Original Article

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Comparative Study on Efficacy of Autologous Platelet Gel versus Topical Phenytoin in Chronic Wounds: A Prospective, Randomized Controlled Study

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Abstract

Introduction: Platelets are commonly known to release certain factors from alpha (α) granules which include platelet-derived growth factor and epidermal growth factor, which act locally on the wound and hasten the healing process. The most common side effect of phenytoin treatment for epilepsy is gingival hyperplasia.

Aims: The objective of this study was to assess the efficacy of Autologous Platelet gel compared to topical phenytoin in improving the healing process and to prove it as a relatively low cost and easy to use the option in the management of chronic wounds.

Materials and Methodology: In this experimental study, the data from 30 patients with chronic ulcers were collected, 15 patients underwent topical phenytoin dressing, and remaining 15 patients underwent autologous platelet gel. Variables like the rate of granulation tissue formation as percentage of ulcer area covered, percentage of graft take up, and duration of hospital stay were compared.

Results: Mean reduction in the area of ulcer, 237.67 mm2 for the platelet dressing was more than that of phenytoin dressing, 17.04 mm2 after the initiation of treatment. The percentage reduction in platelet dressing was 46.95% ± 15.16% and 2.28% ± 2.54% in phenytoin dressing, which was statistically significant. The maximum number of days in which granulation tissue was seen in platelet dressing is 1-10 days, i.e., 80% and in phenytoin dressing the maximum number of days in which granulation tissue was seen is 11-20 days, i.e., 53.0%.

Conclusions: Autologous platelet gel helps in faster healing with better graft take up and reduces hospital stay.

Key words: Chronic wounds, Dressing, Granulation tissue, Healing, Phenytoin, Platelet gel

INTRODUCTION

Platelet extract has shown to enhance and accelerate both soft tissue and hard tissue healing. Its effectiveness is based on its high level of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β, epidermal growth factor (EGF), vascular EGF, and insulin-like growth factor.[1]

A common side effect of phenytoin is the development of fibrous overgrowth of gingiva. This apparent stimulatory effect of phenytoin on connective tissue suggested an exciting possibility for its use in wound healing. 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.[2]

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MATERIALS AND METHODOLOGY

This is a prospective, randomized controlled study, to test the efficacy of autologous platelet gel versus topical phenytoin in epithelialization and wound reduction in chronic wounds. The study was conducted in the Department of Surgery, JSS hospital for a period of 6 months from July 2014 to December 2014.

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30 patients were studied, 15 cases were randomly chosen for study with autologous platelet gel and 15 cases received topical phenytoin as dressing for the chronic wound.

- Study type:
  - Prospective, observational, randomized study.

Inclusion Criteria

- Age group: 18-80 years
- Ulcer ≥ 8 weeks
- Hemoglobin > 10 g%
- Fasting blood sugar ≤ 110 mg% and Post-prandial blood sugar ≤ 140 mg% if diabetic.

Exclusion Criteria

- Ulcers with evidence of malignancy
- Active infection with pus discharge, slough
- Evidence of gangrene in the ulcer or on any other part of limb
- Patient is currently receiving or has received radiation or chemotherapy within the last 3 months
- Patient has known or suspected osteomyelitis
- Patient with active cancer, decompensated liver disease, or on renal dialysis
- Patients on steroids for another illness
- Patients on oral phenytoin
- Patients hypersensitive to phenytoin.

Preparation of Platelet Gel

- 12 ml of blood was drawn intravenously from the antecubital region
- Blood centrifuged at 1000 rpm for 10 min
- The supernatant formed is platelet poor plasma which is discarded
- Remaining PRP is collected in another vacutainer and again centrifuged at 1000 rpm for 10 min. The upper half is discarded, and the lower half yields concentrated platelet rich plasma
- 2 ml of PRP which is thoroughly mixed with 0.08 ml of 10% calcium gluconate.

Topical Phenytoin

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 total body surface area.

RESULTS

In this study, 90% of the patients were males as compared to females who were 10% of the total cases as shown in Table 1 and Graphs 1 and 2.

In this study, 50% of the wounds were of non-specific traumatic etiology. The next most common wounds were pressure sores at 16.6%. There is no statistical difference between platelet dressing and Phenytoin dressing with regard to the etiology of the wounds ($P = 0.797$) as shown in Table 2.

The mean duration of the wound in platelet dressing was 103.73 ± 130.75 weeks and 52 ± 98.2 weeks in the phenytoin dressing group. The difference of mean duration of the wound in platelet dressing and phenytoin dressing was not statistically significant ($P = 0.231$) as shown in Table 3 and Graph 3.

The mean area at the beginning of the study was 518.73 ± 383.02 mm^2 in the platelet dressing and 517.73 ± 506.91 mm^2 in the phenytoin dressing. There was no statistical difference between the two groups ($P = 0.995$) before initiation of treatment as shown in Table 4.

