



A COMPARITIVE STUDY BETWEEN PHENYTOIN TOPICAL DRESSING AND NEUTRAL PH SOLUTION OF HYPOCHLOROUS ACID ON DIABETIC AND CHRONIC ULCERS

General Surgery

Dr. Nichenametla Vishnu Keshav	Post graduate (Department of General Surgery) Meenakshi Medical College Hospital and Research Center.
Dr. Niveditha V	Post graduate (Department of General Surgery), Meenakshi Medical College Hospital and Research Center.
Professor Dr P S Saravanan	HOD, Department of General Surgery, Meenakshi Medical College Hospital and Research Center.
Dr Ravi R	Associate Professor, Department Of General Surgery, Meenakshi Medical College Hospital and Research Center.
Dr Dorababu	Post Graduate, Department Of General Surgery, Meenakshi Medical College Hospital and Research Center.

ABSTRACT

Treatment of wounds, which is being a difficult to treat because of chronic nature in many patients in day-to-day practice. There are so many topical treatments which are being used. In our study we are going to compare the efficacy two different type of dressing to Select and make rapid decisions. Phenytoin and hypochlorous acid are widely used in the management of chronic ulcers, their efficacy in terms of time taken for granulation tissue formation, duration of hospital stay, time taken for complete healing of ulcer and cost effectiveness remains unclear. Hence this study was conducted to compare the outcome of phenytoin or neutral pH hypochlorous acid solution dressings in the management of diabetic and chronic ulcers.

KEYWORDS

Chronic Ulcer, Phenytoin, Hypochlorous acid, Granulation tissue, Healing

INTRODUCTION

Diabetic ulcers or other chronic ulcers are the most frequent type of ulcers reported in the surgical outpatient department. Due to the chronicity of the ulcers it requires continuous treatment even as inpatients. The majority of the chronic ulcers are due to diabetes mellitus, venous disorders and pressure point ulcers. The challenge in the management of chronic ulcers is that even after regular cleaning, dressing, use of topical applicants, etc., the ulcer remains unhealed. Thus, treating these chronic ulcers remains a challenge for the surgeons. During the recent times there were several newer treating techniques were introduced. Apart from the techniques there are several drugs which were used in the treatment of chronic ulcers including topical phenytoin, hypochlorous acid, betadine, etc. Phenytoin is one of the commonly used anticonvulsant drugs which is readily available throughout the world. It was found to act by blocking the neuronal excitation by binding with the sodium channels during rest and preventing its functional properties which results in generating excitatory action potentials¹. It was first used in the dental science, as a healing agent during the year 1939, which results in hypergranulation of gingival tissues^{2,3}. The mechanism of phenytoin in the process of healing remains unclear⁴. However, the findings of various studies⁵⁻¹⁰ suggest that phenytoin has properties which in healing mechanism among the cases with vascular ulcers, diabetic ulcers and pressure ulcers. Phenytoin is also readily available at low-cost with better healing property. Studies have proven that with the use of phenytoin the process of granulation tissue formation occurs earlier than the conventional saline dressings¹¹. It was shown that it helps in wound healing by stimulation of proliferation of fibroblast¹². Another drug which is being used in the treatment of chronic ulcer is hypochlorous acid (HOCL). Hypochlorous acid is nothing but water along with sodium chloride electrolyzed to form reactive oxygen and chlorine in a neutral pH which has antimicrobial property¹³. HOCL acts by disrupt and preventing the biofilm and it has bactericidal characteristic in the low concentrations. However, these agents, phenytoin and hypochlorous acid are widely used in the management of chronic ulcers, their efficacy in terms of time taken for granulation tissue formation, duration of hospital stay, time taken for complete healing of ulcer remains unclear. Hence this study was conducted to compare the outcome of phenytoin or neutral pH hypochlorous acid solution dressings in the management of diabetic and chronic ulcers.

