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## Original Research Paper

# A Randomized Control Study of Autologous Platelet Rich Plasma and Normal Saline Dressing In Management of Pressure Ulcer In Spinal Cord Injury Patients

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**Objectives:** Pressure ulcers (PrUs) are the common complications following SCI and there are various options available for PrUs management. In this study the author compared the effect of platelet rich plasma gel dressing of pressure ulcer with normal saline dressing in SCI patients.
**Design:** This randomized comparative study was conducted in PMR department of SMS medical college.
**Method:** Fifty eight SCI patients with PrUs, were randomized into PRP gel treatment group (n=29) and normal saline treatment group (n=29) equally. In PRP group, pressure ulcer dressing was done with autologous PRP gel twice weekly for 5 weeks and in NS group, ulcer dressing was done with 9% normal saline on the daily basis for 5 weeks. Evaluation of PrU healing was done by ulcer staging, measuring wound surface area, Pressure Ulcer Scale for Healing (PUSH), histopathological features of ulcer.
**Results:** The mean age of the patients was 37.79±9.90 and 35.14±9.05 years in PRP and NS group respectively. Statistically significant reduction in the stages of ulcer was observed only in PRP gel dressing group only ($p<0.001$ S) after 5 weeks. The wound area, wound volume and PUSH score of PrU decreased significantly in both groups but on compression among the groups significant decrease in ulcer surface area, and PUSH score was observed in PRP group as compare to NS group. Significant improvement in histopathological of the ulcer was observed after 5 weeks both in PRP (P value= 0.001) and NS (P value= 0.001) group but on comparison among the groups, ulcer treated with PRP gel showed more significant improvement as compare to NS group (P value= 0.001)
**Conclusion:** PRP gel dressing is a better alternative as compare to normal saline dressings in PrU healing in SCI patients.
**Key Words:** SCI, Pressure Ulcer, Platelet Rich Plasma, histopathology, Biopsy

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## INTRODUCTION

Spinal Cord injury (SCI) is one of the most devastating and demoralizing injury both for the patient as well as for the health care providers. The expensive treatment cost and long recovery treatment in SCI patients always bring great influence to the individual, the family and also bring a heavy burden on the society. [1] Life expectancy of the SCI population is steadily improving through modern spinal unit care but this is also associated with secondary complications in these populations that continue to pose management challenges and impair the quality of life of such patients. Spinal cord injury lead to multiple complication such as cardio-respiratory, urological complications, pressure ulcer, neurogenic bowel and bladder, Autonomic Dysreflexia (AD), spasticity, sexual dysfunction, deep vein thrombosis etc.

Pressure ulcers are one of the commonest secondary complications following SCI. [2] The incidence of pressure ulcer in SCI population may vary from 25–66%. The prevalence of pressure ulcer in general acute care setting is around 10–18%, in long-term facilities 2.3–28%, and home care from it is around 0–29%. [3] In Indian setting the prevalence of pressure ulcer in hospitalized patients has been reported to be 4.94 in study conducted by Chauhan et al. [4] The common extrinsic risk factors for development of pressure ulcers in SCI population are prolonged pressure, surface shear, friction and local micro- environment and the intrinsic risk factors includes anemia, muscle weakness/atrophy, impaired nutrition, impaired mobility and impaired sensation. Other risk factors associated with ulcer development in SCI population are such as spasticity, heterotrophic ossification, and bladder & bowel incontinence.

In clinical practice, assessment of pressure ulcer can be done by length/width measurement, surface area measurement (length x width), wound volume measure by (surface area x depth or amount of saline that fills into the wound cavity), Pressure Ulcer Score of Healing (PUSH),[5] Wound Healing Scale (WHS) etc. The assessment of the histological state of the wound healing is also important in clinical practice for management of ulcer. Histopathological evaluation should include the basic components of healing process including inflammation, angiogenesis, fibroplasia, restoration of the connective tissue matrix, wound contraction and remodeling. Histopathological feature of the wound can be assessed in terms of the formation of granulation tissue and can be divided in four categories; 1) Necrosis and suppuration, 2) Early granulation tissue, 3) Neo-vascularization and late granulation tissue and 4) Well-formed granulation tissue with epithelialization.[1]

The pressure ulcer is one of the commonest and most serious complications following SCI and once developed; its wide spectrum impact can be appreciated by overall decline of quality of life of the patient. Thus; management of pressure ulcer is one of the most important aspects of SCI management. Management of pressure ulcer involves local wound care, identify and remove the risk factor. Local wound care includes; clean the wound bed surface with normal saline and mechanical debridement (if required), and dressing. Various kinds of dressings are used for ulcer management such as alginate, hydrocolloid, hydrogel, silver (silver stream and aquacel dressing), iodine and autologous platelet rich plasma dressing etc. Other treatment may include therapeutic agent for infection control, therapeutic agent for wound healing, therapeutic ultrasound, nutritional support, hyperbaric oxygen therapy, stem cell therapy, surgical management (skin graft or flap surgery), negative wound pressure therapy, and electric stimulation etc.

