

ORIGINAL RESEARCH

Comparative Study Of The Efficacy Of Autologous Prp, Phenytoin Sodium Powder & Conventional Dressing In Healing Of Non Healing Ulcers

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ABSTRACT:

Aim

To observe the efficacy of autologous PRP and phenytoin sodium powder in the healing of non healing ulcer.

Material & methods

This prospective randomized controlled study included Sample size of 90 patients (at least 30 in each group). Patients of all age groups with non healing ulcers of more than 3 months duration, irrespective of its aetiology. Debridement of dead necrotic tissue which was done every week after opening the dressing before measuring ulcer size. Every ulcer was tested for culture & sensitivity & treated with specific antibiotics before specific interventions were applied. The patients were randomly allocated to one of the three groups as per their presentation first patient in A, second in B, third in C, fourth again in A, fifth in B & so on.

Results:

Diabetic ulcers (50%) were the commonest, followed by venous (25%), traumatic & pressure sores in the same order. The patients subjected to Group A, that were treated with autologous PRP gel, showed a statistically significant mean reduction in volume of the ulcer ($17.86 \pm 15.63 \text{ cm}^3$) by the end of 3 weeks leading to partial or total granulation in 22 patients & complete re-epithelization in 6 out of 30 cases. The patients subjected to Group B, that were treated with Phenytoin sodium suspension, showed a reduction in the mean ulcer volume ($7.32 \pm 5.32 \text{ cm}^3$) by the end of 3 weeks of treatment which was not statistically significant, leading to partial or total granulation in 70% patients & complete re-epithelization in 13 % out of 30 cases. Almost no healing was seen in 16% of the total cases. The patients subjected to Group C, that were treated with conventional normal saline dressings, showed a reduction in the mean ulcer volume ($6.21 \pm 6.21 \text{ cm}^3$) by the end of 3 weeks of treatment which was not statistically significant when compared to other groups, leading to partial or total granulation in 70% patients & complete re-epithelization in none of

the cases. The results with PRP were better than with Phenytoin group. Total healing rate of 20% was seen with PRP group as compared to zero patients with complete re-epithelization in conventional normal saline dressing group. The results with PRP as compared to Normal saline group. Total healing rate of 13.3% in Phenytoin group as compared to zero patients with complete re-epithelization in conventional normal saline dressing group. The results were better with phenytoin as compared to normal saline group. Autologous PRP gel showed significant reduction in mean ulcer volume of all aetiology when compared to phenytoin sodium suspension. No side effects were documented in any of the three groups.

Conclusion:

Autologous PRP therapy is a safe, efficacious & cost effective method in the healing of chronic non-healing ulcers. There was no risk of adverse effects. Moreover, even phenytoin sodium powder suspension is cost-effective, more efficacious as compared to conventional normal saline dressings in treating chronic non-healing ulcers.

Keywords: non-healing ulcers, PRP therapy, phenytoin sodium powder.

Introduction

The terms "chronic ulcers" or "non-healing ulcers" refer to lesions that are unresponsive to initial therapy or that persist despite adequate care and do not progress toward healing within a specific time frame and have an underlying aetiology that may be related to systemic disease or local disorders.[1] This is because the usual healing process cannot occur when growth factors and cytokines, which are essential for tissue regeneration and remodelling, are insufficient.[2]

The prevalence of chronic non-healing ulcers in patients visiting surgical OPD or getting admitted to the surgical unit, ranges from 1.9 to 13% worldwide.[3] Chronic non-healing ulcers are more prevalent in elderly persons or the ageing population due to lifestyle problems such as obesity, diabetes, and atherosclerosis occlusion.[4]

These non-healing ulcer patients are usually treated by control of infection, desloughing or debridement of wound followed by normal saline or povidone iodine dressing, may or may not be combined with mupirocin. The common treatment methods include applying a dry or wet gauze bandage, repeatedly cleaning the area with salt water, and removing dead tissue.[5] However, the ideal dressing should be devoid of contaminants, capable of removing excessive exudates and toxic substances, able to maintain a moist environment at the wound-dressing interface, impermeable to microorganisms, able to allow gaseous exchange and should be simple to remove & affordable. A plenty of dressings are available, and studies have shown that they help prevent infection and promote wound healing.[6]

