

## Original Research Article

# Intralesional autologous platelet rich plasma therapy in chronic nonhealing cutaneous ulcers: an interventional study from a tertiary care centre in North Kerala

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### ABSTRACT

**Background:** Treatment of chronic nonhealing cutaneous ulcers is a challenge to clinicians. When wounds fail to achieve sufficient healing after 4 weeks of conventional therapy reassess the underlying pathology and consider advanced therapeutic options. Autologous platelet rich plasma is a novel treatment for nonhealing cutaneous ulcers, which can provide growth factors directly onto the wound.

**Methods:** 34 patients with non-healing cutaneous ulcers satisfying inclusion and exclusion criteria were included in the study. All patients were treated with PRP therapy weekly for 6 weeks. Every week ulcer area and volume was measured and outcome expressed as improvement in area and volume of ulcers before and after PRP therapy.

**Results:** In our study majority were males (64%) and the mean age of population was  $51.0 \pm 10.4$  years. Of 34 patients 18 had venous ulcers. All ulcers healed within 12 weeks and mean duration of healing was  $7.51 \pm 2.9$  weeks. 8 (24.24%) patients had their ulcer completely healed within 6 weeks. Larger ulcers took long duration to heal and smaller ones healed within short duration. The total improvement in area and volume of ulcers was 85.7% and 90.7% (median) respectively at the end of 6 weeks.

**Conclusions:** PRP is an effective, safe, readily available and cheap outpatient procedure which can be widely used for the treatment of chronic recalcitrant ulcers which improves the quality of life and reduces the financial burden of patients. Further research and controlled, randomized prospective clinical trials on larger population are necessary to validate the results.

**Keywords:** Platelet rich plasma, PRP, Non healing ulcers, Growth factors

### INTRODUCTION

An ulcer is a sore on the skin or mucous membrane, accompanied by disintegration of the tissue. It is a defect with loss of the epidermis and at least part of the dermis and even subcutaneous fat.<sup>1</sup> Ulcers always heal with scarring. Consensus has been reached such that a wound may be defined as chronic if it persists for more than 6 weeks and shows no tendency to heal after 3 or more months.<sup>2</sup>

Chronic ulceration of the lower leg, including foot, is a frequent condition, causing pain, social discomfort and generating considerable costs for the patients. These wounds cause severe emotional and physical stress and create a significant financial burden on patients and healthcare system.<sup>3</sup>

Chronic ulcer does not heal in an orderly set of stages and in a predictable amount of time the way the acute wounds do. Chronic wounds seem to be detained in one or more

of the phases of wound healing.<sup>4,5</sup> To overcome that stage and to start the healing process a number of factors need to be addressed such as bacterial burden, necrotic tissue, and moisture balance of the whole wound.<sup>6</sup> In chronic wounds precise balance between production and degradation of molecules such as collagen is lost and degradation plays the major role.<sup>7,8</sup>

Conventional therapies like dressings, surgical debridement and even skin grafting can't provide satisfactory healing of chronic ulcers since they aren't able to provide growth factors that can modulate healing process.<sup>9</sup> Autologous platelet rich plasma (PRP) therapy is a safe, simple, easily available and inexpensive procedure in the treatment of chronic non-healing ulcers and it represents a newer technology that is part of tissue engineering and cellular therapy.

PRP is a concentrate of platelet rich plasma protein derived from whole blood, centrifuged to remove red blood cells. It is a portion of plasma fraction of autologous blood having platelet concentration 5 times above the baseline.<sup>10</sup> Since PRP therapy is an autologous method, it is biocompatible, safe and does not carry the risk of transmissible infections. This procedure can be safely done on patients with co-morbid conditions. PRP has been used to encourage a brisk healing response across several specialties, in particular dentistry, orthopaedics and dermatology.

PRP enhances wound healing since it contains growth factors which are important in modulating mesenchymal cell recruitment, proliferation, and extracellular matrix synthesis during the healing process.<sup>11</sup> Platelet-rich preparations with wound healing potential are defined by a platelet concentration above 1 million per  $\mu$ l.

There are many prospective studies conducted in western countries on the effect of PRP therapy in chronic non-healing ulcers. But there is scarcity of studies from Indian population.