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Platelet-rich plasma (PRP) is currently considered to be an advanced wound therapy for chronic and acute wounds managements in regenerative medicine. PRP is a good source of growth factors and these growth factors released by platelets, regulate the orchestrated and complex events in normal wound healing phase. Effectiveness of PRP is based on its high level of growth factors such as platelet derived growth factor (PDGF), transforming growth factor (TGF), epidermal growth factor (EGF), vascular endothelial growth factor(VEGF), and insulin-like growth factor (IGF) etc.[6] These growth factors pay important role in modulating mesenchymal cell recruitment, proliferation, and extracellular matrix synthesis during the wound healing process.[7] PRP has high level of leukocytes so it also plays an important role in antimicrobial activity that may contribute to the prevention of infection

Normal saline dressing is use as common conventional dressing for wound cleaning and healing. Saline dressings are physiologically normal and isotonic, giving a moist environment to the wound, which is require for healing of ulcer. NS dressing is inexpensive and also convenient to apply. Saline dressings work as an osmotic dressing, with evaporation of water from NS gauze and the dressing becomes hypertonic. The hyper-tonicity of the normal saline dressing provides an osmotic gradient for absorption of wound discharge/fluid from the wound by osmosis and contributing to its effectiveness as a wound dressing. This may explain why frequent dressing changes are required to maintain adequate tonicity and permeability for the dressing to be effective of wound healing. [8]

There are many studies in the literature provide support for clinical use of PRP in the treatment of acute and chronic wounds. But very few studies are available which support the clinical use of PRP in pressure ulcer treatment in SCI patients. The author also came across that there are only few Indian studies available which support the clinical use of PRP in pressure ulcer in SCI patients. This study was designed to compare the efficacy of local applications of autologous platelet rich plasma in the treatment of pressure ulcer with common traditional management (0.9% NS dressing) in spinal cord injury patients.

**OBJECTIVES**:- The objective of the present study was to evaluate the effect of local application of autologous PRP in pressure ulcer healing in comparison with normal saline dressing on the basis of pressure ulcer grading, wound surface area, wound volume, PUSH score measurement and ulcer histopathological features of the ulcers.

**MATERIAL AND METHODS:-**

This was an interventional comparative randomized control study. The indoor SCI patients with pressure ulcers in the department of physical medicine and rehabilitation of Sawai Man Singh hospital was recruited between July 2019 and September 2020. Patients were evaluated at baseline and follow up at week 5.

Traumatic SCI patients of both genders of age between 20 to 50 years with vertebral level below C4 and a clean pressure ulcer of grade II, III, or IV were recruited in this study. Patients were excluded if they had serum protein level deficiency, low hemoglobin level (<10gm/dl), smoker or nicotine users, non-traumatic spinal cord patients, malignant disorder, major psychiatric disorders or any medical conditions that interferes pressure ulcer healing, obese patients (> 30 BMI) and sensory intact patients.

All the patients were given detailed information about the purpose of study and written consent was obtained from all the participants. The complete history of patients was taken to rule out any other occult medical or neuropsychological problem and the complete general physical and neurological examination was done. X-rays of the injury site as well as of PrUs

sites were done. Routine hematological investigations (viz. hemoglobin, bleeding time, clotting time, blood urea, blood sugar, serum sodium ion, serum potassium ion, total serum protein and serum albumin) were done.

Sample size was calculated at 80% study power and alpha error of 0.05. Total 29 patients in each group were required as a sample size, which was further enhanced to 32 patients in each group as final sample size assuming 10% drop out/lost follow up/attrition.

Fifty eight patients of SCI with pressure ulcers were recruited in the study and were equally randomized into PRP treatment group (n=29) and NS dressing treatment group (n=29).

**INTERVENTIONS**

Participants who were satisfying our inclusion criteria was randomly assigned to the Group-A (PRP gel dressing) or the Group-B (Normal saline dressing) using the random number generation functions in a commercially available software program.