Venous, diabetic, arterial, traumatic, neurotrophic, or lymphatic chronic non-healing ulcers are among the possible causes.[7] Chronic, non-healing ulcers, diabetes and venous disorders such as venous hypertension are thought to be the main contributing causes. [8] Most diabetes patients acquire chronic ulcers in their lower extremities that are difficult to cure because of diabetic neuropathy; since these diabetic ulcers are persistent, bacteria can infect them and cause infection.[9]

In patients with chronic non-healing ulcers, a lengthy hospital stay, constant wound cleaning, and routine antibiotic are used to avoid microbiological infection cause physical, psychological, and financial anguish. Rapid wound closure is the goal of the management and therapy strategies used for chronic non-healing wound ulcers.[5]

However, quite a few factors, like microbial infection in ulcer, presence of debris or necrotic tissues, tissue hypoxia, immunodeficiency, malnutrition, systemic diseases like diabetes mellitus, use of corticosteroids, limit the effectiveness of the conventional strategy used for management of chronic non-healing ulcers.[10]

We have used autologous PRP and Phenytoin sodium powder in the present study for the purpose of studying the efficacy of these newer agents helping in wound contraction leading to healing of wound.

Aim & objectives

Aim

To observe the efficacy of autologous PRP and phenytoin sodium powder in the healing of non healing ulcer.

Objectives

Primary objective

1. To test the efficacy of autologous PRP in non healing ulcer.
2. To test the efficacy of phenytoin sodium powder in non healing ulcer.
3. To compare the efficacy of autologous PRP, phenytoin sodium powder & conventional methods in healing of non healing ulcer.

Secondary objective

1. To study the side effects of autologous PRP when used locally for treatment of non healing ulcer.
2. To study the side effects of phenytoin sodium powder when used locally for treatment of non healing ulcer.

Material & methods

Study Design and Setting: After obtaining approval from the institutional ethics committee, this Prospective randomized Study was undertaken in department of General Surgery, School Of Medical Sciences & Research, Greater Noida, UP.

Study Sample Size: Sample size of 90 patients (at least 30 in each group) were included in the study.

Study Period: December 2020 to July 2022

Study Area: Department of general surgery Sharda Hospital , School of Medical sciences and Research (Greater Noida)

Study Design: Prospective randomized controlled study

Study Population: Patients of all age groups with non healing ulcers of more than 3 months duration, irrespective of its aetiology.

Inclusion criteria: Patient with ulcer > 3 months duration having >18 years of age and Hemodynamically stable patients were included.

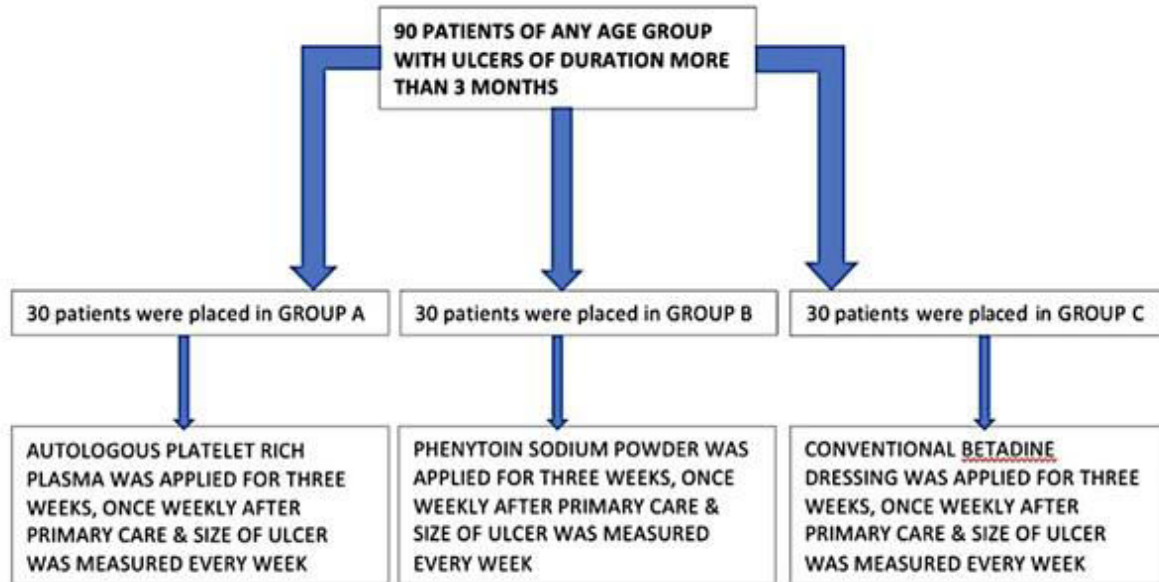
Patients with Active infection, Anaemia (HB < 10), Thrombocytopenia, Malignancy, Immunodeficiency, Culture positive were excluded from study.