OBJECTIVES

To compare the outcome of phenytoin or neutral pH hypochlorous acid solution dressings in the management of diabetic and chronic ulcers in

terms of - Time taken for Granulation tissue formation - Duration of Hospital stay - Time taken for complete healing of ulcer

MATERIALS AND METHODS

Study Design: This cross sectional study was conducted to compare the outcome of phenytoin or neutral pH hypochlorous acid solution dressings in the management of diabetic and chronic ulcer.

Study Area: This study was conducted in the department of General Surgery in Meenakshi Medical College Hospital and Research Institute, a tertiary care teaching hospital located in Enathur, Kanchipuram.

Study population: Patients attending outpatient and inpatient department of General surgery with chronic ulcers during the study period were included in the study.

Study period: The study was conducted during the period of March 2021 to March 2022.

Inclusion Criteria:

Cases with chronic ulcers including diabetic ulcers, venous ulcers, pressure ulcers and Cases of aged more than 18 years were included in this study.

Exclusion Criteria:

Cases with Burn ulcers Malignant ulcers Traumatic ulcer Tuberculosis ulcer and Syphilis ulcer were excluded from the study.

Sample size:

a total of hundred patients with chronic ulcers were included in the study and among them fifty cases were assigned to topical phenytoin group and another fifty cases were assigned to neutral pH hypochlorous acid group through computer generated random numbers.

RESULTS

In the present study a total of 100 cases were included. Group phenytoin refers to phenytoin group and group hypochlorous acid refers to hypochlorous acid, which were used for the treatment of chronic ulcers. In phenytoin group there were 10%, 22%, 34%, 28% and 6% of cases belongs to age group 31-40 years of age, 41-50 years of age, 51-60 years of age, 61-70 years of age and more than 70 years of age, respectively. Similarly in hypochlorous acid group, there were

8%, 18%, 36%, 24% and 14% of cases belongs to age group 31-40 years of age, 41- 50 years of age, 51-60 years of age, 61-70 years of age and more than 70 years of age, respectively. The association between age group in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.7185$).table 1

In the present study, in phenytoin group there were 76% and 24% of cases were males and females, respectively. Similarly in hypochlorous acid group there were 70% and 30% of cases were males and females, respectively. Association between gender in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.4992$).table 2

On assessing the proportion of cases with habit of smoking, in the phenytoin group there were 28% and 72% of cases with and without habit of smoking, respectively. Similarly, in the hypochlorous acid group there were 30% and 70% of cases with and without habit of smoking, respectively. Association between habit of smoking in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.8255$). table 3

In phenytoin group there were 58% and 42% of cases with and without history of diabetes mellitus, respectively whereas in the hypochlorous acid group there were 54% and 46% of cases with and without history of diabetes mellitus, respectively. On assessing the association between diabetes mellitus in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.6870$).table 4

In phenytoin group there were 24% and 76% of cases with and without history of hypertension, respectively whereas in the hypochlorous acid group there were 20% and 80% of cases with and without history of hypertension, respectively. On assessing the association between hypertension in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.6292$).table 5

Among the study participants, in phenytoin group there were 24%, 38% and 20% of cases with HbA1c levels of less than 6.5%, 6.5-8% and more than 8%, respectively. Similarly, in hypochlorous acid group there were 40%, 42% and 18% of cases with HbA1c levels of less than 6.5%, 6.5-8% and more than 8%, respectively. On assessing the association between HbA1c levels in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.9152$).Table 6

Based on type of ulcer, in phenytoin group there were 38%, 34%, 10% and 18% of cases with diabetic ulcer, venous ulcer, necrotizing ulcer and pressure wound, respectively. Similarly, in hypochlorous acid group there were 34%, 38%, 8% and 20% of cases with diabetic ulcer, venous ulcer, necrotizing ulcer and pressure wound, respectively. On assessing the association between type of ulcers in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.9431$). Table 7