## METHODS

Aim of the study was to assess percentage improvement in area and volume of ulcer(s) and the duration of ulcer(s) healing with PRP therapy. This was an interventional study of 34 consecutive patients with non-healing cutaneous ulcers of various aetiologies attending Department of Dermatology, MES medical college.

### Study period

1<sup>st</sup> January 2016 to 30<sup>th</sup> June 2017.

### Inclusion Criteria

Inclusion criteria were age more than 18 years; sterile ulcers with duration more than 6 weeks and size more

than 2 cm<sup>2</sup>; patients who had received conventional therapies for at least 6 weeks.

### Exclusion criteria

Exclusion criteria were patients with bleeding disorders; patients with uncontrolled sugar levels; patients not giving consent.

### Instruments

- Sociodemographic proforma
- Cotton tip applicator
- Centimeter ruler
- 10 ml syringe
- Rotary centrifuge
- 4 INR tubes (Sodium citrate as anticoagulant)
- 2 plain tubes
- Pipette
- Insulin syringe
- 10% calcium chloride

### Data collection

Patients undergoing PRP therapy and those who satisfy the inclusion and exclusion criteria were selected. After getting informed written consent, socio-demographic data of the patient was collected using a proforma. After general physical examination, ulcer size (length, breadth, width) was measured by the "clock-face" method described by Sussman using cotton tip applicator and centimeter ruler before starting PRP therapy.<sup>12</sup> Autologous platelet rich plasma was prepared by double centrifugation technique under strict aseptic precautions. 10 ml blood was withdrawn from antecubital vein and 2.5 ml transferred to four anticoagulated (sodium citrate) tubes. It was centrifuged at 1800 rpm for 5 minutes and the supernatant plasma is taken and transferred to 2 plain tubes which again centrifuged at 2500 rpm for 5 minutes. Bottom layer in the tube that containing platelet rich plasma is harvested and taken to an insulin syringe containing 10% calcium chloride (0.3 ml for 1 ml PRP). After proper surgical debridement PRP was injected onto the edges of the wound and was covered with a non-absorbent dressing. Patient was then instructed to remove the dressing after 24 hours and to keep the wound clean. This process was repeated weekly for 6 weeks from the department. Every week the wound area and volume was calculated by  $\text{length} \times \text{width} \times 0.7854$  and  $\text{length} \times \text{breadth} \times \text{depth} \times 0.7854$  (formula for an ellipse) respectively.<sup>13</sup> Photographs were taken before each application for 6 weeks, thereafter weekly till ulcers healed.

### Statistical analysis

Data analyzed using Microsoft Excel and Epi info. Outcome of the study is expressed in mean and standard deviation and statistical comparison of ulcer size (in terms of area and volume) before and after PRP therapy

is done using paired 't' test, Friedman's test and chi-square test.

**RESULTS**

34 patients with non-healing cutaneous ulcers of various aetiologies were selected for the study. The results of the study are discussed in the following headings: Demographic characteristics and ulcer characteristics.

**Demographic characteristics**

*Age and gender distribution*

Out of 34 patients, 26 were males (76.5%) and 8 were females (23.5%). Mean age of patients was 51.0±10.4 years. Majority of patients were in the age group of 41-50 years in both males (38.5%) and females (62.5%).

*Comorbidities*

Out of 34 patients 20 patients had diabetes mellitus (58.8%), 18 had varicose veins (52.9%), 9 had systemic hypertension and 2 patients had peripheral occlusive vascular disease.

*Treatment received for ulcer before PRP therapy*

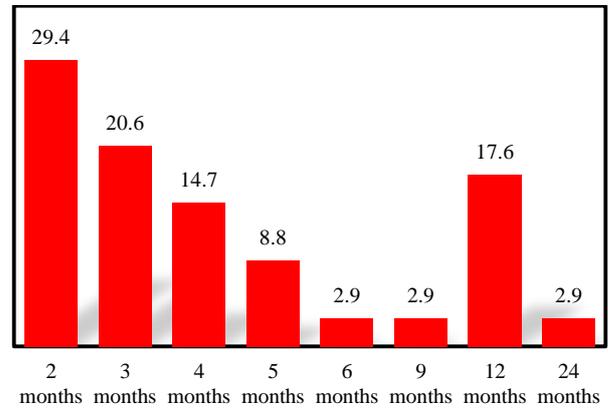
Among the 20 diabetic patients 8 were on insulin and 12 were on oral hypoglycemic agents. Out of 18 venous ulcers, 10 patients had undergone varicose vein surgery. One patient had undergone left femoropopliteal bypass grafting for PVOD. Among the 34 patients, ulcers of 26 patients were treated with conventional dressings alone and 8 were treated with wound debridement and dressings and one patient had received vacuum therapy. Among 26 patients 10 had been doing dressings from home daily and 16 patients from hospital on alternate days.

