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A Comparative Study Of Efficacy Of Topical Phenytoin Vs Oxum Dressings In Chronic Non Healing Ulcers

KEYWORDS

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INTRODUCTION

In this millennium where mankind has succeeded in deciphering the human genetic code, theissue of chronic wound management still remains an enigmatic challenge. Chronic wounds,especially non healing types, are one of the most common surgical conditions a surgeoncomes across. For time immemorial doctors have been trying many methods to treat thesetypes of wounds.

The peculiarity of a chronic wound is that, whatever management you give, theyrefuse to heal, especially pressure ulcers or bed sores. The notion that woundsshould be kept dry, although still held by a considerable number of clinicians, issteadily losing ground. We now know that wounds re-epithelialiase much faster ordevelop granulation tissue faster when treated with dressings which allow moistwound healing. We recognize that occluding wounds does not lead to infection.

Even though many modalities of wound care have come up to assist a surgeon,

example the use of compression bandages to treat venous ulcers, the problem ofchronic wound still remains.[1]

A wound care revolution is currently in the making. Many techniques have been tried overthe centuries to heal chronic leg ulcers. Although wound dressing have been used for at leasttwo millennia, there exist no ideal dressing. Surgical dressing of both open and closed woundis based mainly on tradition, training and surgeons own philosophy. During the last twodecades a wide variety of innovative dressings have been introduced.[2]

People have tried various non-conventional topical therapies in wound healing,such as aloe vera, antacids, Benzoyl peroxide, collagen, gentian violet,impregnated guaze, insulin, mercurochrome, oxygen therapy, sugar, vinegar andphenytoin.[3]

Studies have also shown that topical phenytoin promotes healing of Decubitus

ulcers, venous stasis ulcers, traumatic wounds, burns, leprosy , trophic ulcers,and was found to be superior management of diabetic ulcers. The present studywas conducted to assess the efficacy of topical phenytoin dressing as comparedto oxum dressing in healing process in ulcers and prove that Topical phenytoincan be used as much better alternative option in the management of chronic non healingulcers.[4,5,6,7,8,9,10,11]

NEED FOR STUDY

Chronic non healing ulcer is a common clinical entity and continues to be a therapeuticproblem

Clinical, animal, and in vitro studies suggest that phenytoin may be involved in the healingprocess at several levels including stimulation of fibroblast proliferation, enhancing theformation of granulation tissue, decreasing collagenase activity (by reducing its production orsecretion or both), promoting deposition of collagen and other connective tissue components,decreasing bacterial contamination and decreasing wound exudates Biopsies of phenytointreated open wounds show neovascularization, collagenization, decreased polymorphonuclearinfiltrate cells, and eosinophils.

This apparent stimulatory effect of phenytoin on connective tissue suggested an excitingpossibility for its use in wound healing. We aim to take up this study to evaluate the efficacyof topical phenytoin in chronic non healing ulcers in our institution.

OBJECTIVES OF THE STUDY

To compare the efficacy of topical phenytoin with that of a controlgroup using conventional wound dressings,in healing of diabeticulcers, in terms of:

1. Number of days required for healing.
2. Rate of granulations tissue formation.
3. Rate of reduction in mean ulcer surface area.
4. Quality of graft bed.
5. Skin graft take up.
6. Serial culture and sensitivity of wound swabs to assess the effect of topical phenytoin on bacterial load.

REVIEW OF LITERATURE

Phenytoin (diphenylhydantoin) was introduced into therapy in 1937 for the effective control of convulsive disorders. It was in 1939 that Kimball first observed gingival hyperplasia in some epileptics treated with phenytoin and this stimulated the use of phenytoin in wound healing. Shapiro carried out the first controlled clinical trial in 1958, finding that periodontal patients with surgical wounds who were pre treated with oral phenytoin had less inflammation, less pain and accelerated healing compared with controls. A common side effect with phenytoin is the development of fibrous overgrowth of gingiva. This apparent stimulatory effect of phenytoin on connective tissue suggested

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an exciting possibility for its use in wound healing. Healthy granulation tissue appears earlier with phenytoin than with conventional dressings. It has been reported that phenytoin has contributed to the removal of various Gram-positive and Gram-negative organisms from wounds. Local pain relief has been observed with topical phenytoin therapy, which can be explained by its membrane stabilizing action and by reducing the inflammatory response. Facilitation of nerve regeneration has also been reported with phenytoin.