In phenytoin group there were 84%, 4% and 12% of cases with ulcers in their lower extremities, upper extremities and other areas, respectively. Similarly, in hypochlorous acid group there were 84%, 6% and 10% of cases with ulcers in their lower extremities, upper extremities and other areas, respectively. On assessing the association between location of ulcers in phenytoin group and hypochlorous acid group was found to be statistically insignificant ($p=0.8646$).Table 8

Mean ulcer size before the treatment in the phenytoin group was reported as 9.5 ± 4.2 cms and in the hypochlorous acid groups it was reported as 8.4 ± 5.1 cms. The mean dissimilarity in size of ulcer before the treatment in phenytoin group and in the hypochlorous acid group was found to be similar with no statistically significant dissimilarity noted (0.2419). Table 9

Mean ulcer size after the treatment in the phenytoin group was reported as 4.1 ± 1.2 cms and in the hypochlorous acid groups it was reported as 6.7 ± 2.2 cms. The mean dissimilarity in size of ulcer after the treatment in phenytoin group was comparatively lower than the hypochlorous acid group and the dissimilarity was significant (0.0001). Table 10

In phenytoin group, granulation tissues were observed on 14th day of treatment in 94% of cases and 6% without any granulation tissue growths were reported. Similarly, in the hypochlorous acid group, granulation tissues were observed on 14th day of treatment in 78% of

cases and 22% without any granulation tissue growths were reported. On assessing the association between granulation tissue after 14 days of treatment in phenytoin group and hypochlorous acid group was significant ($P=0.0211$). Table 11

In phenytoin group, there were 82%, 12% and 6% of cases with complete healing of ulcer, partial healing and no improvement in the ulcer, respectively following the treatment. Similarly, in hypochlorous acid group, there were 52%, 28% and 20% of cases with complete healing of ulcer, partial healing and no improvement in the ulcer, respectively following the treatment. On assessing the association between the ulcers status following treatment phenytoin group was found to be much better than hypochlorous acid group and the dissimilarity in proportion was significant ($p=0.0057$). Table 12

On assessing the time taken for complete healing, in the phenytoin group, 84%, 14% and 2% of cases were reported with complete healing of ulcer in less than or equal to 3 weeks of treatment, 4-6 weeks and more than 6 weeks of treatment, respectively. Similarly, in the hypochlorous acid group, 62%, 24% and 14% of cases were reported with complete healing of ulcer in less than or equal to 3 weeks of treatment, 4-6 weeks and more than 6 weeks of treatment, respectively. On assessing the association between time taken for complete healing of ulcer in phenytoin group and hypochlorous acid group, phenytoin group tend to heal faster than hypochlorous acid group and it was found to be statically significant ($p=0.0238$). Table 13

Mean duration of stay in the hospital in the phenytoin group was reported as 10.6 ± 8.2 days and in the hypochlorous acid groups it was reported as 13.5 ± 11.4 days. The mean dissimilarity in duration of stay in the hospital for the treatment in phenytoin group was comparatively lower than the hypochlorous acid group and the dissimilarity was significant (0.0006). Table 14

DISCUSSION

In the present study a total of 100 cases were included. Group phenytoin refers to phenytoin group and group hypochlorous acid refers to hypochlorous acid, which were used for the treatment of chronic ulcers.

The association between Age group ,Gender, Habit of Smoking, Diabetis Mellitus,Hypertension in phenytoin group and hypochlorous acid group was found to be statistically insignificant.

On assessing the association between HbA1c levels, Type of Ulcers, Location of Ulcers in phenytoin group and hypochlorous acid group was found to be statistically insignificant.

The mean dissimilarity in size of ulcer before the treatment in phenytoin group and in the hypochlorous acid group was found to be similar with no statistically significant dissimilarity noted.

The mean dissimilarity in size of ulcer after the treatment in phenytoin group was comparatively lower than the hypochlorous acid group and the dissimilarity was significant.