**Ulcer characteristics**

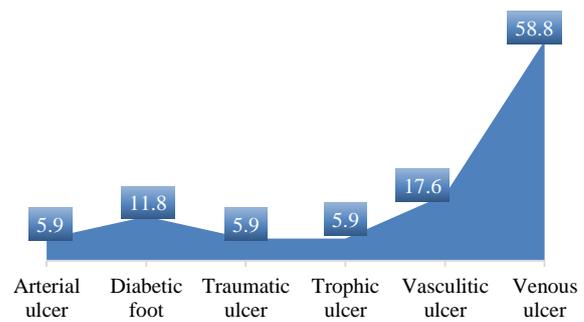
Duration of ulcers among the study population ranged from 2 months to 24 months with a mean duration of 5.5±4.8 months (Figure 1). In all patients ulcers were located in lower limbs with a majority (41.1%) in the medial malleolus followed by shin (17.6%) and big toe (11.8%). Out of 34 ulcers there were 18 (58.8%) venous ulcers, 6 (17.6%) vasculitic ulcers, 4 (11.8%) diabetic foot, 2 (5.9%) each of traumatic, trophic and arterial ulcers (Figure 2).

The ulcer size was examined before the commencement of treatment and thereafter every week. There was a reduction in mean ulcer area from day zero of 27.5±19.3 to 7.3±8.1 cm<sup>2</sup> at 6<sup>th</sup> week of follow-up (Figure 3). There was a reduction in mean ulcer volume from day zero of 28.72±20.38 to 5.47±7.3 cm<sup>3</sup> at 6<sup>th</sup> week of follow-up (Figure 3). Average improvement in the area and volume of ulcers were 85.7% and 90.7% (median) respectively at

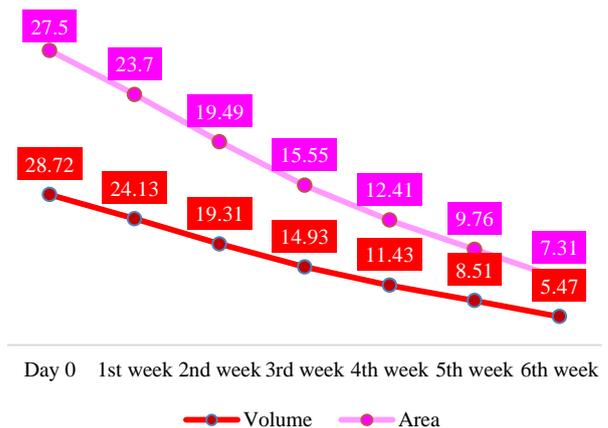
the end of 6 weeks and this improvement is statistically significant (p<0.001) (Friedman test). Area of all ulcers were reduced by >30% (varying from 33% to 100%) within 4 weeks.



**Figure 1: Duration of ulcer.**



**Figure 2: Types of ulcers.**



**Figure 3: Graph showing reduction in area and volume of ulcers after PRP therapy.**

Mean duration of ulcer healing was 7.67±2.314 weeks for 33 patients. One patient was lost follow-up. Majority of the patients 18 (54.55%) had their ulcer healed within 7 to 9 weeks, and 8 ulcers healed within ≤6 weeks and 7 took ≥10 weeks to heal (Table 1).

