



Comparative Study of Efficacy of Platelet Rich Plasma Vs Superoxidised Solution in Treatment of Chronic Non- Healing Foot Ulcers

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Abstract

Background: Wounds and their management are fundamental in the practice of surgery. A chronic ulcer of the foot is a frequent condition and is a major health challenge and growing health problem all over the world.

Aims & Objectives: To compare the efficacy of Platelet rich plasma and Superoxidised solution in the management of chronic foot ulcers to observe: Wound disinfection, Rate of wound healing, Appearance of granulation tissue, Duration of hospital stay.

Materials: Randomized prospective comparative study of patients with chronic non healing foot ulcers admitted at our hospital from October 2018 to January 2020, patients were randomized into 2 groups- PRP and SOS with 25 patients in each group. Wound assessments done at regular intervals and various wound outcome variables compared. Statistical analysis of data done.

Results: In a study of 50 patients, most patients were in the age group of 51- 60years, 76% were diabetics and 78% were males. There was a rapid decrease in wound size in PRP group compared to SOS group at day 21, and earlier appearance of granulation and epithelialization in PRP group. The duration of hospital stay was almost equal in both groups.

Conclusion: This study shows more favorable results for PRP as compared to SOS in healing of chronic non healing foot ulcers which are highly statistically significant.

Keywords: Platelet Rich Plasma, Superoxidised Solution, Chronic non healing foot ulcers.

Introduction

Wounds and their management are basic and fundamental in the practice of surgery. An **Ulcer** can be defined as 'break in the continuity of the covering epithelium either skin or mucous membrane due to molecular death'. The prevalence of leg ulceration is approximately 1 to 2%, and is slightly higher in the adult population.¹

The Words quoted by Luodon and published in 1805² very much summarizes leg ulcer management, —ulcers on the leg form an extensive and important class of disease, the treatment of such cases is generally looked upon as an inferior branch of practice and inglorious task where much labour must be bestowed and little honor gained²

An ideal wound care product is the one which in addition to controlling the infection should also protect the normal tissues and not interfere with the normal wound healing. Apart from conventional methods to facilitate wound healing, newer methods like PRP dressing and Superoxidised solution dressing is emerging.

PRP is an effective concentration of multiple growth factors by virtue of platelets alone, which contain plasma proteins namely fibrin, fibronectin and vitronectin. This cocktail of GFs is pivotal in diabetic foot for modulation of tissue repair and regeneration of plasma proteins as a scaffold for connective tissue and epithelial migration.

The efficacy of certain growth factors in healing various injuries and the concentrations of these growth factors found within PRP are the theoretical basis for the use of PRP in tissue repair.

Platelet rich plasma contain following growth factors:

- Platelet-derived growth factor
- Transforming growth factor beta
- Fibroblast growth factor
- Insulin-like growth factor 1
- Insulin-like growth factor 2
- Vascular endothelial growth factor
- Epidermal growth factor
- Interleukin 8
- Keratinocyte growth factor.

Superoxidised solution is an electrochemically processed aqueous solution with neutral pH, nontoxic, non-irrigating, no rinse dermal wound irritant which is rich in reactive oxygen species. It is bactericidal in its action, which acts by denaturing proteins of bacterial cell wall and imbalances the osmolarity of bacterial cell.

Both are affordable solutions for the patient population of this study. Very few studies have been conducted to study the efficacy of PRP dressing and SOS dressing in wound healing, but no study has compared the efficacy of both dressings.

Chronic leg ulcers are usually associated with significant morbidity, high cost of healthcare, loss

of productivity, and reduced quality of life^[3-6] As wounds is a great burden on the Healthcare system, hence the need for the study.

Aims and Objectives

To compare the efficacy of Platelet rich plasma and Superoxidised solution in the management of chronic foot ulcers to observe:

- 1) Wound disinfection
- 2) Rate of wound healing
- 3) Appearance of granulation tissue
- 4) Duration of hospital stay.

Material and Methods

This study was conducted over a period of 18 months in the Department of General Surgery, KIMS hospital, Bangalore.

Inclusion Criteria: Patients aged between 18-80 years with hemoglobin levels above 10g/dL having ulcers of more than four weeks duration and size less than 15cm², secondary to diabetes mellitus or trauma.

Exclusion Criteria: Patients with necrotizing fasciitis, peripheral vascular disease, decubitus, venous or trophic ulcers, osteomyelitis, renal impairment, immunocompromised status, bleeding or platelet disorders.