On assessing the association between granulation tissue after 14 days of treatment in phenytoin group and hypochlorous acid group was significant.

On assessing the association between time taken for complete healing of ulcer in phenytoin group and hypochlorous acid group, phenytoin group tend to heal faster than hypochlorous acid group and it was found to be statically significant.

The mean dissimilarity in time taken for complete healing of ulcer after the treatment in phenytoin group was comparatively lower than the hypochlorous acid group and the dissimilarity was significant.

Mean duration of stay in the hospital in the phenytoin group was reported as 10.6 ± 8.2 days and in the hypochlorous acid groups it was reported as 13.5 ± 11.4 days. The mean dissimilarity in duration of stay in the hospital for the treatment in phenytoin group was comparatively lower than the hypochlorous acid group and the dissimilarity was significant.

CONCLUSION

Findings of this study show that topical phenytoin is comparatively

better than neutral pH hypochlorous acid in terms of early formation of granulation tissues and reduction the size of the ulcer. Also more proportion of cases with complete healing of ulcer and early clearance of wound discharge was reported among the cases those who were treated with topical phenytoin than neutral pH hypochlorous acid. With respect to time taken, the overall time taken for complete healing of the ulcer and reduced duration of hospital stay were reported in the phenytoin group compared to neutral pH hypochlorous acid group. Thus we conclude that topical phenytoin is comparatively more efficacious than neutral pH hypochlorous acid.

List Of Tables

Table 1: Comparison Of Age Between Groups

Age group	Group P N (%)	Group H N (%)	Total	P value
31-40 years	05(10)	04(08)	09	0.7185
41-50 years	11(22)	09(18)	20	
51-60 years	17(34)	18(36)	35	
61-70 years	14(28)	12(24)	26	
> 70 years	03(06)	07(14)	10	
Total	50 (100)	50 (100)	100	

Table 2: Comparison Of Gender Between Groups

Gender	Group P	Group H	Total	P value
Male	38(76)	35(70)	73	0.4992
Female	12(24)	15(30)	27	
Total	50 (100)	50 (100)	100	

Table 3: Comparison Of Habit Of Smoking Between Groups

Habit of smoking	Group P	Group H	Total	P value
Present	14(28)	15(30)	29	0.8255
Absent	36(72)	35(70)	71	
Total	50 (100)	50 (100)	100	

Table 4: Proportion Of Cases With Diabetes Mellitus In Both The Groups

Diabetes mellitus	Group P	Group H	Total	P value
	29(58)	27(54)	56	0.6870
No	21(42)	23(46)	44	
Total	50 (100)	50 (100)	100	

Table 5: Proportion Of Cases With Hypertension In Both The Groups

Known case of hypertension	Group P	Group H	Total	P value
	12(24)	10(20)	22	0.6292
No	38(76)	40(80)	78	
Total	50 (100)	50 (100)	100	

Table 6: Comparison Of HbA1c Levels In Both The Groups

HbA1c levels	Group P	Group H	Total	P value
< 6.5%	21(24)	20(40)	41	0.9152
6.5-8 %	19(38)	21(42)	40	
> 8%	10(20)	09(18)	19	
Total	50 (100)	50 (100)	100	

Table 7: Comparison Of Type Of Ulcers Between Groups

Type of Ulcer	Group P	Group H	Total	P value
Diabetic ulcer	19(38)	17(34)	36	0.9431
Venous ulcer	17(34)	19(38)	36	
Necrotizing wound	05(10)	04(08)	9	
Pressure	09(18)	10(20)	19	
Total	50 (100)	50 (100)	100	

Table 8: Comparison Of Location Of Ulcer Between Groups

Ulcer location	Group P	Group H	Total	P value
Lower extremity	42(84)	42(84)	84	0.8646
Upper	02(04)	03(06)	05	
Other	06(12)	05(10)	11	
Total	50 (100)	50 (100)	100	