****Primary care:** Debridement of dead necrotic tissue which was done every week after opening the dressing before measuring ulcer size.

Every ulcer was tested for culture & sensitivity & treated with specific antibiotics before specific interventions were applied.

The patients were randomly allocated to one of the three groups as per their presentation first patient in A, second in B, third in C, fourth again in A, fifth in B & so on.

No.	Group	Intervention done	Number of Patients
I	A	Autologous PRP	30
II	B	Phenytoin Sodium suspension	30
III	C	Conventional Normal Saline dressing	30



First on presentation and every week after opening the dressing, the ulcers were measured in their longest length, breadth & depth. This was recorded in centimetres.

Considering the shape to be ellipsoid in general, the surface area was calculated by using following formula on every visit:

Volume of the ulcer = (length in cm x breadth in cm x depth in cm) * 0.7854

Preparation of Phenytoin sodium powder dressing -

- The required concentration of phenytoin was measured based on ulcer size, 0-5 cm² 100mg, 5.1-10 cm² 150 mg, and 10.1-15 cm² 200 mg, respectively.
- The calculated concentration of phenytoin sodium powdered tablet was mixed with 100ml of Normal Saline.
- The suspension was directly applied to the ulcer.
- Aseptic dressing was applied over it.

Preparation of Autologous Platelet rich plasma -

- A 30cc venous blood draw yielded 3-5 cc of PRP.
- Whole blood of the patient was collected.
- Centrifuged Whole blood at a speed of 3200 RPM for 20 min.
- Three layers were formed because of their density: The bottom layer consisting of RBCs, the middle layer being buffy coat & topmost being platelets in plasma.
- Removed supernatant plasma from the top of the container.
- Centrifuged the plasma at 3200 RPM for 20 min to separate the platelet-rich plasma from platelet-poor plasma.

The patients were subjected to leading questions asking about the following side effects, if present, on every follow up visit : Peri-lesional itch; Burning sensation; Dermatitis; Pain; Stinging; Allergic rash anywhere on the body or General malaise

Results

Table 1: Distribution of study population according to Age between all 3 study groups

Study groups	Age			
	Mean	Std. Deviation	F-value	p-value
PRP	47.20	11.31	0.510	0.602
Phenytoin powder	49.43	6.54		
Conventional dressing	48.50	7.18		
Total	48.38	8.56		

The mean age was compared between PRP, Phenytoin powder and Conventional dressing groups using the one-way ANOVA test with post-hoc test for inter-group comparisons. There was no significant difference in mean age between PRP, Phenytoin powder and Conventional dressing groups.

Table 2: Distribution of study population according to Age (Overall)

Age group (years)	Number of patients
20-30	1
31-40	15
41-50	42
51-60	29
61-70	3

Maximum patients belonged to age group 41-50 years, followed by age group 51-60 years.

Table 3: Distribution of study population according to Gender between all 3 study groups

Gender	Groups			Total
	PRP	Phenytoin powder	Conventional dressing	
Male	20	20	24	64
	66.7%	66.7%	80.0%	71.1%
Female	10	10	6	26
	33.3%	33.3%	20.0%	28.9%
p-value = 0.421				

There was no significant difference in distribution of males and females between PRP, Phenytoin powder and Conventional dressing groups.

Distribution of study population according to Gender between all 3 study groups

Table 4: Distribution of study population according to Gender (Overall)

Patients with chronic non-healing ulcers	n
MALES	64
FEMALES	26
TOTAL PATIENTS	90

Table 5: Distribution of study population according to Aetiology of ulcer (Overall)

Aetiology	Male	Female
Diabetic ulcer	35	10
Venous ulcer	16	7
Traumatic ulcer	8	4
Pressure sore	5	5

