. Saudi Med J. 2002;23:373–8.
2. Nalini S, David G, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA.2005;293:217–28.
3. Reiber GE, Vileikyte L, Boyko EJ, del AM, Smith DG, Lavery LA, et al. Causal pathways for incident lower extremity ulcers in patients with diabetes from two settings. Diabetes Care. 1999;22:157–62.
4. American Diabetes Association. Consensus development conference on diabetic foot wound care.Diabetes Care. 1999;22:1354– 60.
5. Armstrong DG, Lavery LA. Diabetic foot ulcers: prevention, diagnosis and classification. AmFam Physician. 1998;57:1325–32.
6. Frykberg RG. Diabetic foot ulcerations. In: Frykberg RG, editor. The high risk foot in diabetes mellitus.New York: Churchill Livingstone; 1991. pp. 151–95.
7. Frykberg RG. Diabetic foot ulcers: current concepts. J Foot Ankle Surg. 1998;37:440–6.
8. Frykberg RG, Armstrong DG, Giurini J, Edwards A, Kravette M, Kravitz S, et al. Diabetic foot disorders: a clinical practice guideline. American College of Foot and Ankle Surgeons. J Foot Ankle Surg. 2000;39(5 Suppl):S1–60.
9. White R, McIntosh C. Topical therapies for diabetic foot ulcers: standard treatments. J Wound Care.2008;17:426–32.