Methodology

Patients with Chronic Foot Ulcers admitted during October 2018 - January 2020 at KIMSH&RC General Surgery Dept. were screened and selected for this study.

50 patients were randomized into 2 groups with 25 patients in Group A being Platelet Rich Plasma (PRP) and 25 patients in Group B being Superoxidised Solution (SOS) using a computer-based randomization.

Patients included in the study were subjected to detailed clinical history and examination. Routine blood investigations such complete blood count, renal function test, blood sugars and swab culture sensitivity from ulcer was taken on D1 in all patients. X ray was taken wherever indicated.

For Group A: 10ml of blood was collected and centrifuged at 3200 rpm for 15 mins, this freshly prepared PRP was injected at healing margins of the wound with insulin syringe after cleansing with normal saline. Dressing was done. This was repeated after 5 days and was done for 5 sessions.

For Group B: Superoxidised solution was sprayed after cleansing the wound and dressing done with. This was also done for 5 weeks.

Patients were put on antibiotics according to culture and sensitivity, sugars were controlled for diabetic patients.

Wound assessment was done on 1, 5, 9, 12, 18, 21 days and observations were noted in terms of wound reduction between two groups.

Wound healing between the two groups were compared based on:

- Wound size
- Appearance of Granulation tissue

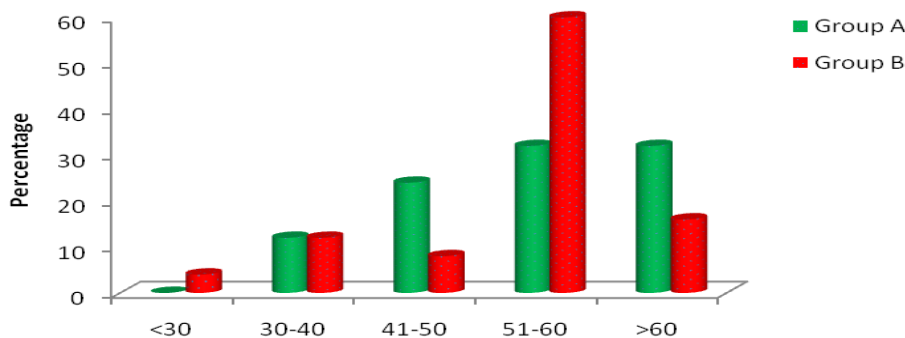
- Appearance of Epithelialization
- Organisms isolated/ Growth on culture sensitivity
- Duration of hospitalization
- Day of wound disinfection.

The end point of the study was taken as the complete closure or end of follow up.

Descriptive and inferential statistical analysis was carried out in the study with p-value less than 0.05 considered as significant.

Results

Age Distribution: The overall mean age of patients in both groups was 55.64 ± 12.46, of Group A – 57.24± 12.93 and Group B - 54.04±12.02. The maximum number of patients were in the age group of 51-60 years in both Group A(8 patients) and Group B(15 patients).



2. Sex Distribution: In Group A, there are 19 male and 6 female patients. In Group B there are 20 male, 5 female patients in group B, with overall 78% male and 22% female patients in both groups.

3. Etiology: The total number of diabetics in the study included 38 patients (76%), while 12 patients (24%) were not diabetic. Both in Group A and Group B, 76% were Diabetic and 6 patients in each group had history of minor trauma.

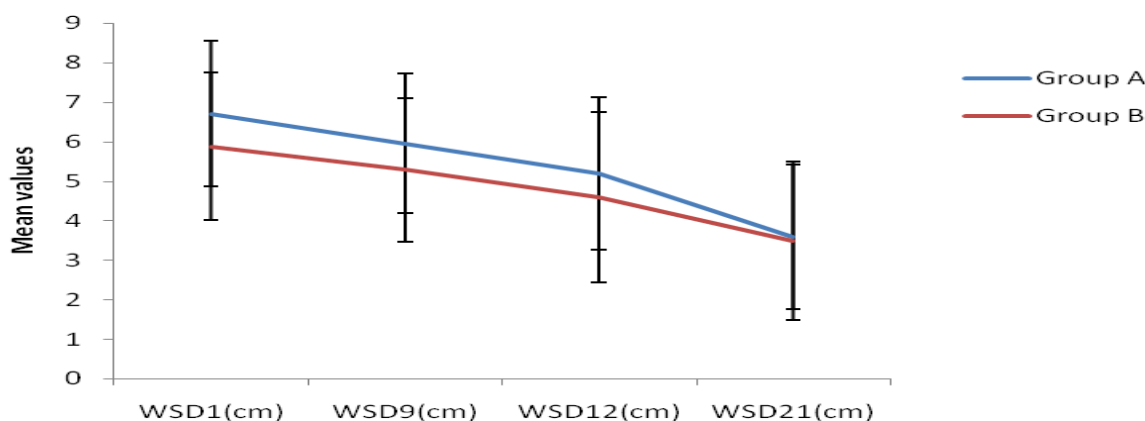
ETIOLOGY	Group A	Group B	Total
T2DM	19(76%)	19(76%)	38(76%)
Traumatic	6(24%)	6(24%)	12(24%)
Total	25(100%)	25(100%)	50(100%)