Table 9: Mean Size Of Ulcer Before Treatment In Both The Groups

Mean ulcer size	Group P	Group H	P value
Before (in cms)	9.5±4.2	8.4±5.1	0.2419

Table 10: Mean Size Of Ulcer After Treatment In Both The Groups *Significant

Mean ulcer size	Group P	Group H	P value
After (in cms)	4.1±1.2	6.7±2.2	0.0001*

Table 11: Comparison Of Granulation Tissue Formation In Both The Groups *Significant

Granulation tissue after 14 days of treatment	Group P	Group H	Total	P value
	47(94)	39(78)	86	0.0211*
Absent	03(06)	11(22)	14	
Total	50 (100)	50 (100)	100	

Table 12: Comparison Of Time Taken For Complete Healing In Both The Groups *Significant

Time taken for healing	Group P	Group H	Total	P value
≤ 3 weeks	42(84)	31(62)	73	0.0238*
4-6 weeks	07(14)	12(24)	19	
> 6 weeks	01(02)	07(14)	08	
Total	50 (100)	50 (100)	100	

Table 13: Mean Time Taken For Complete Healing In Both The Groups *Significant

Mean Time taken for complete healing (in days)	Group P	Group H	P value
	16.7±13.5	25.6±17.2	0.0001*

Table 14: Mean Duration Of Hospital Stay In Both The Groups *Significant

Mean Duration of hospital stay (in days)	Group P	Group H	P value
	10.6±8.2	13.5±11.4	0.0006*

REFERENCES

- Hasamnis AA, Mohanty BK, Patil S. Evaluation of wound healing effect of topical phenytoin on excisional wound in albino rats. J Young Pharm. 2010;2(1):59-62.
- Arya R, Gulati S. Phenytoin-induced gingival overgrowth. Acta Neurol Scand. 2012; 125(3):149-55.
- Shaw J, Hughes CM, Lagan KM, Bell PM. The clinical effect of topical phenytoin on wound healing: a systematic review. Br J Dermatol. 2007;157(5):997-1004.
- Firmino F. Potencial terapêutico da fenitoína na cicatrização de radiodermite. Esc Anna Nery Rev Enferm. 2007;11(1):143-9.
- Simpson GM, Kunz E, Slaughter J. Use of sodium diphenylhydantoin in the treatment of leg ulcers. NY State J Med 1965;65:886-8.
- Muthukumarasamy MG, Sivakumar G, Manoharan G. Topical phenytoin in diabetic foot ulcers. Diab Care 1991;14:909-11.
- Pai MR, Sitaraman N, Kotian MS. Topical phenytoin in diabetic ulcers: a double blind controlled trial. Indian J Med Sci 2001;55(11):593-9.
- Bansal NK, Mukul. Comparison of topical phenytoin with normal saline in the treatment of chronic trophic ulcers in leprosy. Int J Dermatol 1993;32(3):210-3.
- Carneiro PM, Nyawawa ET. Topical phenytoin versus EUSOL in the treatment of nonmalignant chronic leg ulcers. East Afr Med J 2003;80(3):124-9.
- Rhodes RS, Heyneman CA, Culbertson VL, Wilson SE, Phatak HM. Topical phenytoin treatment of stage II decubitus ulcers in the elderly. Ann Pharmacother

- 2001;35(6):675e81.87
11. Pendse AK, Sharma A, Sodani A, Hada S. Topical phenytoin in wound healing. *Int J Dermatol* 1993;32:214e7.
 12. Anstead GM, Hart LM, Sunahara JF, Liter ME. Phenytoin in wound healing. *Ann Pharmacother* 1996;30:768e75.
 13. Selkon JB, Cherry GW, Wilson JM, et al. Evaluation of hypochlorous acid washes in the treatment of chronic venous leg ulcers. *J Wound Care* 2006;15:33–7.