Pressure ulcer dressing with PRP: On the day of the ulcer dressing, PRP was prepared in the Department of PMR, SMS Medical College using the standard preparation techniques from the patient's own blood in a sterile environment using a REMI R-8C centrifuge machine. Blood (amount-according to the size of pressure ulcer) was collected using 21 gauge needle from ante-cubital vein into an 8.5ml vacutainer tubes containing citrate anticoagulant. PRP was prepared with double centrifugation method. First the blood was centrifuged at 3200 R.P.M. for 14-min, the blood was layered in three basic components: red blood cell, platelets and platelet-poor plasma. Due to different sediment coefficients, the red blood cells layer was seen at the lowest level, the platelet layer was in the middle and the platelet-poor plasma layer was at the top. The lower the red blood cells layer was removed and then the vacutainer tube was agitated for approximately 1 minute and was centrifuged again at 3500 R.P.M. for 5 min. The blood was separated into two layers, the supernatant platelet-poor plasma layer and lower platelet-rich plasma layer. About three quarters of the supernatant was discarded and in the residual PRP, calcium chloride (10%) was added in a ratio of 6:1 (PRP: 10% calcium chloride) to activate the PRP. Then the vacutainer tube was agitated for 5–10 seconds to initiate the PRP gel formation. PRP was assessed for platelets concentration randomly after every 7 patients for adequate platelets concentration.

For the dressing with the PRP group, pressure ulcer was cleaned with normal saline and debrided (if needed). Activated PRP was applied to the ulcer and was spread over the wound to transform into a gel. Non-absorbent vaseline gauze was applied over the wound after application of PRP, and then dry cotton gauze and cotton pad was applied to absorb the any discharge from the wound. A transparent drape (opsite) was used to cover the wound. The PRP gel dressing of ulcer was done twice-weekly for 5 weeks (total 10 dressings in 5 weeks were applied).

Pressure ulcer dressing with NS: In the NS group, pressure ulcer was cleaned, debrided (if needed) and was dressed daily with normal saline (0.9%) dressing up-to 5 weeks.

**OUTCOME MEASURES-**

Detailed evaluation of pressure ulcer was done at base line and after $5^{th}$ weeks of treatment with the following measuring tools:-

**1) Pressure ulcer grading:-** As per NPUAP staging system, stages of pressure ulcer was

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assessed at baseline and at the end of 5th week in both the groups.

2) **Wound surface area measurement (in cm2):-** The wound surface area was calculated by Prime Ruler area measuring application with the help of android mobile (Prime Ruler application available on Google play store).
3) **Wound volume (in ml):-**Wound volume was assessed by measured the amount of normal saline that occupies or fills into the pressure ulcer cavity.
4) **Pressure Ulcer Scale for Healing (PUSH):-** PUSH score was used for wound assessment as described in below.

PUSH criteria was used for wound assessment in term of length x width = wound surface area, amount of exudate and type of tissue at the base line and follow-ups as described in the table. The total score is ranged from 0 to 17, with 0 representing a healed wound. The score would go down with wound improvement and would go up with wound deterioration. (Table: 1)

**Table 1: PUSH criteria for PUSH scoring of pressure ulcer**

| | | | | | | |
|---|---|---|---|---|---|---|
| Length x width = Surface area (cm2) | 0<br>0 | 1<br><0.3 | 2<br>0.3-0.6 | 3<br>0.7-1.0 | 4<br>1.1-2.0 | 5<br>2.1-3.0 |
| | 6<br>3.1-4.0 | 7<br>4.1-8.0 | 8<br>8.1-12.0 | 9<br>12.1-24.0 | 10<br>>24.0 | Sub score |
| Exudate amount | 0<br>None | 1<br>Light | 2<br>Moderate | 3<br>Heavy | | Sub Score |
| Tissue type | 0<br>Closed | 1<br>Epithelial tissue | 2<br>Granulation tissue | 3<br>Slough | 4<br>Necrotic tissue | Sub score |
| PUSH Score (minimum score = 0, maximum score = 17) | | | | | | Total score |

Directions: Observe and measure the pressure ulcer. Categorize the ulcer with respect to surface area, exudate and type of wound tissue. Record a sub-score for each of these ulcer characteristics. Add the sub-scores to obtain the total score. A comparison of total scores measured over time provides an indication of the improvement or deterioration in pressure ulcer healing. [9]

5) **Histopathological findings in tissue:-** A punch biopsy was taken from the margins of the wound at base line and at 3$^{rd}$ week and at the end of study (end of 5$^{th}$ weeks) to monitor histopathological features of pressure ulcer healing. Histopathology of the wound was assessed in terms of the formation of granulation tissue and was divided in four categories; 1) Necrosis and suppuration, 2) Early granulation tissue, 3) Neo-vascularization and late granulation

## STATISTICAL ANALYSIS

Categorical variables were expressed frequency and percentage and analyzed using chi-square test for comparison between the two groups. Before - after comparison for categorical variables was done using McNemar's test. Continuous variables were expressed as mean and standard deviation and analyzed using independent sample t-test for comparison between the two groups. Paired t-test was used for before after comparison. Wilcoxon sign rank test was used for ordinal variables. P value<0.05 was taken as statistically significant.

