



TO COMPARE THE EFFICACY OF PLATELET RICH PLASMA AND NORMAL SALINE IN DRESSING OF NON HEALING TROPHIC ULCER IN PATIENTS OF HANSEN'S DISEASE

Medicine

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ABSTRACT

Objective: - This study was done to compare efficacy of platelet rich plasma and normal saline dressing of non healing trophic ulcer in patients of Hansen's disease.

Methodology: - 50 cases of non healing trophic ulcer in patients of Hansen's disease were included (M:F=1.5:1) and divided into two groups (PRP group & Normal saline group). Dressing of PRP group with normal saline and PRP injected at wound base and margin at different interval, dressing of normal saline group with normal saline only. Outcome was compared by assessment of wound area and PUSH score over a period of 6 weeks.

Result: - PRP group showed significant decrease in area of wound and PUSH score as compared to normal saline group at the end of study. There is no significant complication during study period in both groups.

Conclusion: - Use of PRP in dressing of trophic ulcer has enhanced healing reduced duration of treatment, and improving the patient's quality of life.

KEYWORDS

INTRODUCTION

The term Leprosy is a tribute to the Norwegian physician Gerhard Armauer Hansen, who identified the bacillus *Mycobacterium leprae* as the cause of the disease in 1873. Leprosy is caused by *Mycobacterium leprae* and has been known since biblical times. It is still endemic in many regions of the world. Impairment results in a set of sensory, motor and autonomic disturbances, with ulcers originating primarily on the hands and feet. The absence of innervations of the foot, leading to anesthesia, the paralysis of intrinsic muscles, and hemodynamic disturbances, predisposes patients to ulcer formation. Superimposed pressure and repetitive stress over weight bearing areas lead to pre ulcerative conditions as blisters, callosities, and cracks over plantar surfaces of the feet. Trophic ulcers secondary to leprosy pose a great stigma to the patients and remain a challenge to the treating physician. In the absence of proper care, these may lead to the development of full-blown ulcers, leading to the absorption of affected parts, which in turn leads to mutilation. Different methods of treatment have been used in ulcer management, but the outcomes are frequently dissatisfactory, and many people must live with chronic wounds that result in high economic and social costs¹. Various treatment in practice are total plaster cast immobilization, saline or collagen dressings, topical phenytoin or metronidazole application, topical growth factors like platelet derived growth factor (becalpermin), epidermal growth factor and other reconstructive surgical procedures². The discovery of Platelet Rich Plasma (PRP) with its favorable role in wound healing is a boon for the patients. The autologous PRP is prepared from one's own blood by process of centrifugation and platelet activation. On application to the wound, it directly introduces growth factors and cytokines, thereby normalizing the metabolic process, promoting neoangiogenesis, improving cellular metabolism and activating local immunity.³

METHODOLOGY

In this study, we enrolled 50 patients who satisfied inclusion criteria like age between 18 to 65yrs, negative for pus culture and sensitivity and negative for serology viral markers for HIV, HCV and HBV. Enrolled patients were divided into two groups (PRP group & Normal saline group) with non healing trophic ulcers. Patients were recruited after taking Ethical clearance from Institutional Ethical Committee and written informed consent taken from the patients. Dressing of PRP group was done with normal saline followed by PRP injection at wound base and margin at 0, 2 weeks and 4 weeks, dressing of Normal saline group was done with normal saline only. Dressing was done

every alternate day in both the groups. Outcome was compared in form of healing measured by decrease in ulcer size and improvement in PUSH scores over 0, 2, 4 and 6 weeks. All patients with gross necrotic infection underwent surgical debridement in a clean setting; preferably in an operation theater. All infected wounds were put on a course of systemic antibiotic and considered for the study only once they were free of all infection as proved by bacteriological culture and sensitivity.

Study design

This comparative observational study was conducted at Physical medicine and rehabilitation OPD, AIIMS Patna from September 2017 to August 2018. Enrolled patients were randomly assigned into two groups by computer generated system.

PRP preparation

Following routine monitoring processes, such as examining blood pressure, heart rate, and an electrocardiogram, a 20-mL blood sample was drawn under sterile condition. Under strict aseptic precautions, the process was carried out with temperature maintained at 22–26°C by manual double spin method⁶. Blood was collected from the patient in centrifuge test tubes labeled with identification data (name and age) and mixed with anticoagulant Acid Citrate Dextrose (ACD) in the ratio of 10:1.5. The tube was then placed for first centrifugation at the rate of 2000 rpm for 10 minutes when plasma separated; plasma, Buffy coat and upper layers of RBCs were pipette into another test tube. This was subjected to second centrifugation at the rate of 3000 rpm for ten minutes. Platelets settled down, upper 3/4th supernatant was discarded and the lower PRP was obtained.

