Clinical Study to Compare the Efficacy of Platelet Rich Plasma versus Conventional Dressing in Chronic Diabetic Non Healing Ulcers

Authors
Dr S.Praveenkumar*1, Dr J.Kabalimurty2, Dr C.Stalinraja3
*1Post Graduate, Department of General Surgery, Rajah Muthiah Medical College, Chidambaram
2Professor and Head, Department of General Surgery, Rajah Muthiah Medical College, Chidambaram
3Associate Professor, Department of General Surgery, Rajah Muthiah Medical College, Chidambaram

Abstract
Diabetic non healing ulcers are a frequent of amputation and represent substantial expenses to fitness care and decrease patient best of existence. The purpose of wound management is to attain wound closure as expeditiously as possible. Apart from these conventional methods to facilitate wound numerous new methods are emerging such as cellular therapies like platelet-rich plasma (PRP). Platelets release certain factors from alpha granules which can be placed in thromboocyte cell membrane which include platelet derived growth factor (PDGF), platelet derived angiogenesis factor, epidermal growth factor (EGF), and platelet factor 4. These elements act regionally on wound and promotes the recovery process. This was a prospective study conducted at Rajah Muthiah Medical College, Chidambaram. Total of forty six patients were assigned. They have been grouped into two by computerized randomization. Patients in control group were treated with traditional dressing and patients in study group have been handled with PLATELET RICH PLASMA (PRP) dressing and observed for decrease in the wound size. This have a look at intends to demonstrate the healing function of autologous platelet rich plasma in healing of chronic non-healing diabetic ulcers.

Keywords: Platelet rich plasma, chronic diabetic non healing ulcers.

Introduction
Chronic wounds are characterised by a long inflammatory period that hinders regenerative wound healing. Chronic wounds, specifically in patients with diabetes mellitus (DM), are a prime fitness venture. Accepted therapeutic objectives and requirements of take care of diabetic foot ulcers encompass wound debridement, pressure comfort within the wound place, suitable wound management, infection management, ischemia control, control of co-morbidity, and surgical management as needed. Apart from these traditional strategies to facilitate wound healing many new methods are emerging consisting of cellular remedies which include platelet-rich plasma (PRP). This could have an important role in a standardized, quality care.
Platelets release growth factors from alpha granules which include platelet derived growth component (PDGF), epidermal growth factor (EGF), platelet derived angiogenesis factor and platelet component 4. These factors act regionally on wound and hasten the wound healing. Platelet extract has been used in lots of studies and has
shown astonishing effects in healing of chronic non healing diabetic ulcers.

**Objective**
- To test the efficacy of autologous platelet rich plasma in chronic non-healing diabetic ulcers in comparison to traditional dressing.

**Subjects and Methods**
Type of have a look at: Prospective, time bound study.
Duration of study: 2 Year
Sampling method: Simple random sampling.

**Inclusion criteria**
1. Age organization of 20 to 65 years with chronic non healing diabetic ulcers.
2. Patients with type 1 or type 2 diabetes
3. Ulcer ≥ three weeks duration.
4. Ulcer ≤ 13 cm² in size.
5. Hb ≥ 11 gm%.

**Exclusion criteria**
1. Screening platelet matter < 100 × 10⁹/l.
2. Patients with known or suspected osteomyelitis.
3. Patients with other comorbid condition.
4. Severe infection (presence of obvious pus or copious wound exudates).
5. Presence of cellulitis, gangrene, insufficient perfusion, ischemia.
6. Patient not accepting the consent.

**Methodology**
Written informed consent was obtained from all patients.
For traditional dressing:
Ulcer was washed with normal saline and saline soaked gauze piece and was placed over the ulcer .then pad and roller bandage was applied.
For platelet rich plasma dressing:
The ulcer was washed with Normal Saline. Platelet rich plasma (PRP) was prepared from patients blood and implemented over the ulcer two times weekly.
The wounds in both the groups were examined. The dressings have been changed as informed before in both control and study groups and presence of healthy granulation tissue was noted. Final area was obtained and statistical evaluation was done.