## RESULTS

Fifty eight patients, 29 in each group were recruited into this study. Mean age of the

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participants was 34.79 ±9.90 in PRP and 35.14±9.05 in NS group, this difference of mean age in both the group was statistically non-significant (P = 0.89) and the groups were comparable. Mean BMI at enrolment was 20.56±6.15 of PRP group and 21.11±4.69 of NS group and this difference was also non-significant (P = 0.701). Male to female ratio was 26:3 and 23:6 in PRP and NS group respectively and most of the patients were of cervical and dorsal spine injuries in both the groups. Patients with complete SCI (ASIA – A) were more frequent as compare to incomplete injury in both the groups (n=18 and n=16 in PRP and NS group respectively). Most of the pressure ulcers were situated at sacral region and grade 2 and 3 pressure ulcer were more frequent in both the groups then grade 4. (Table: 2)

**Table 2: Demographic and characteristics of the study population**

| Characteristic | | Incidence (PRP Group) | Incidence (NS Group) |
|---|---|---|---|
| Mean age (years) | | 34.79 ±9.90 | 35.14±9.05 |
| Gender | Male | 26 | 23 |
| | Female | 3 | 6 |
| Mean BMI ($Kg/m^2$) | | 20.56±6.15 | 21.11±4.69 |
| Mode of trauma | Fall of heavy object | 3 | 7 |
| | Fall from height | 16 | 28 |
| | Road traffic accident | 10 | 23 |
| Level of spine injury | Cervical | 12 | 11 |
| | Dorsal | 13 | 03 |
| | Lumber | 04 | 05 |
| Neurological level of injury | ASIA- A | 18 | 16 |
| | ASIA- B | 7 | 8 |
| | ASIA- C | 3 | 5 |
| | ASIA- D | 1 | 0 |
| | ASIA- E | 0 | 0 |
| Neurological Injury | Complete | 18 | 16 |
| | Incomplete | 11 | 13 |
| Grade of pressure ulcer at baseline | Grade 2 | 10 | 12 |
| | Grade 3 | 12 | 09 |
| | Grade 4 | 07 | 08 |
| Blood parameters | Mean Hb (gm/dl) | 12.11 ± 1.49 | 11.64 ± 1.17 |
| | Mean protein (gm/dl) | 6.29 ± 0.44 | 6.28 ± 0.47 |
| Site of pressure Ulcer | Sacrum | 19 | 14 |
| | IT | 03 | 05 |
| | GT | 07 | 08 |
| | Malleolus | 00 | 02 |

After 5 weeks of ulcer treatment with PRP gel dressing, it was observed that 10 pressure ulcer of stage II increased to 15 ulcers, 12 pressure ulcer of stage III decreased to 6 pressure ulcers, 7 pressure ulcer of stage IV decreased to 2 pressure ulcer and 6 pressure ulcers healed completely. Study result revealed that with the PRP gel dressing, the number of high grade ulcer decreased where the number of low grade ulcers increased which was statistically significant (P<0.001). The study also showed that after 5 weeks dressing of the ulcers with

0.9% NS dressing; 12 pressure ulcer of grade II converted into 15 ulcer of grade II, 9 pressure ulcer of grade III converted into 8 ulcer of grade III, 8 pressure ulcer of grade IV changed to 5 ulcer of grade IV and 1 pressure healed completely. This change in ulcer staging with NS dressing group was statistically non- significant (P<0.152). (Table: 3)

**Table 3: Pressure grading in PRP and NS group at baseline and end of 5th weeks**

| Grade of ulcer | PRP Group | | | | NS Group | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | | 5 weeks | | Baseline | | 5 weeks | |
| | N | % | N | % | N | % | N | % |
| Healed | 0 | 0 | 6 | 20.69 | 0 | 0 | 1 | 3.45 |
| II | 10 | 34.48 | 15 | 51.72 | 12 | 41.38 | 15 | 51.72 |
| III | 12 | 41.38 | 6 | 20.69 | 9 | 31.03 | 8 | 27.59 |
| IV | 7 | 24.14 | 2 | 6.90 | 8 | 27.59 | 5 | 17.24 |
| Total | 29 | 100 | 29 | 100 | 29 | 100 | 29 | 100 |
| P value | <0.001 (S) | | | | 0.152 (NS) | | | |