Measurement of Ulcer

Cotton-tipped applicators and disposable scales were used to measure length, width of the visible ulcer. Measurement of ulcer size was done by using clock face method in which length was 12:00 to 6:00 with 12:00 toward the head; width was 3:00 to 9:00 side by side^{7,8}.

Elements in PUSH Tool⁵

LENGTH X WIDTH (in cm ²)	0	1	2	3	4	5	Sub-score
	0	< 0.3	0.3 – 0.6	0.7 – 1.0	1.1 – 2.0	2.1 – 3.0	
	6	7	8	9	10		
	0	1	2	3			
EXUDATE AMOUNT	None	Light	Moderate	Heavy			Sub-score
	0	1	2	3			
TISSUE TYPE	0	1	2	3	4		Sub-score
	Closed	Epithelial Tissue	Granulation Tissue	Slough	Necrotic Tissue		
							TOTAL SCORE

RESULTS

Out of 50 patients of Hansen disease with trophic ulcer, male and female ratio in both groups was not significant (p=0.083). Most of the patients belonged to lower socio economic status in which common cause for trophic ulcer was breakdown of substandard foot with normal or excessive walking as evidenced in our study with 40% patients being farmers and 24% manual labourers.

In our study, 24% patients were on Multibacillary Multidrug Therapy (MBMDT) and 38 patients (76%) completed MBMDT. Our study showed treatment with MBMDT did not influence wound healing. Whatever may be the site of ulcer, it showed no statistical significance on ulcer healing with PRP therapy. At the beginning of the study, surface area of the wound, 16.09±4.97 in PRP group and 15.79±5.55 in normal saline group which significantly reduce in both groups at the end of study, on comparison between both groups found that reduction in area of wound is more in PRP group (16.09±4.97 to 1.20±1.27) as compared to normal saline group (15.79±5.55 to 4.93±2.49). PUSH score at regular interval also showed significant variation in PRP group in comparison to Normal saline group. We observed that in the PRP group PUSH score decreased subsequently from 12.72±1.31 at first visit to 10.72±1.57 in second, to 7.40±1.71 in third and finally to 3.28±2.59 at the end of study period. However, in Normal saline group PUSH score varied from 12.96 ±1.17 at first visit to 11.36±1.38 at second visit to 9.72 ±1.62 and finally 7.96±1.79 at the end of study.

Table 1: Age distribution of patients studied

Age in years	PRP Group	NS Group	Total
<30	1(4%)	0(0%)	1(2%)
30-40	9(36%)	6(24%)	15(30%)
41-50	7(28%)	9(36%)	16(32%)
51-60	5(20%)	3(12%)	8(16%)
61-70	3(12%)	7(28%)	10(20%)
Total	25(100%)	25(100%)	50(100%)
Mean ± SD	45.16±10.50	49.68±0.48	47.42±10.63

P=0.134

Table 2: Gender distribution of patients studied

Gender	PRP Group	NS Group	Total
Female	7(28%)	13(52%)	20(40%)
Male	18(72%)	12(48%)	30(60%)
Total	25(100%)	25(100%)	50(100%)

Table 3: Socio Economic Status

Socio Economic Status	PRP Group	NS Group	Total
Lower	21(84%)	17(68%)	38(76%)
Middle	4(16%)	8(32%)	12(24%)
Total	25(100%)	25(100%)	50(100%)

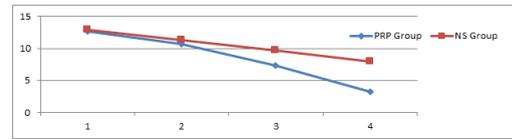
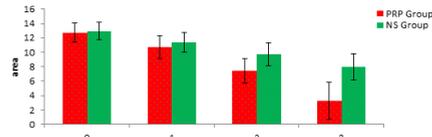
P=0.185

Table 4: Area

Area	PRP Group	NS Group	Total	P value
0	16.09±4.97	15.79±5.55	15.94±5.21	0.843
1	8.42±3.78	10.37±4.36	9.39±4.16	0.098+
2	3.57±2.39	7.84±3.23	5.7±3.55	<0.001**
3	1.20±1.27	4.93±2.49	3.06±2.71	<0.001**