Simpson, Kunz and Slafta, reported that phenytoin promoted the healing of chronic leg ulcers.Measurements were made by means of a planimeter reading of the ulcer area as well as the actual scaling area around the ulcer and clinical rating. All 3 indices measured showed improvement in the phenytoin group compared with the placebo group.

Strean, reported phenytoin was effective in promoting the complete healing of an antecubital ulcer, a diabetic ulcer and two peptic ulcers, all of long duration. It was found that phenytoin provided for the regeneration of healthy tissue in the denuded zone.

El-Zayat, conducted pilot clinical trials to evaluate topical phenytoin's effectiveness in treating decubitus ulcers resulting from war-related wounds.Prompt pain relief, decreased wound exudate and bacterial contamination, enhanced granulation tissue formation, and more rapid healing characterized the phenytoin group. The author emphasizes that topical phenytoin is not only effective in promoting wound healing, but is also readily available, safe, inexpensive, and easy to use.[4]

Muthukumarasamy, Sivakumar and Manoharan, conducted a study of application of phenytoin on diabetic foot ulcers,(applied as a thin layer over the ulcer). The patients were matched for age, sex, ulcer area, depth, chronicity and infection. There was improvement, in the ulcers treated with topical phenytoin which healed more rapidly.[5]

Adjei, Evans and Asiedu, presented three cases of Ghanaian children (ages 8-17) with Buruli ulcers which were treated successfully with topical phenytoin. Fresh granulation tissue appeared within two to six weeks of treatment and complete healing was achieved in six to sixteen weeks with the time to healing correlating with ulcer duration.[6]

Bansal and Mukul compared topical phenytoin with sodium chloride (0.9 %) dressing in the treatment of leprosy trophic ulcers. In the phenytoin group, granulation tissue was well established and wound discharge was eliminated within 1 week whereas in the control group discharge persisted through the second and third weeks and comparable degree of granulation required 2 weeks.[7]

Rhodes, Heyneman, Culbertson, Wilson and Pkatak, report on a study of patients with stage II decubitus ulcers.Results indicated that, the phenytoin group showed more rapid results in all aspects of ulcer healing. All wounds in the phenytoin group showed greater reduction in ulcer size, appearance of healthy granulation tissue, and reduction in wound exudates. No adverse drug reactions or interactions were noted throughout the study.[8]

Carneiro and Nyawawa, evaluated the effectiveness of topical phenytoin compared to that of EUSOL (Edinburgh University solution of lime) with respect to rate of healing and analgesic and antibacterial properties in patients with chronic, non-malignant leg ulcers, over a fourteen-month period.The authors found that pain reduction and ulcer discharge reduction was greater with the phenytoin group than for EUSOL.[9]

Oluwatosin et al. compared topical phenytoin with honey dressings for the treatment of chronic leg ulcers and found that phenytoin was superior to honey as a topical agent.[10]

OBSERVATION AND RESULT

The 100 patients admitted for the study were divided into two equal and comparable groups. Patients subjected to topical phenytion dressing were classified under Studyand those who underwent oxum wound dressings were classified as control. The patients characteristics of the two groups were well matched in the table below:

	Study	Control
No. of patients	50	50
Range of age in years	25-75	25-75
Male – Female ratio (M : F)	28:22	35:15
Range of Ulcer surface area cm	6-100	4-80

RESULTS

GROUP A –PHENYTOIN DRESSINGS GROUP B – OXUM DRESSINGS

Table 1:AGE DISTRIBUTION OF PATIENTS STUDIED

Age in years	Group A		Group B	
	No	%	No	%
<=40	4	8.0	5	10.0
41-50	11	22.0	16	32.0
51-60	16	32.0	16	32.0
61-70	16	32.0	10	20.0
71-80	2	4.0	2	4.0
>80	1	2.0	1	2.0
Total	50	100.0	50	100.0

Samples are age matched with P=0.323

The age of the patients were varied from 25 to 75 years. Maximum number of cases(40%)belong to the age group of 50 to 70 years. The average age of diabetic foot lesion in ourcountry is 60 years.

Table 2: GENDER DISTRIBUTION OF PATIENTS

Gender	Group A		Group B	
	No	%	No	%
Male	35	70.0	35	70.0
Female	15	30.0	15	30.0
Total	50	100.0	50	100.0

Samples are gender matched with P=1.000

In both study and control group males had more ulcers and were subjected to the study compared to females. Among them 70% of the patients were male and 30% were female.