The study showed that dressing with PRP gel and with 0.9% NS for 5 weeks results in significant reduction in mean wound surface area from 13.5 ± 14.49 to 6.32 ± 11.27 (P <0.001) and from 20.63 ± 12.08 to 14.54 ± 11.24 (P <0.001) respectively. On compression among the PRP and NS group, result showed significant reduction in mean wound surface area at the end of the 5th week (p<0.007) in PRP group as compare to NS group. The study results revealed that at the end of 5 week, there was a significantly reduction in mean wound volume from 4.16 ± 3.25 ml to 1.78 ± 2.77 (P value <0.001) in PRP group and from 4.3 ± 2.78 ml to 2.99 ± 2.53 ml (P value <0.001) in NS group and on comparison of mean wound volume among the groups, the author observed that there was non-significant difference (P<0.315) in mean wound volume at the end of 5th week among the groups. The study showed that both in PRP and NS groups there was a significant reduction in PUSH score from 1.93 ± 3.43 to 6.45 ± 5.07 (P value <0.001) and 13.55 ± 3.04 to 10.55 ± 3.64 (P value <0.001) respectively at end of 5th week and on compression of mean PUSH score in between the groups, results showed that significant decrease in PUSH score in PRP group as compare to NS group (p Value = .001) at the end of 5th week. (Table: 4, Fig. 1)

**Table 4: Mean wound surface area, volume and PUSH score at baseline and at 5 weeks**

| | Baseline | | 5 weeks | | P Value |
|---|---|---|---|---|---|
| | PRP Group | NS Group | PRP Group | NS Group | |
| **Wound area in $cm^2$ (Mean ± SD)** | 13.5 ± 14.49 | 20.63 ± 12.08 | 6.32 ± 11.27 | 14.54 ± 11.24 | 0.007 |
| **Wound volume in ml (Mean ± SD)** | 4.16 ± 3.25 | 4.3 ± 2.78 | 1.78 ± 2.77 | 2.99 ± 2.53 | 0.086 |
| **PUSH Score (Mean ± SD)** | 11.93 ± 3.43 | 13.55 ± 3.04 | 6.45 ± 5.07 | 10.55 ± 3.64 | 0.001 |

The histopathological features of the wound were observed in both the groups at baseline and at 5th week, in term of necrosis and suppuration, early granulation tissue, neo-vascularization and late granulation tissue and well-formed granulation tissue with epithelialization. At the base line, in PRP group, 20 pressure ulcers had necrosis and suppuration tissue, 7 ulcers had early granulation tissue and 2 ulcers had neo-vascularization and late granulation tissue. At the end of 5th week in PRP group 2 ulcers showed necrosis and suppuration tissue, 3 ulcers had early granulation tissue, 7 ulcers had neo-vascularization and late granulation tissue and

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17 ulcers had well-formed granulation with epithelialization tissue. At the baseline, in NS group, 23 pressure ulcers had necrosis and suppuration, 5 ulcers had early granulation tissue, and 1 ulcer had neo-vascularization and late granulation tissue and at the end of 5th week, 8 ulcers showed necrosis and suppuration tissue, 10 ulcers had early granulation tissue, 10 ulcers had neo-vascularization and late granulation tissue and 1 ulcer had well-formed granulation with epithelialization tissue. On analysis the author observed significant improvement in histopathological features of wound both in PRP ($P < 0.001$) and NS ($P < 0.001$) group at the end of 5th week. (On compression of histopathological findings in the ulcers among the PRP and NS groups, the result showed a significant histopathological improvement in ulcers in patients whose wound dressing was done with PRP gel (17 pressure ulcer converted into well-formed granulation with epithelialization in PRP group) as compare to patients whose dressing was done with normal saline (only one pressure ulcer converted into well-formed granulation with epithelialization in NS group) at the end of 5th weeks ($p<0.001$). ) (Fig. 2, 3and Table: 5)