Table 5: PUSH

PUSH	PRP Group	NS Group	Total	P value
0	12.72±1.31	12.96±1.17	12.84±1.23	0.498
1	10.72±1.57	11.36±1.38	11.04±1.50	0.132
2	7.40±1.71	9.72±1.62	8.56±2.02	<0.001**
3	3.28±2.59	7.96±1.79	5.62±3.23	<0.001**



DISCUSSION

In 1959, Price introduced the term trophic ulcer. Trophic means nutrition. It is characterized by chronic ulceration of anesthetic foot, overlying bony prominences with increased tendency to recur. It is associated with morbidity, psychosocial stigma and it finally cripples the patient. The management of patients with trophic ulcers is difficult, as it is a recurrent and recalcitrant problem. By shortening the wound healing phase, the quality of life of these patients can be improved, and they can be rehabilitated at the earliest. Various treatment modalities are available for trophic ulcers such as moist wound dressings, vacuum-assisted closure, hyperbaric oxygen therapy, reconstructive surgeries and topical application of growth factors, in the form of platelet-rich plasma. Recently, the usefulness of PRP has been published as a potential and inexpensive means for treatment of ulcers. A total of 135485 new cases were detected during year 2016-2017 which gives Annual New Case Detection Rate of 10.17 per 100000 populations¹⁰.

Plantar ulcers in leprosy differ from traumatic ulcers as the pathological process begins with loss of sensation and autonomic imbalances superimposed on intrinsic muscle paralysis. Ulcers which have been treated by conservative methods like plaster cast immobilization recurs soon, as some inflammation still persist with friable adhesions. The process of wound healing is complex, requiring cellular events brought about by various mediators. PRP (autologous platelet gel, plasma rich growth factor and platelet concentrated plasma) provide abundant platelets that are concentrated into a small volume of plasma¹¹. The growth factors released from the α-granules of the activated platelets, along with plasma proteins namely fibrin, fibronectin and vitronectin play a pivotal role in modulation of tissue repair and regeneration. Platelets trigger biological effects including directed chemotaxis, angiogenesis and cell proliferation and differentiation, which play a key role in the process of tissue repair and regeneration. They contain a large number of growth factors and cytokines which play a key role in inflammation and tissue repair. These characteristics of platelets have led to the idea of using platelets as a therapeutic tool to promote wound healing, particularly in patients in whom tissue repair is compromised¹². In 1986, Knighton et al; showed that the use of autologous platelet factors accelerated epithelialization of granulation tissue leading to complete repair of chronic non-healing ulcers. This was the first clinical study that demonstrated the promising role of locally acting factors derived from autologous blood in promoting healing of chronic cutaneous ulcers. A study conducted by Frykberg et al; on 49 patients with 65 non-healing ulcers application of PRP showed that 63 of 65 ulcers responded with significant result. Driver et al; conducted a multicentric randomized study on 72 patients with diabetic foot ulcers who were treated with autologous platelet-rich plasma gel or control (saline gel). Their study results showed that significantly more wounds healed in patients treated with platelet-rich plasma gel (13 out of 16 or 81.3%) than patients treated with control gel (8 out of 19 or 42.1%). Our study goes in concordance with literature that Hansen's disease and deformities are more common and severe in males. In elderly patients, wound healing is slow with reduced inflammatory response and altered cytokine profile but our study showed that ageing had no statistical significance in ulcer healing with PRP treatment. Plantar ulcers are not distributed evenly in the sole and more common over the forefoot and lateral malleolus especially in Indians because of cultural habits; our study is in concordance with literature. In the PRP group we achieved full closure in seven wounds, while in Normal saline group two wounds achieved full closure.

Limitation of study

Small sample size, lack of morphological assessment of ulcer bed and tissue, short time of follow up and assessment, PRP need specific kit like centrifuge machine and centrifuge vial; so the cost is high.

Conflict of interest

None

CONCLUSION

The use of PRP has greatly reduced the duration of treatment, thus shortening the inpatient hospital stay and improving the patient's quality of life. PRP therapy is the preferable treatment option in leprosy patients with chronic non-healing ulcers and should be included in treatment of all Hansen's disease patients with chronic trophic ulcers. It is a simple, safe and cost effective in-office procedure, albeit requiring an optimal set-up and expertise.

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