**Results**
**Table -1 Age Distribution**

| Age in years | Study group | Control Group |
|--------------|-------------|---------------|
|              | No | %  | No | %  |
| <30          | 1  | 4.3| 1  | 4.3|
| 31-40        | 3  | 13.0| 3  | 13.0|
| 41-50        | 7  | 30.4| 8  | 34.8|
| 51-60        | 8  | 34.8| 9  | 39.1|
| 61-70        | 1  | 4.3| 0  | 0.0|
| 71-80        | 3  | 13.0| 2  | 8.7|
| Total        | 23 | 100.0| 23 | 100.0|
| Mean ± SD    | 51.78±12.29| 50.48±11.58|

The mean age in the study group was 51.78 years and in control group was 50.48 years. Samples are age matched with P=0.713
Table - 2 Sex Distribution

| Gender | Study group | Control Group |
|--------|-------------|---------------|
|        | No  | %   | No   | %   |
| Female | 10  | 43.5| 8    | 34.8|
| Male   | 13  | 56.5| 15   | 65.2|
| Total  | 23  | 100.0| 23   | 100.0|

Incidence of chronic lower limb ulcers were more in males in both the groups as compared to females.

Table - 3 Onset

| Onset | Study group | Control Group |
|-------|-------------|---------------|
|       | No  | %   | No   | %   |
| T     | 14  | 60.9| 15   | 65.2|
| S     | 9   | 39.1| 8    | 34.8|
| Total | 23  | 100.0| 23   | 100.0|

In this study, Traumatic ulcers were 60.9 % in study group and 65.2 % in control group and spontaneous ulcers were 39.1% in study group and 34.8 % in control group. It was observed traumatic ulcers were more in both the groups.

Table - 4 Comparison of Initial Area and Final Area

|                  | Study group    | Control Group | P value |
|------------------|----------------|---------------|---------|
| Initial Area(IA) | 1328.57±128.68| 1338.08±131.54| 0.805   |
| Final Area(FA)   | 749.99±99.97  | 1149.84±114.74| <0.001**|
| CA=IA-FA         | 579.03±63.55  | 214.39±148.20 | <0.001**|

Table - 5 Percentage % area reduction in two groups of patients

| % area reduction | Study group | Control Group |
|------------------|-------------|---------------|
|                  | No  | %   | No   | %   |
| <15              | 0   | 0.0 | 17   | 73.9|
| 15-30            | 0   | 0.0 | 6    | 26.1|
| >40              | 23  | 100.0| 0    | 0.0|
| Total            | 23  | 100.0| 23   | 100.0|
| Mean ± SD        | 43.40±3.74| 14.03±3.45   |

Study group (PRP dressing) had better wound contraction of Mean±SD43. 40±3.74 in comparison to control group (conventional dressing), the mean wound contraction was Mean±SD 14.03±3.45. These was observed to be statistically significant P<0.001**, in Student t test.

Discussion

Chronic diabetic non healing ulcers treatment remains difficult in this advanced clinical generation as it relies upon various factors. The idea of wound dressing to prevent the wound from infection and to provide the healthy environment for healing. Diabetic wounds have been treated with various types of dressings.

The study was carried out at Rajah Muthiah Medical College and Hospital. Platelet rich plasma (PRP dressing), it's been used additionally in periodontal, maxillofacial surgical treatment, orthopaedic and trauma management.
Platelet-rich plasma (PRP) is defined as plasma with a platelet level above peripheral blood concentration\(^1,2\). When platelets come into contact with exposed endothelium, various factors are released and act along with chemotaxis, cellular proliferation, angiogenesis, extracellular matrix deposition, and aids in wound healing\(^3\). Hence, increasing platelet concentration in an injured tissue could bring about increased growth factors and, finally, aid in wound healing\(^4\).

PRP also referred to as platelet-enriched plasma, platelet rich concentrate, autologous platelet gel, and platelet releasate\(^5\). Platelet release were used to deal with wounds since 1985.\(^6\) PRP serves as a growth factor agonist\(^4\) and has both mitogenic and chemotactic action\(^7,8,9,10\).

PRP dressing acts as a tissue sealant and drug delivery system\(^11,1\), and platelets initiate healing by releasing various growth factors\(^10,12,13\) via \(\alpha\)-granules degranulation.\(^13\) \(\alpha\)-granules of platelets contains\(^10,13,14,15,16,17\).

Platelet-derived growth factor (PDGF-AA, BB, and AB isomers), Transforming growth factor-\(\beta\) (TGF-\(\beta\)), platelet factor- four (PF-4), Interleukin-1 (IL-1), platelet derived angiogenesis component (PDAF), Vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), Platelet-derived endothelial growth factor (PDGEF), epithelial cell growth factor (ECGF), Insulin like growth factor (IGF), osteonectin (On), vitronectin (Vn), fibronectin (Fn), thrombospondin-1 (TSP-1), fibrinogen (Ff), osteocalcin (Oc).