Mean reduction in the area of ulcer, 237.67 mm^2 for the platelet dressing was more than that of phenytoin dressing, 17.04 mm^2 after the initiation of treatment, and

Table 1: Age at presentation

Age group (in years)	No of patients	Percentage	*n*=15 (%)	
			Platelet dressing	Phenytoin dressing
<20	1	3	0 (0)	1 (7)
20-40	7	24	4 (27)	3 (20)
40-60	16	53	8 (53)	8 (53)
60-80	6	20	3 (20)	3 (20)

Table 2: Various etiologies of wounds

Etiology	Platelet dressing (%)	Phenytoin dressing (%)	Total (%)
Non-specific traumatic	8 (53.3)	7 (46.6)	15 (50)
Pressure sore	3 (20)	2 (13.3)	5 (16.6)
Diabetes	1 (6.7)	3 (20)	4 (13.3)
Snake bite	2 (13.3)	2 (13.3)	4 (13.3)
Varicose veins	1 (6.7)	1 (6.7)	2 (6.7)

Table 3: Duration of wound

Type of dressing	Duration in weeks		*P*
	Mean	SD	
Platelet dressing	103.73	130.75	0.231
Phenytoin dressing	52	98.2	

SD: Standard deviation

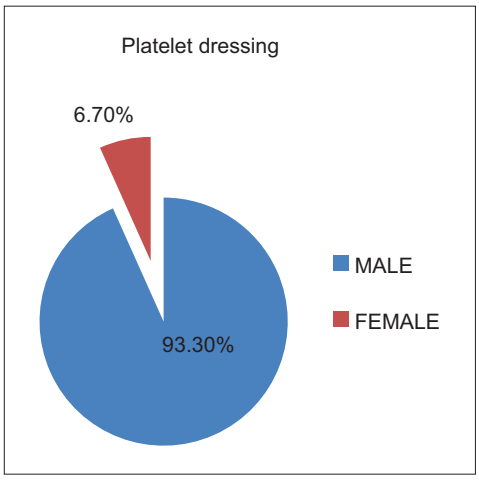
Table 4: Initial wound area in mm²

Type of dressing	Before		*P*
	Mean	SD	
Platelet dressing	518.73	383.02	0.995
Phenytoin dressing	517.73	506.91	

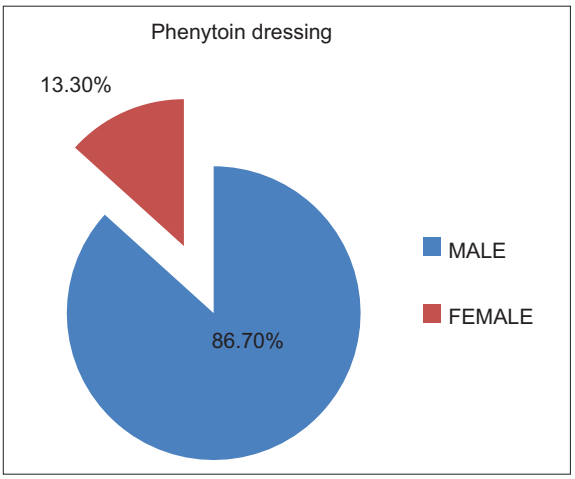
SD: Standard deviation

the difference was statistically significant ($P < 0.001$) as shown in Table 5 and Graph 4.

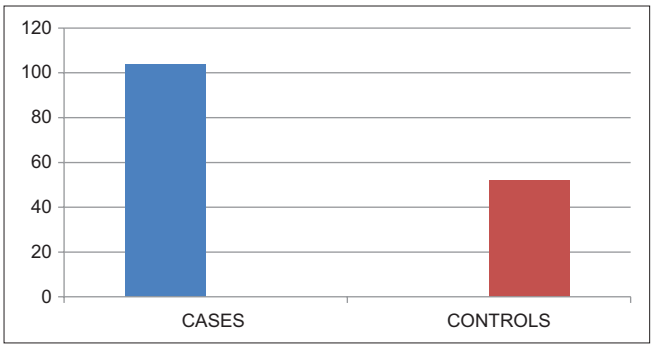
The percentage reduction in platelet dressing was 46.95% ± 15.16% and 2.28% ± 2.54% in phenytoin dressing which was statistically significant ($P = 0.000$) as shown in Table 6.



Graph 1: Platelet dressing



Graph 2: Phenytoin dressing



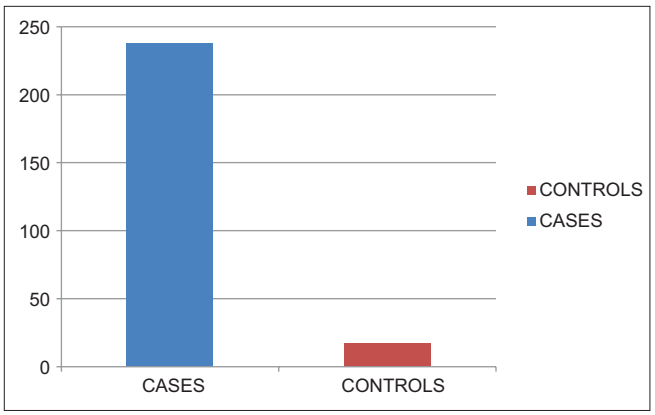
Graph 3: Mean duration of wound in cases and controls

Mean granulation is significantly less in platelet dressing with $P \leq 0.001$. The maximum number of days in which granulation tissue was seen in platelet dressing is 1-10 days, i.e., 80% and in phenytoin dressing the maximum number of days in which granulation tissue was seen is 11-20 days, i.e., 53.0% as shown in Table 7, Graph 5 and Figure 1.