4. Wound Size: Wound size was measured at baseline-Day 1 for all patients. The change in wound size was calculated from baseline (Day 1) and last day of measurement, i.e., Day 21 and in patients who underwent Split skin grafting (SSG)

before 21 days it was calculated one day prior to SSG.

In this study few patients underwent SSG after Day 9 and Day 12. The largest diameter of wound size was considered for analysis.

Variables	Group A	Group B	Total	P Value
WSD1(cm)	6.71±1.85	5.88±1.87	6.30±1.89	0.125
WSD9(cm)	5.96±1.77	5.29±1.82	5.63±1.81	0.193
WSD12(cm)	5.20±1.93	4.59±2.15	4.90±2.04	0.295
WSD21(cm)	3.60±1.83	3.49±2.01	3.55±1.90	0.838
Difference				
□ D1-D9	0.744	0.592	0.668	-
□ D1-D12	1.50	1.292	1.39	-
□ D1-D21	3.10	2.392	2.745	-
P value				
□ D1-D9	<0.001**	<0.001**	<0.001**	-
□ D1-D12	<0.001**	0.001**	<0.001**	-
□ D1-D21	<0.001**	<0.001**	<0.001**	-



5. Appearance of Granulation tissue: In Group A (PRP), the mean duration for Day of appearance of Granulation tissue was 6.44 ± 1.35 days. In Group B (SOS), the mean duration for day of appearance of Granulation tissue was 8.36 ± 2.01

days. Chi-Square test was used to analyze the outcomes. There was significant difference between Group A and Group B on Chi-Square Test for day of appearance of granulation tissue.

Appearance of granulation on day	Group A	Group B	Total
1-5	10(40%)	2(8%)	12(24%)
6-10	15(60%)	19(76%)	34(68%)
10-15	0(0%)	4(16%)	4(8%)
Total	25(100%)	25(100%)	50(100%)

6. Appearance of Epithelialization: In Group A, the mean duration for day of appearance of Epithelialization was 9.16 ± 1.84 days. In Group B, the mean duration for day of appearance of

Epithelialization was 11.04 ± 2.29 days. There was significant difference between Group A and Group B on Chi-Square Test for day of appearance of Epithelialization.

Appearance of epithelialisation tissue on day	Group A	Group B	Total
1-5	0(0%)	0(0%)	0(0%)
6-10	19(76%)	10(40%)	29(58%)
10-15	6(24%)	15(60%)	21(42%)
Total	25(100%)	25(100%)	50(100%)

7. Wound Disinfection: In Group A, the mean duration for day of Wound Disinfection (Culture negative) was 7.88 ± 1.01 days. In Group B, the mean duration for day of Wound Disinfection

(Culture negative) was 8.28 ± 0.97 days. There was no significant difference between Group A and Group B.

A Comparison of Granulation day/ Epithelialization day/ Disinfection day in two groups studied:

Variables	Group A	Group B	Total	P Value
GRANULATION DAY	6.44 ± 1.35	8.36 ± 2.01	7.40 ± 1.95	<0.001**
EPITHELIALISATION DAY	9.16 ± 1.84	11.40 ± 2.29	10.28 ± 2.34	<0.001**
DISINFECTION DAY	7.88 ± 1.01	8.28 ± 0.97	8.08 ± 1.00	0.162

8. Organism on Culture Sensitivity:

The commonest organism on Culture sensitivity taken on day 1 for all patients was Staphylococcus aureus – 9 patients, Enterococci – 5 patients, no growth in 11 patients.

9. Duration of Hospitalization: In Group A, the mean duration of hospitalization was 11.96 ± 2.11 days. In Group B, the mean duration of hospitalization was 11.88 ± 2.53 days. There was no significant difference between Group A and Group B on Student t Test.