Table 6: Distribution of total study population according to volume of ulcer

Volume		Mean	Std. Deviation	F-value	p-value	post-hoc comparisons
At presentation	PRP	23.18	24.10	0.806	0.450	
	Phenytoin powder	26.39	24.24			
	Conventional	31.64	29.47			
At 1st week	PRP	16.01	17.55	2.271	0.043*	
	Phenytoin powder	18.99	20.50			
	Conventional	27.18	26.93			
At 2nd week	PRP	9.70	11.97	2.854	0.030*	
	Phenytoin powder	14.10	19.25			
	Conventional	21.59	25.00			
At 3rd week	PRP	5.32	8.47	3.930	0.023*	
	Phenytoin powder	10.46	19.69			
	Conventional	18.88	24.79			

The mean Ulcer Volume at 1st week, 2nd week and 3rd week was significantly more among Conventional compared to Phenytoin powder which was significantly more than PRP.

Table 7: Comparison of efficacy of various interventions on volume of Diabetic ulcers

Volume		Diabetic ulcers				
		Mean	Std. Deviation	F-value	p-value	post-hoc comparisons
At presentation	PRP	30.01	29.20	0.042	0.959	
	Phenytoin powder	32.90	23.90			
	Conventional	30.86	29.76			
At 1st week	PRP	21.01	22.30	0.160	0.853	
	Phenytoin powder	23.71	23.46			
	Conventional	26.11	27.56			
At 2nd week	PRP	13.68	15.25	2.306	0.048*	
	Phenytoin powder	17.77	24.13			
	Conventional	20.19	26.83			
At 3rd week	PRP	8.66	11.38	0.623	0.045*	
	Phenytoin powder	13.61	25.15			
	Conventional	17.93	27.21			

The mean Ulcer Volume at 2nd week and 3rd week was significantly more among Conventional compared to Phenytoin powder which was significantly more than PRP.

Table 8: Comparison of efficacy of various interventions on volume of Pressure sores

Volume		Pressure sore				
		Mean	Std. Deviation	F-value	p-value	post-hoc comparisons
At presentation	PRP	16.15	15.96	1.051	0.399	
	Phenytoin powder	12.70	4.76			
	Conventional	26.40	3.34			
At 1st week	PRP	8.28	11.36	2.084	0.043*	
	Phenytoin powder	9.29	5.43			
	Conventional	22.58	3.05			
At 2nd week	PRP	5.32	5.97	6.747	0.023*	
	Phenytoin powder	6.11	2.23			

	Conventional	17.90	1.33			
At 3rd week	PRP	2.93	4.03	10.252	0.008*	
	Phenytoin powder	2.87	0.79			
	Conventional	13.19	2.67			

The mean Ulcer Volume at 1st week, 2nd week and 3rd week was significantly more among Conventional compared to Phenytoin powder which was significantly more than PRP.

Table 9: Comparison of efficacy of various interventions on volume of Venous ulcers

Volume		Venous ulcers				
		Mean	Std. Deviation	F-value	p-value	post-hoc comparisons
At presentation	PRP	16.05	6.11	1.049	0.369	
	Phenytoin powder	12.39	4.73			
	Conventional	24.25	26.52			
At 1st week	PRP	8.65	4.91	2.209	0.041*	
	Phenytoin powder	10.01	6.24			
	Conventional	20.02	20.12			
At 2nd week	PRP	5.79	3.05	2.789	0.034*	
	Phenytoin powder	7.66	7.05			
	Conventional	16.28	15.82			
At 3rd week	PRP	2.22	2.08	3.123	0.022*	
	Phenytoin powder	5.51	7.91			
	Conventional	13.60	12.46			

The mean Ulcer Volume at 1st week, 2nd week and 3rd week was significantly more among Conventional compared to Phenytoin powder which was significantly more than PRP.

Table 10: Comparison of efficacy of various interventions on volume of Traumatic ulcers

Volume		Traumatic ulcers				
		Mean	Std. Deviation	F-value	p-value	post-hoc comparisons
At presentation	PRP	19.06	26.66	1.734	0.231	
	Phenytoin powder	49.44	46.21			
	Conventional	61.45	39.00			
At 1st week	PRP	11.86	16.14	2.984	0.047*	
	Phenytoin powder	32.29	33.45			
	Conventional	57.43	39.55			
At 2nd week	PRP	7.26	10.51	3.156	0.035*	
	Phenytoin powder	23.57	24.20			
	Conventional	47.42	38.77			
At 3rd week	PRP	2.20	2.42	3.908	0.029*	
	Phenytoin powder	18.02	24.52			
	Conventional	43.56	40.66			

The mean ulcer dimension at 1st week, 2nd week and 3rd week was significantly more among Conventional compared to Phenytoin powder which was significantly more than PRP.