DISCUSSION

Autologous platelet-rich plasma for the treatment of chronic wounds has been under development as a theory and for clinical application since 1986 when Knighton *et al.*[3] demonstrated for the first time its use in stimulating repair of non-healing human wounds.

In the Knighton *et al.* study,[3] the experimental group had a longer duration than the control group (119 weeks compared to 47 weeks), whereas in the Anitua *et al.* study,[4] the wound duration was longer in the control group (110 weeks vs. 68 weeks). The remaining studies including



Graph 4: Mean reduction in area of ulcer between cases and control

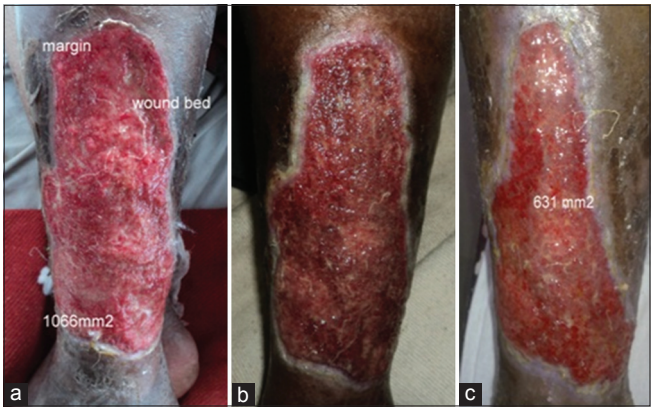


Figure 1: Rate of granulation formation at day 1 and day 4 after platelet dressing. (a) Day 1 platelet dressing, (b) Filling of wound bed and Rim of epithelialization, (c) Day 4 platelet dressing

Table 5: Reduction of mean area of ulcer of platelet dressing and phenytoin dressing after treatment

Type of dressing	Mean area reduced in mm²	SD	*P*
Platelet dressing	237.67	194.02	<0.001
Phenytoin dressing	17.07	33.30	

SD: Standard deviation

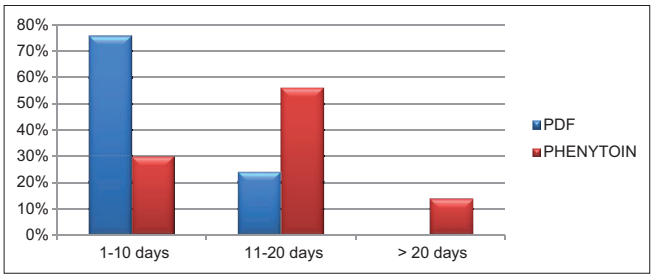
Table 6: Percentage reduction of wounds

Type of dressing	Percentage reduction		*P*
	Mean	SD	
Platelet dressing	46.95	15.16	0.000
Phenytoin dressing	2.28	2.54	

SD: Standard deviation

Table 7: Comparison of number of days in which granulation tissue appeared in both the groups

Granulation	Platelet dressing (*n*=15)		Phenytoin dressing (*n*=15)	
	No.	%	No.	%
1-10	12	80.0	4	26.0
11-20	3	20.0	8	53.0
>20	0	0.0	3	20.0



Graph 5: Rate of granulation tissue formation in days

the present study had no statistical difference of wound duration between cases and controls.

The mean size of the wounds in the present study was 51.7 cm^2 which is much higher than in the other studies being 4 times more than the next largest in the series, 13 cm^2 of the Krupski *et al.* study.[5]

In the present study, the rate of healing in the phenytoin group was 0.85 ± 1.67 cm^2/week and in the platelet group was 11.87 ± 9.71 cm^2/week ($P < 0.05$).[6]

The final area of the wounds was significantly reduced in the platelet group as compared to the phenytoin group at the end of the study.

The time taken per platelet dressing was 30-40 min. No cost was incurred by the patient as all materials required were available as hospital supply. No adverse effects were seen with platelet dressing. The growth factors present in platelets are the individual patient's natural growth factors in their biologically determined ratio. Because it is autologous, it presents no risk of immunogenic reactions or human to human disease transmissions like HIV or hepatitis B, thus making it a safe modality of treatment.

The study, in spite of its shortcomings, does indicate that topical application of autologous platelet is more effective than topical phenytoin therapy in helping a chronic ulcer to heal and that it has the potential to be a useful, safe, and cost-effective adjunct to wound healing.

CONCLUSION

With the use of autologous PDGF dressings in comparison with topical phenytoin therapy for the treatment of chronic ulcers, the following conclusions were derived.

- PDGF showed faster and better healing rates among the study group
- Area reduction was statistically significant in the study group
- There were no adverse effects or reactions seen both the group
- The overall hospital stay and post-operative complications were less in both groups.

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