Hospital stay	Group A	Group B	Total
1-5	0(0%)	0(0%)	0(0%)
6-10	11(44%)	12(48%)	23(46%)
11-15	14(56%)	11(44%)	25(50%)
16-20	0(0%)	2(8%)	2(4%)
Total	25(100%)	25(100%)	50(100%)
Mean \pm SD	11.96 ± 2.11	11.88 ± 2.53	11.92 ± 2.31

Discussion

It is every surgeon's desire that after dressing the wound, it should heal without any complications. Successful wound dressing should keep the wound moist and be devoid of any adverse reactions such as infection, maceration and allergy.

In the present study, the effect of Platelet Rich Plasma versus Superoxidised solution in the management of lower limb ulcers in a group of 25 patients each was studied.

The mean age of patients in the study was 55.64 ± 12.46 years, 78% of patients were male. 76% of patients were diabetic and 24% of patients had traumatic etiology.

Various wound outcome variables were compared between both groups. The average reduction in wound size from day 1 to day 21 was statistically significant, with the Platelet Rich Plasma group showing more rapid reduction in wound size compared to Superoxidised solution group. There

was a 3.10cm average reduction in wound size in Group A (PRP) as compared to 2.39cm in Group B (SOS) at Day 21.

In the Group A (PRP), there was earlier appearance of granulation tissue (6.44 ± 1.35 days) as compared to Group B (SOS) (8.736 ± 2.01 days). The appearance of epithelialization was earlier in Group A (PRP) (9.16 ± 1.84 days) as compared to Group B (SOS) (11.40 ± 2.29 days). Both the results were statistically significant ($p < 0.001$).

There were no studies in the past comparing the efficacy of PRP and Superoxidised solution for chronic non healing foot ulcers, but there are many studies comparing PRP versus PI solution and SOS versus PI solution in terms of wound healing.

In a study conducted by V.Kapur et al⁷ diabetic foot ulcer and chronic leg ulcers patients and acute abscesses treated with SOS also showed early granulation and epithelization when

compared to PI group at a mean follow up of 21 days. Their study also showed that average reduction in wound size at day 21 was greater in SOS group as compared to PI group.

Ashok Anand⁸, compared efficacy of SOS versus PI in post C-section wounds, showed that 88% had granulation by day 5 in SOS group compared to 80% in PI group and by day 10 there was granulation in all patients.

In Group A (PRP) the average duration for wound disinfection was 7.88 ± 1.01 days compared to 8.283 ± 0.97 days.

In a study conducted by Chittoria RK⁹ et al for role of SOS in the management of diabetic foot ulcers in Andhra Pradesh on 20 patients, 19 out of 20 cases were negative for infection after 5 days.

Most commonly cultured organisms were Staphylococcus aureus 9(18%), pseudomonas- 6 (12%), Enterococci, Acinetobacter, proteus – 5(10%), E.coli and streptococci- 3(6%). Staph aureus was the commonest organism on culture in studies conducted by V.Kapur et al⁷ and Chittoria RK⁹ et al.

Driver et al conducted a prospective randomized-controlled, blinded, multicenter clinical study in 129 patients to evaluate the safety and efficacy of autologous platelet-rich plasma gel for the treatment of non healing diabetic foot ulcers. It was found that significantly more autologous platelet-rich plasma gel(81.3%) than control gel(42.1%) treated wounds healed.¹⁰

Knighton DR et al conducted a prospectively randomized, blinded trial in 32 patients in 1990 at Minnesota, Minneapolis to test whether or not platelet derived wound healing factors accelerate repair. In the study group, 81% of patients had epithelialization compared to 15% in the control group. Results from this study demonstrate a highly statistically significant effect of topically applied platelet derived growth factors on the repair of chronic non healing cutaneous ulcers.¹¹

Robert G Frykberg et al used autologous PRP gel on 49 patients with chronic, non healing wounds and found that 97% of wounds improved, for all wound etiologies. The results of this study suggest

that the application of PRP gel can reverse non healing trends in chronic wounds.¹²

The mean duration of hospitalization was 11.96 ± 2.11 days in Group A (PRP) which included as compared to 11.88 ± 2.53 days in Group B (SOS), Hence, in the current study there was faster healing rate of ulcers treated with Platelet Rich Plasma compared to Superoxidised solution, proving PRP to be safe, efficient and superior as a wound care product compared to Superoxidised solution in the management of chronic non healing foot ulcers.

Conclusion

Platelet Rich Plasma with its moistening effects and cost effectiveness is safe, has faster response in wound healing and gives better results compared to the Superoxidised solution for use in wound care in management of chronic non healing foot ulcers.

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