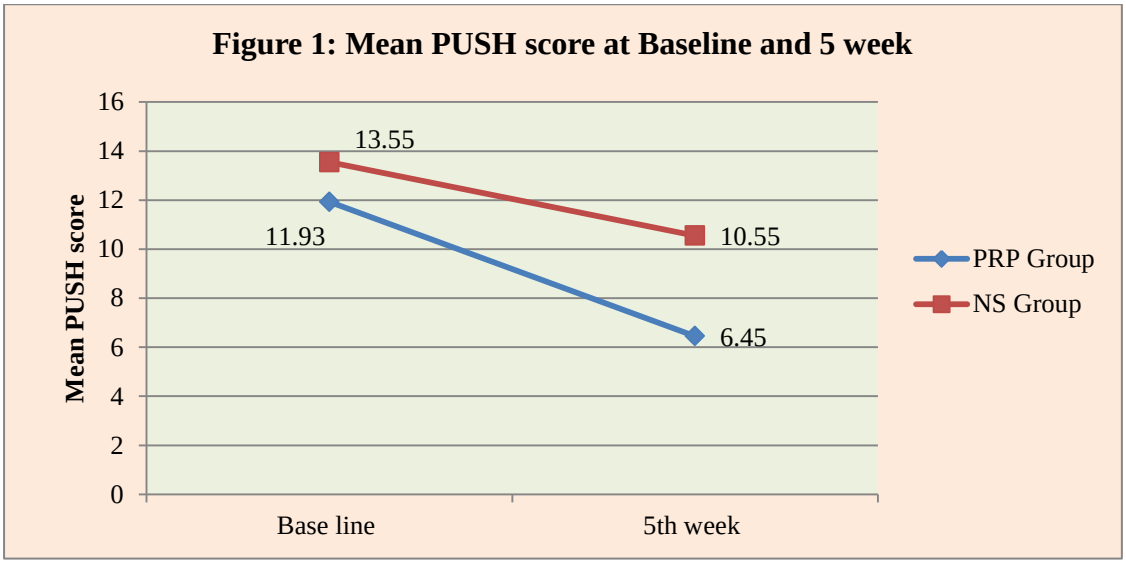


**Figure 1** Showing mean PUSH score at baseline and 5 week in PRP and NS group

**Table no 5: Histopathology of pressure in PRP and NS group at baseline and at 5th week**

| | Baseline | | | | 5 weeks | | | |
|---|---|---|---|---|---|---|---|---|
| | PRP | | NS | | PRP | | NS | |
| | No. | % | No. | % | No. | % | No. | % |
| Necrosis & Suppuration | 20 | 68.97 | 23 | 79.31 | 2 | 6.90 | 8 | 27.59 |
| Early granulation tissue | 7 | 24.14 | 5 | 17.24 | 3 | 10.34 | 10 | 34.48 |
| Neovascularization and late granulation tissue | 2 | 6.90 | 1 | 3.45 | 7 | 24.14 | 10 | 34.48 |
| Well-formed granulation tissue with epithelization | 0 | 0.00 | 0 | 0.00 | 17 | 58.62 | 1 | 3.45 |
| Total | 29 | 100.00 | 29 | 100.00 | 29 | 100.00 | 29 | 100.00 |
| p value | 0.645 (NS) | | | | P<0.001 (S) | | | |

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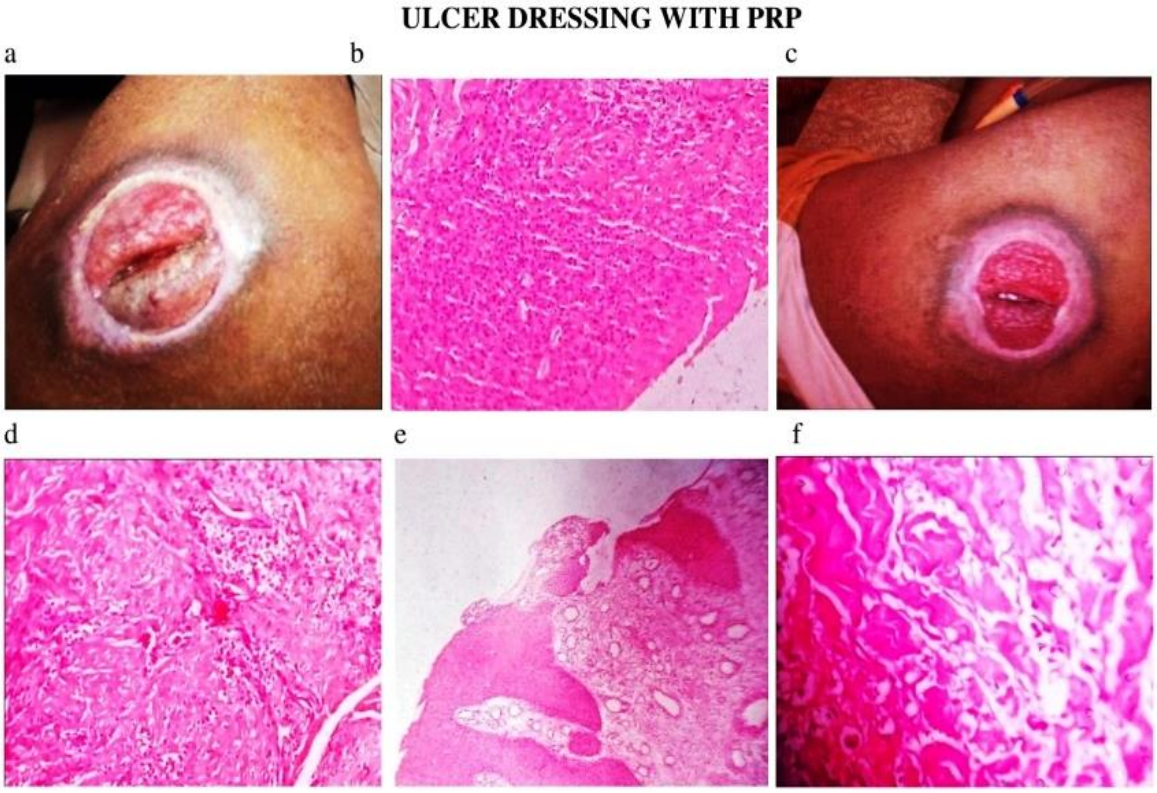