Table 11: Comparison of Wound condition at the end of 3rd week

Wound condition	Groups		
	PRP	Phenytoin powder	Conventional dressing
Healed/Re-epithelized	6	4	0
	20.0%	13.3%	0.0%
Improved/Partial or total granulation	22	21	21
	73.3%	70.0%	70.0%
No healing/ not much change	2	5	9
	6.7%	16.7%	30.0%
χ^2 value = 10.256, p-value = 0.036*			

Healing was significantly more among PRP group. Whereas it was same significantly more among Conventional dressing group.

Table 12: Comparison of side effects with various intervention

	Perilesional itch	Burning sensation	Dermatitis	Pain	Stinging	Allergic rash	General malaise
PRP	0	0	0	3	0	0	0
Phenytoin sodium	0	0	0	4	0	0	0
Conventional NS	0	0	0	3	0	0	0

Discussion

For the management of chronic non-healing ulcers, there is currently a large variety of dressings that are available in the commercial market. There is a consistent stream of new product launches, each of which is geared at a certain facet of the healing process. When applied correctly, a dressing will stop exudate from leaking, eliminate odour, reduce discomfort, and prevent wound infection.[15]

There is no replacement for proper wound debridement, appropriate systemic antibiotic medication, regular (daily) dressing changes, and wound examination. This is true regardless of the kind of dressing that is selected. In our study, autologous PRP & Phenytoin sodium has been used in comparison to conventional normal saline dressing. It has been suggested that phenytoin might be beneficial when used topically as an agent for encouraging the healing of chronic non-healing ulcers. It would appear that using autologous PRP & topical phenytoin as a therapeutic agent is both successful and cost-efficient in the healing of wounds.[15]

When applied to wounds, autologous PRP & topical phenytoin are a well-known and affordable therapeutic treatment that promotes the formation of granulation tissue, angiogenesis, and a reduction in the overall size of the lesion.[10]

Age and Gender

There was no significant difference in distribution of mean age between PRP, Phenytoin powder and Conventional dressing groups after distribution of patients (p value = 0.4), but in the overall study population, the male population with chronic non healing ulcers (n=36) was more than female population (n=24). Overall, maximum patients belonged to age group 41-50 years (n=42), followed by age group 51-60 years (n=29). The mean age of patients was 47.220 years, 49.43 years & 48.50 years in all the three groups respectively, which was parallel to mean age seen in the different studies.

There was no significant difference in distribution of males and female ratio between PRP, Phenytoin powder and Conventional dressing groups. 71.1 % males & 28.9 % females had presented with ulcers which was parallel to the previous literature. While almost equal number of males and females got distributed in between three groups, making it a non-significant variable.

Even in a study by *Ahmed and Ahmed*[15] it was observed that the mean age and gender ratio was consistent with our study.

Chauhan et al.[10] reported that the patients were under the age group of 40-70 years and Males (71) were more affected than females.

Maji et al.[26] reported that the patients' ages ranged from 38-81 years, with mean age of the patients was 59.68 ± 8.70 years. The proportion of patients in the age group of 51 to 60 years (41.9 %) was considerably greater than in the other age groups. There were a total of 160 cases, 105 of which were men, and 55 of which were women.

Dubhashi and Sindwani.[14] reported that maximum patients (52.0%) were in the age group of 41-60 years with 64.0% males and 36.0% females.

Manoj et al. observed that 68.33% were males and 31.66% were females with subjects belonging to the age group of 30-70 years.

Aetiology of ulcers

In the present study, the most common aetiology of chronic non-healing ulcers was found to be diabetic (n=45). The second most common were venous ulcers (n=23), followed by traumatic (n=12) & pressure sores (n=10). The diabetic (70%) & venous ulcers (25%) were more common in males than in female gender which is consistent with the literature. What so ever the aetiology of ulcers may be, most of the ulcers showed some contraction with every intervention.

Similarly, in a study conducted by *Kakagia et al.*[27] and *Ahmed et al.*[15] revealed that one of the common aetiology for chronic nonhealing ulcers was diabetes mellitus. In their study, 70% of the patients were diabetic. However, the main challenge in diabetic patients in their study population was the control of infection and adequate glycaemic control, and 3 of them had an infection due to poor glycaemic control and they were monitored more frequently than others for adequate glycaemic control. In their study subjects, 80% of patients showed near-complete wound healing.