These factors aids in healing through attracting un-differentiated cells in the newly formed matrix and triggering cellular division\(^14\). PRP may additionally suppress cytokine release and limit inflammation, interacting with macrophages to enhance tissue repair and regeneration\(^18\), increase new capillary growth\(^8,19\). And boost up epithelialization in non healing wounds\(^20\).

No adverse effect or complication has been suggested PRP dressing. In this study we have selected patients with chronic non healing diabetic ulcers and PRP dressing was applied for study group and conventional dressing for control group. Result was compared.

A total of forty six patients was taken in this study. Patients with non healing diabetic ulcers of more than three weeks, randomized into study group or control group based on computerized randomization chart.

The mean age in study group was 51.78 years and in control group was 50.48 years.

In this study it was found that patients receiving Platelet rich plasma dressing had better wound contraction of 43.40% (S.D: 3.74) as compared to control group receiving conventional dressing (normal saline dressing). Mean wound contraction for conventional dressing was 14.03%(S.D: 3.45). These were known to be significant on Student T test (p<zero.001) suggesting that Platelet rich plasma augments ulcer healing in chronic diabetic non healing ulcers.

In this study the suggest time taken for complete healing of the ulcers had been 2.74 weeks in study group (PRP dressing) as compared to 5.22 weeks in the control group (conventional dressing).

Table -6 Weeks for complete healing

| Weeks for complete healing | Study group | Control Group |
|---------------------------|-------------|---------------|
|                           | No | % | No | % |
| 1 week                    | 0  | 0.0 | 0  | 0.0 |
| 2 weeks                   | 6  | 26.1 | 0  | 0.0 |
| 3 weeks                   | 17 | 73.9 | 0  | 0.0 |
| 4 weeks                   | 0  | 0.0 | 1  | 4.3 |
| 5 weeks                   | 0  | 0.0 | 16 | 69.6 |
| 6 weeks                   | 0  | 0.0 | 6  | 26.1 |
| Total                     | 23 | 100.0 | 23 | 100.0 |
| Mean ± SD                 | 2.74±0.45 | 5.22±0.52 |
The mean time taken for complete healing of the ulcers were 2.74 weeks in study group as compared to 5.22 weeks in the control group.

**Graph 1:** Age Distribution

![Age Distribution Graph](image1)

**Graph 2:** Sex distribution

![Sex Distribution Graph](image2)

**Graph 3:** Onset of ulcers

![Onset of Ulcers Graph](image3)
Graph 4: Comparison of Initial Area (IA) and Final Area (FA), CA contracted area

Graph 5: % area reduction in two groups of patients

Graph 6: Weeks for complete healing

Statistical Methods: Descriptive and inferential statistical evaluation has been done within the present look at. Results on continuous measurements are supplied on Mean ± SD (Min-Max) and measurements are provided in Number (%). Significance is classified at 5 % level of significance. The following assumptions on records is made, Assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population need to be...
random. Cases of the samples have to be independent.
Chi-square/ Fisher Exact has been used to
discover the significance of study parameters on
categorical scale between two or greater groups.
Significant figures
+ Suggestive significant (P value: 0.05<P<0.10)
* Moderately significant (P value:0.01<P<0.05)
** Strongly significant (P value: P<0.01)
Statistical software: The Statistical software
namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc
9.0.1, Systat 12.0 and R environment ver.2.11.1
were used for the interpretation of the data and
Microsoft excel and word have been used to
generate graphs, tables etc.
Feasibility of this study:
In the present study we have taken 46 patients
suffering from chronic diabetic non healing
Ulcers (>3 weeks). Patients have been taken
included based on inclusion and exclusion
criteria. Out of forty six patients, 23 were study
group (PRP dressing) and 23 were control group
(conventional dressing). Participants included in
study group have been managed with platelet rich
plasma dressing.
We have implemented the formula to calculate %
reduction in area of ulcer after specific duration in
both study and control group.
Rate of contraction of wound after treatment =
Initial area – final area/ initial area * 100
We have observed 14.03% (S.D; 3.45) contraction
of wounds in control group in comparison to
43.40% (S.D:3.74) contraction of wounds in study
group. Therefore study group have a better
percentage of ulcer contraction compared to the
control group.
On applying student T test p<0.001 is significant.
Hence platelet rich plasma dressing therapy
promotes wound healing in patients with non
healing diabetic ulcers.