**Figure 2:** Clinical and histopathology photographs of the pressure ulcer (PRP group) during treatment with PRP. (a) Clinical photograph of pressure ulcer at the time of enrolment (b) Histopathology slide of ulcer tissue at enrollment showing ulceration with sloughed our epidermis (H&E stain, 10X). (c) Clinical photograph after fifth week of PRP application. (d) Histopathology slide after third week of PRP application shows well-formed granulation tissue (H & E stain, 40X). (e) Histopathology slide after fifth week of PRP application showing regenerating epidermis (epithelialization) (H&E stain, 10X). (f) Histopathology slide after fifth week of PRP application shows showing collagenization (H&E stain, 40X).

**DISCUSSION:-**

Many studies in the literature provide support for clinical use of PRP in the management of acute and chronic wounds. Recently very few studies have shown usefulness of PRP in pressure ulcer because it leads to reactivation and accelerated healing in pressure ulcer.[1,10] However inconclusive reports had also been documented by Weed et al and Scevola et al.[11] There are only a few Indian studies which support the clinical use of PRP in pressure ulcer treatment in SCI patients. This study was planned and designed to find out the effect of platelet rich plasma gel dressing in the management of pressure ulcer in spinal cord injury patients as compare to NS dressing on the basis of ulcer grading, wound size measurement, PUSH score and histopathological features.

The study showed significant improvement in the grading of ulcer after 5 weeks treatment with PRP gel dressing (p value – 0.001). The ulcer grading also improved with use of NS dressing but it was statistically non-significant (p value - 0.152). Similar to our findings Sung-AE-Kim et al.[12] reported that out of 16 ulcers 9 ulcers showed 90-100% epithelization after 3 week of PRP gel dressing, Yaun et al.[6] reported that 3 out of 3 pressure ulcer completely healed after 7, 14 week and 17 days with PRP gel dressing. Tsachiridi et al. [13] also observed that 2 patients with pressure ulcer achieved complete epithelization after 8 weeks of PRP dressing.

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**Figure 3:** Clinical and histopathology photographs of the pressure ulcer (NS group) treated with daily saline dressing. Final outcome is deterioration in the ulcer. (a) Clinical photograph pressure ulcer at the time of enrolment (b) Histopathology slide of ulcer tissue at enrollment showing ulceration with sloughed our epidermis (H&E stain, 10X). (c) Clinical photograph after fifth weeks of NS dressing application. (d) Histopathology slide after fifth week of PRP application shows poorly developed granulation tissue with some myofibroblastic proliferation (H&E stain, 40X)

Mean wound surface area reduced significantly both in PRP (53.18% reduction, $P < 0.001$) and NS group (29.52% reduction, $P < 0.001$) but on comparison between the groups, mean wound surface area reduced more with PRP gel dressing as compare to NS dressing, which was statistically significant (P value - 0.007). The result of present study is similar to the study conducted by Somani A et al. [14], who reported significantly reduction in mean surface area of ulcer by 85.51% in PRP group and by 42.74% in saline group. Rapple et al. [15] also observed that average reduction of surface area of pressure ulcer was 53.81% after 4 week PRP gel dressing. Singh et al[2] also concluded in his study that mean wound surface area reduced significantly with PRP gel dressing as compare to NS dressing. All these above studies concluded that mean surface area of ulcer significantly reduce in those patients whose ulcer dressing was done with PRP gel as compare to normal saline dressing, this finding is similar to our study. Inverse to our study, Weed et al. [16] and Knox et al. [17] observed that PRP dressing could not demonstrate statistically significant reduction in mean surface area of ulcer. This inverse finding of Weed et al could be explained as they used different method of PRP gel preparation which was not activated with calcium or thrombin that is essential to

release the of growth factors and another reason could be small sample size of these studies as compare to present study. Knox et al used platelet rich tissue graft, which was also not activated by calcium or thrombin, which could explain the inverse result to this study.