In the same way, purpose of a prospective case series by *Frykberg et al.* (2010) [28] was to evaluate how a physiologically relevant concentration of an autologous platelet-rich plasma (PRP) gel affects initial wound healing trajectories of chronic, nonhealing wounds of various aetiologies and in different care settings. The most common wounds were pressure ulcers (n = 21), venous ulcers (n = 16) and diabetic foot ulcers (n = 14). For all wound aetiologies, 97% of wounds improved.

Contraction of ulcers size

In the present study, the mean decrease in volume of the ulcer ($17.86 \pm 15.63 \text{ cm}^3$) treated with autologous PRP gel was statistically significant with a p-value of 0.023 after completion of the study period. The mean decrease in volume of the ulcers treated with phenytoin sodium powder suspension ($7.32 \pm 5.32 \text{ cm}^3$) & conventional normal saline dressings ($6.21 \pm 6.21 \text{ cm}^3$) was found to be not significant statistically with respective p-values of <0.001. This signifies that if compared, autologous PRP gel was the most efficacious in producing re-epithelization with a healing rate of 20% , followed by phenytoin sodium suspension with a healing rate of 13.3% by the end of 3 weeks of treatment. In the group of patients treated with conventional normal saline dressings 30% showed to have no granulation at all.

Ramakrishna Reddy, Venkata reddy & Padmanabh Inamdar [25] conducted a study with 50 patients where they were treated with autologous PRP and Conventional dressings. Almost similar to what was observed in our study, average time taken for complete healing in PRP treated patients was 3.68 weeks and ones treated with Conventional normal saline dressing took an average of 6.2 weeks.

Moneib et al.[12] found that the mean percentage improvement in the area of the ulcer after PRP and conventional therapy was $67.6\pm36.6\%$ and $13.67\pm28.06\%$, respectively. The mean change in the ulcer's area after PRP and conventional therapy was 4.92 ± 11.94 cm and 0.13 ± 0.27 cm, respectively. This is parallel to findings of our study where decrease in mean ulcer volume with PRP was 17.86 ± 15.63 cm³ compared to 6.21 ± 6.21 cm³ in conventional dressing group.

Singh et al.[19] reported that the ulcer area in Autologous PRFM was reduced by a mean of 8.26 mm² (74.9%), which is a very significant change. The ulcer area in Triple combination paste (zinc oxide, phenytoin, and mupirocin ointment) decreased by a mean of 4.799 mm² (47.75%), which is a significant reduction (P-value = 0.017). Two patients in autologous PRFM obtained roughly 80% healing by 5 weeks and total re-epithelialization by the end of 8 weeks; however, none of the patients in triple combination paste (zinc oxide, phenytoin, and mupirocin ointment) achieved complete re-epithelialization during their treatment. This is parallel to findings of our study where decrease in mean ulcer volume with PRP was 17.86 ± 15.63 cm³ compared to 7.32 ± 5.32 cm³ in phenytoin group.

Similarly in a study by Somani and Rai[22] among PRF group, the mean reduction in the area of the ulcer size was 85.51%, whereas in the Saline group, the mean reduction in the area of the ulcer size was 42.74%. This was in accordance with the findings of our study where mean reduction in volume of ulcer with PRP is more than Conventional normal saline dressings at the end of 3 weeks.

Elsaid et al.[20] reported that Group I received dressing with PRP gel and group II received regular saline dressing. Compared to none of the patients in group II, just three (25%) patients in group I had full recovery. 8.3% of patients in group I and 41.6% of patients in group II overall did not respond to therapy. The longitudinal and horizontal DFU decrease percentages in group I were substantially higher than those in group II (43.2% vs. 4.1% and 42.3% vs. 8.2%, respectively).

Prabhu et al.[5] stated that at the end of 5-week period, 81.73 percent of the patients demonstrated full healing, whereas 12.50 percent of the patients required skin grafting.

Sringeri et al.[13] compared the effectiveness of autologous platelet gel to that of topical phenytoin. Platelet dressing demonstrated a larger mean decrease in ulcer area (237.67 mm²) than phenytoin dressing did. Platelet dressing (17.04 mm²). The fact that the percentage of platelet dressing that was used was reduced by $46.95\pm15.16\%$ while the percentage of phenytoin dressing that was used was reduced by just $2.28\pm2.54\%$ was statistically significant.