Table 3:DURATION OF HOSPITAL STAY IN DAYS

Duration stay in days	Group A (n=50)		Group B (n=50)	
	No	%	No	%
1-12	1	2.0	0	0.0
13-24	8	16.0	0	0.0
25-36	9	18.0	8	16.0
37-48	24	48.0	15	30.0
>48	8	16.0	27	54.0
Mean ±SD	38.70±12.07		56.78±22.92	

Mean duration of hospital Stay in days is significantly less in Group A with **P=<0.001****

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Mean duration of hospital Stay in days is significantly less in Group A with**P=<0.001**.**The Mean ±SD in group A(phenytoin dressings) is 38.70±12.07 and in group B(oxum dressings) is 56.78±22.92.

This graph shows that patient s treated with phenytoin dressings had lesserduration of stay in the hospital.

Table 4:COMPARISON OF NUMBER OF DAYS IN WHICHGRANULATION TISSUE APPEARED IN BOTH THE GROUPS

Granulation	Group A (n=50)		Group B (n=50)	
	No	%	No	%
1-10	38	76.0	15	30.0
11-20	12	24.0	28	56.0
>20	0	0.0	7	14.0
Mean ±SD	9.49±4.32		14.72±5.27	

Mean Granulation is significantly less in Group A with P=<0.001**. The maximum number of days in which granulation tissue was seen in group A is **1-10 days** i.e **76%** and in group B the maximum number of days in which granulation tissue was seen is **11-20 days** i.e **56 %**. The Mean ±SD in group A is 9.49±4.32 and in group B is 14.72±5.27.

Table 5: COMPARISON OF CULTURE SENSITIVITY AFTER 7 DAYS IN TWO GROUPS

Culture Sensitivity	Group A		Group B	
	No	%	No	%
Negative	24	48.0	17	34.0
Positive	26	52.0	33	66.0
Total	50	100.0	50	100.0

Granulation tissue appeared much faster in patients treated with phenytoin dressings than patients treated with oxum dressings.

Culture sensitivity positive are more in Group B (66.0% vs 52.0%) with **P=0.155**

Culture sensitivity was positive in both the study and control groups after 7 days. Both the groups were continued on the antibiotics required.

Table 6: COMPARISON OF GRAFT TAKE UP IN TWO GROUPS

Graft Take up	Group A (n=50)		Group B (n=50)	
	No	%	No	%
<30	0	0.0	4	8.0
30-50	1	2.0	17	34.0
51-70	0	0.0	10	20.0
>70	49	98.0	19	38.0
Mean ±SD	86.39±8.17		58.72±21.44	

Graft take up is significantly more in Group A with **P=<0.001**,**the % of graft up take was in group A 98% and in group B it was 38%. The Mean ±SD in group A was 86.39±8.17 and in group B was 58.72±21.4.

The patients treated with phenytoin dressings had better graft up take than patients treated with oxum dressings.

Table 7: TYPE OF ULCER

Type of Ulcer	Group A (n=50)		Group B (n=50)		P value
	No	%	No	%	
Diabetic	28	56.0	37	54.0	0.059+
Pressure	6	12.0	5	10.0	0.749
Skin graft	3	6.0	2	4.0	1.000
Traumatic ulcer	6	12.0	4	8.0	0.505
Venous stasis ulcer	7	14.0	2	4.0	0.081+

The commonest ulcer seen is the diabetic ulcer for which in group A **56 %** cases were diabetic and in group B **54%** were diabetic ulcers.

SUMMARY

Increased rate of granulation tissue formation was seen in topical phenytoin dressing group when compared to conventional dressing group. Better graft take up was seen in topical phenytoin dressing group as compared to the conventional dressing group. Shorter duration of hospital stay was observed in the topicalphenytoin dressing group.

Topical phenytoin dressing appears to be an effective, inexpensive and widely available therapeutic agent in wound healing. Follow up observations revealed that topical phenytoin dressing group suffered lesser post skin grafting complications like wound contractures, residual raw area and pain compared to the conventional dressing group.

CONCLUSION

In our present study it was concluded that the rate of granulation tissue formation, overall graft survival and patient compliance was better in topical phenytoin dressing group as compared to oxum dressing group. It was also seen that the overall hospital stay and post operative complications were less in the topical phenytoin dressing group. Thus, topical phenytoin moist wound dressing can be considered as a superior option in the management of chronic non healing ulcers. But further studies with larger population will be needed in the future before topical phenytoin dressing can be added to the wide spectrum of treatment modalities available in the management of diabetic ulcers and ulcers of other etiology.