Mean wound volume reduced significantly both in PRP group from 4.16 ± 3.25 ml to 1.78 ± 2.77 ml (57.21% reduction, $p<0.001$) and in NS group from 4.3 ± 2.78 ml to 2.99 ± 2.53 ml (30.46% reduction, $p<0.001$) groups after 5 week treatment. On comparison among the groups, mean wound volume reduced more in PRP gel dressing as compare to NS dressing but it was statistically non-significant ($P = 0.086$). This finding of the present study is similar as observed by Sell et al. [1], Rappl et al. [15] and Frykberg Robert et al. [18] Sell et al observed that wound volume reduced significantly in those patient whose ulcer dressing was done with PRP gel. Rappl et al. also demonstrated that 56% mean volume was reduced with PRP gel dressing and Frykberg Robert et al. also concluded that 51% mean wound volume reduced with use of PRP gel dressing over 3-4 week treatment period. Small sample size of the present study may explain the non-significant improvement in wound volume with PRP gel dressing as compare to NS dressing.

Mean PUSH score reduced significantly from 11.93 ± 3.43 to 6.45 ± 5.07 in PRP group (45.93% reduction, $P <0.001$) and from 13.55 ± 3.04 to 10.55 ± 3.64 in NS group (22.10% reduction, $P <0.001$) group. Singh et al. [2] also reported that PUSH score reduced significantly in both groups (PRP and NS groups). When PUSH score was compared in between the groups, significant reduction in PUSH score in PRP was observed as compare to NS group. Inverse to our finding Singh et al. reported that there was no significant reduction in PUSH score in between the groups. This inverse finding of Singh et al could be explained; that Singh et al. used different tool to measure the ulcer surface area and they recruited grade III and IV pressure ulcer in his study whereas in the present study Prime ruler Android mobile based application used to measure ulcer surface area and grade II, III and IV pressure ulcer were recruited.

In both the groups significant improvement in histopathological features of pressure ulcers were observed at the end of 5th week, but on comparison the histopathological findings of the ulcer in the PRP versus NS group, it was observed that significant improvement in histopathological features of ulcers in those patients whose ulcer's dressing was done with PRP gel as compare to NS group. In the PRP group, 17 pressure ulcers converted into well-formed granulation tissue with epithelialization and 5 ulcers were completely healed; while in NS group only one pressure ulcer converted into well-formed granulation tissue with epithelialization and 1 ulcer was completely healed at the end of 5th week. A similar findings were also observed by R Singh at el.[2] sell et al.[1] and Rapple et al.[15] R Singh et al. reported that 60% (n=15) ulcers were converted into well-formed granulation tissue and epithelialization after 5 weeks in PRP group. R Singh et al. concluded that 96% (n=24) ulcers improved and only 1 deteriorated at end of the 5th week with PRP dressing. Singh et al also reported that in control group 17 (68%) ulcers improved, 7 (28%) deteriorated and 1 wound showed no change. Sell et al reported that all 3 recruited patients showed that granulation tissue, vascularization and epithelization development in all three ulcers treated with PRP dressing. Mazzuco et al.[19] also observed that angiogenesis development with PRP therapy. Anitua et al reported that platelet derived growth factor in PRP had a role in stimulating fibroblast proliferation and inducing myofibroblast, which promoting of the healing of pressure ulcer.

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During our study we did not observe any major complication with the treatment of PRP gel and NS dressings of the pressure ulcer.

**CONCLUSION:-**

This is the probably one of few studies in human beings that has demonstrated potential efficacy of PRP both clinically and histopathologically in enhancement of healing in PrUs in SCI patients. The study concluded significant improvement in ulcer healing both with NS and PRP gel dressing but the advanced wound therapy with use of local applications of PRP seems to be a promising and better alternative to standard saline dressings in PrU healing. The study concluded that PRP releases high concentrate of growth factors to enhance healing of ulcer by promoting of formation of granulation tissue and epithelization in healing phase. Thus PRP gel dressing of ulcer results in better improvement in term of histopathological features of, grading of and size of ulcer as compare to comparison to NS dressing. Hence, we finally concluded that PRP gel dressing is a better alternative to normal saline dressings and also an advanced treatment method for pressure ulcer healing in patients with Spinal cord injury patients.

**LIMITATION:**

There are some limitations inherent with this study. First, there is diversity in the sites and the grade of ulcers in PRP group and NS group, so the healing pattern may be varying, depending on the site and grade of the ulcer. Study duration was short (5 weeks) and the patients were not followed for long follow-up period to observe the sustained effect of PRP gel dressing. Another potential limitation is that we have not undertaken analysis to validate that the composition of PRP did not differ from case to case. Further future research is needed to test the efficacy of PRP in pressure ulcers healing, taking into consideration the methodological limitations of this study.

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**CONFLICT OF INTEREST**

None

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