Dubhashi and Sindwani [14] reported that in comparison to the group that was treated with saline, the phenytoin-treated group both had a considerable reduction in the wound area at the conclusion of the three weeks of therapy (104.4 mm² vs 47.96 mm² respectively).

Comparison of various studies with the present study

SNO.	Name of Authors	Sample size	Interventions used	Results
1	Present study	90	Autologous PRP gel, Phenytoin powder suspension, Conventional NS dressing	Mean decrease in volume of the ulcer (17.86 ± 15.63 cm ³) treated with autologous PRP gel, with phenytoin sodium powder suspension (7.32 ± 5.32 cm ³) & conventional normal saline dressings (6.21 ± 6.21 cm ³).
2	Ramakrishna Reddy,	50	Autologous PRP,	Time taken for complete healing in

	Venkata Reddy, Padhmanabh Inamdar		Conventional normal saline dressing	PRP group was 3.68 weeks compared to 6.2 weeks in conventional dressing. Percentage reduction in size of ulcer in PRP group was 43.96 % & in conventional dressing group was 13.81%.
3	Raxith Sringeri, MS Anil Kumar, K Sindhuri	30	Autologous PRP, Phenytoin	Mean reduction in area for PRP group was 23.67mm ² & 17.04mm ² in phenytoin group. Granulation took 1-10 days in PRP group while 11-20 days in phenytoin group.
4	Hoda A Moneib et al.	40	Autologous PRP, Conventional normal saline dressing	Mean change in the area in PRP group was 4.92±11.94 cm ² while in conventional dressing group it was 0.13±0.27 cm ² . Mean percentage improvement was 67.6±36.6 % in PRP group vs 13.67±28.06% in conventional dressing group.
5	Ravi Prabhu et al.	104	PRP	85% patients had healed ulcers & 12.5% had non healing. Mean ulcer area at start was 5.03cm ² and at the end was 1.69cm ² .
6	Akanksha Singh, Yatendra S Chahar, Shaiphali Chhabra	10	Autologous PRP, Triple (zinc oxide, phenytoin, mupirocin) paste	Decrease in mean area with PRP was 8.26mm ² vs 4.79mm ² with triple combination paste. Complete epithelization was achieved with PRP in 8 weeks vs none achieved epithelization with triple combination paste.
7	Somani and Rai	15	Autologous PRP, Conventional normal saline dressing	Among PRP group, the mean reduction in the area of the ulcer size was 85.51%, whereas in the Saline group, the mean reduction in the area of the ulcer size was 42.74%.
8	Dubhashi and Sindwani	120	Phenytoin, Normal saline dressing	Significant reduction in the wound area at the end of treatment in the phenytoin-treated group compared to the saline-treated group (104.4mm ² vs 47.96mm ²).

Side effects of treatment methods

In the present study, no side effects were seen in any of the groups.

A study by *Ashima Bhatia & Surya Prakash (2004)[23]* also mentioned that side effects from topical phenytoin are rare. Some patients may have a transient burning sensation when the powder is initially applied, but this can be prevented by using pure phenytoin powder instead of phenytoin sodium. A generalized rash that resolved when treatment was stopped has also been reported. Hypertrophic granulation tissue was noted in 10-36 percent of patients in two studies. This is reversed by stopping treatment, and it is suggested that stopping treatment when the wound area is covered with a granulation base can prevent this effect.

Montero et al. (2017)[24] also mentioned no adverse effects or hypersensitivity reactions have been detected in clinical trials with autologous platelet rich plasma. Similarly, an article published in 2021 by *Catherine Hannan on medical news today*, also mentioned that injecting PRP involves using a one's own platelets, which is why patients do not have adverse reactions to this. However, they may experience irritation, pain, or bleeding at or around the injection site.

Conclusion

To conclude, in our study, we found that autologous PRP therapy is a safe, efficacious & cost effective method in the healing of chronic non-healing ulcers. There was no risk of adverse effects. Moreover, even phenytoin sodium powder suspension is cost-effective, more efficacious as compared to conventional normal saline dressings in treating chronic non-healing ulcers. Due to certain constraints a longer study period & follow-up could not be achieved. Hence, further research and controlled randomized prospective clinical trials on larger patient population & longer study period are necessary to validate the results.

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