Conclusion
The ulcers in subjects managed with platelet
rich plasma dressing contracted more than the
ulcers in conventional dressing group (43.40%
(S.D:3.74)Vs 14.03% (S.D; 3.45); P = < 0.001
Significant) which suggests platelet rich plasma
dressing is an effective management to
promotes wound contraction in patients with
diabetic non healing ulcers.

Summary
The study is conducted on 46 patients to evaluate
the efficacy of platelet rich plasma versus
conventional dressing in chronic diabetic non-
healing ulcers in Rajah Muthiah Medical college
and Hospital between Oct 2015 to Sep 2017.
Patients had been divided into two groups of 23
patients each and detailed history was taken and
required investigations was taken. All the 46
patients have been assessed. We concluded
significant decrease in ulcer size in PRP dressing.
There were no adverse effect seen in both groups.

References
1. Nurden AT, Nurden P, Sanchez M, Andia
I, Anitua E. Platelets and wound healing. Front Biosci. 2008;13:3532-3548.
2. Marx RE. Platelet-rich plasma (PRP): What is PRP and what is not PRP? Implant
Dent. 2001;10(4):225-228.
3. Sclafani AP. Applications of platelet-rich fibrin matrix in facial plastic surgery.
Facial Plast Surg. 2009; 25(4):270-276.
4. Middleton KK, Barro V, Muller B, Terada
S, Fu FH. Evaluation of the effects of platelet-rich plasma (PRP) therapy
involved in the healing of sports-related soft tissue injuries. Iowa Orthop J. 2012;
32:150-163.
5. MehtaS, Watson JT. Platelet rich concentrate: basic science and current
clinical applications. J Orthop Trauma. 2008; 22(6):432-8.
6. Driver VR, HanftJ, Fylling CP, Beriou JM,
Autologel Diabetic Foot Ulcer Study Group. A prospective, randomized,
controlled trial of autologous platelet rich
plasma gel for the treatment of diabetic
foot ulcers. Ostomy Wound Manage. 2006; 52(6):68-70,72,74 passim.
7. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent. 2001;10(4):225-8
8. Millington JT, Norris TW. Effective treatment strategies for diabetic foot wounds. J Fam Pract. 2000; 49 (11Suppl): S40-8.
9. Steed DL, Goslen JB, Holloway GA, Malone JM, Bunt TJ, Webster MW. Randomized prospective double-blind trial in healing chronic diabetic foot ulcers. CT-102 activated platelet supernatant, topical versus placebo. Diabetes Care. 1992;15(11):1598-1604.
10. Everts PA, Brown Mahoney C, Hoffmann JJ, et al. Platelet-rich plasma preparation using three devices: implications for platelet activation and platelet growth factor release. Growth Factors. 2006;24(3):165-71.
11. Eppley BL, Woodell JE, Higgins J. Platelet quantification and growth factor analysis from platelet-rich plasma: implications for wound healing. Plast Reconstr Surg. 2004; 114(6):1502-8.
12. Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic non healing wounds. Successful treatment with autologous platelet-derived wound healing factors (PDWBF). Ann Surg. 1986; 204(3):322-30.
13. Knighton DR, Doucette M, Fiegel VD, Ciresi K, Butler E, Austin L. The use of platelet derived wound healing formula in human clinical trials. Prog Clin Biol Res. 1988;266:319-29.
14. Nikolidakis D, Jansen JA. The biology of platelet-rich plasma and its application in oral surgery: literature review. Tissue Eng Part B Rev. 2008;14(3):249-58.
15. Henderson JL, Cupp CL, Ross EV, et al. The effects of autologous platelet gel on wound healing. Ear Nose Throat J. 2003; 82(8):598-602.
16. Weibrich G, Kleis WK, Kunz-Kostomanolakis M, Loos AH, Wagner W. Correlation of platelet concentration in platelet-rich plasma to the extraction method, age, sex, and platelet count of the donor. Int J Oral Maxillofac Implants. 2001; 16(5): 693-9.
17. Harrison P, Cramer EM. Platelet alpha-granules. Blood Rev. 1993;7(1):52-62.
18. Bhanot S, Alex JC. Current applications of platelet gels in facial plastic surgery. Facial Plast Surg. 2002;18(1):27-33.
19. Mishra A, Woodall J Jr, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. Clin Sports Med. 2009; 28(1):113-25.
20. McAleer JP, Sharma S, Kaplan EM, Persich G. Use of autologous platelet concentrate in a non healing lower extremity wound. Adv Skin Wound Care. 2006; 19(7):354-63.