**Table 1: Duration of healing of ulcers.**

Duration of healing (n=33)	Frequency	Percentage (%)
≤6 weeks	8	24.24
7 to 9 weeks	18	54.55
≥10 weeks	7	21.21
<b>Total</b>	<b>33</b>	<b>100.0</b>

**Table 2: Comparison of duration of healing with duration of ulcers.**

No of ulcers	Duration of healing	Mean ulcer duration
<b>8</b>	≤ 6 weeks	14±9.3 weeks
<b>7</b>	≥ 10 weeks	18.3±13.6 weeks

**Table 3: Comparison of duration of healing of ulcers with baseline ulcer volume.**

No of ulcers	Duration of healing	Baseline ulcer volume
<b>8</b>	≤6 weeks	7.76±8.4 cm <sup>3</sup>
<b>7</b>	≥10 weeks	35.2±21.7 cm <sup>3</sup>

Ulcer duration is an important factor in the final healing process. Those ulcers healed within ≤6 weeks had a mean duration of 14±9.3 weeks and those which took ≥10 weeks for healing were present for a mean duration of 18.3±13.6 weeks (Table 2).

**Table 5: Comparison of duration of healing of ulcers in various studies**

Studies reviewed	Year of study	Number of ulcers	Healing duration (in weeks)
<b>Present study</b>	2017	34	<b>7.67</b>
<b>Knighton et al<sup>14</sup></b>	1986	49	7.5
<b>Suryanarayanan et al<sup>9</sup></b>	2014	33	5.6
<b>Bernuzzi et al<sup>17</sup></b>	2010	17	6.2
<b>Crovetti et al<sup>28</sup></b>	2004	24	4.5
<b>Sakata et al<sup>19</sup></b>	2012	40	4.8
<b>Steenvoorde et al<sup>29</sup></b>	2008	13	4.2

## DISCUSSION

Common causes of chronic non-healing cutaneous ulcers include diabetic foot ulcers, venous leg ulcers, and pressure ulcers. Management of these ulcers consume a great deal of healthcare resources around the globe. There are many modalities of treatment for non-healing ulcers. However, selection of an appropriate therapy is often not evidence based. More evidence for the efficacy of current and future advanced wound therapies is required for their appropriate use.

Advanced treatment options include negative pressure wound therapy (NPWT), hyperbaric oxygen therapy (HBOT), laser application, biological and bioengineered therapies. As an adjunct to standard chronic wound care,

Of the 33 ulcers, those ulcers healed within ≤6 weeks duration had a mean baseline ulcer volume of 7.76±8.4cm<sup>3</sup> and those which took ≥10 weeks for healing had a mean baseline ulcer volume of 35.2±21.7 cm<sup>3</sup> (Table 3).

**Table 4: Comparison of improvement in area and volume with other studies.**

Study	Percentage improvement in area	Percentage improvement in volume
<b>Present study</b>	85.7	90.7%
<b>Suryanarayanan et al<sup>11</sup></b>	91.7±18.4	95±14%

Re-epithelialisation of the wound is an indicator of healing of the wound. Complete re-epithelialisation of the ulcer indicates that the wound has healed totally. How long PRP should be injected weekly in the treatment for non-healing ulcers is not yet defined. Even after the stoppage of weekly injections at 6 weeks, we followed up all the patients for 12 weeks and all ulcers healed completely by 12 weeks and 3 of them took only 3 weeks.

Arbitrarily we classified ulcers into those with good epithelialisation and poor epithelialisation by assessing the improvement in ulcer area by at least 50% at 6 weeks. 88.2% ulcers had good epithelialisation.

NPWT and HBOT very efficiently manages wound drainage and provide granulation tissue, wound area reduction, preparation for delayed closure or grafting, or primary healing.

Concurrent with the explosive growth of NPWT and HBOT for the management of chronic wounds in the last two decades, there has been an enormous amount of research and interest in advanced biological therapies. In this regard, biological therapies refer to tissue-based treatments (acellular and cellular), stem cell therapy, autologous platelet-rich plasma (PRP), as well as recombinant human growth factor therapies.

Platelet rich plasma therapy is a novel method of treatment for non-healing cutaneous ulcers, which

popularized due to its ability to provide growth factors directly onto the wound. First clinical application of PRP in the wounds was done by Knighton et al in 1986.<sup>14</sup> PRP can be applied directly on the base of the ulcer or can give as intralesional injection to the edges and floor of the wound. One of major drawbacks with the use of PRP is the short biological activity after topical application, and thus the need for repetition of the procedure.

Intralesional injection is a recently introduced method for application of PRP and represents an effective therapeutic option when dealing with non-healing wounds. In 2013 it was Dionyssiou et al who introduced intralesional injection of PRP in chronic wounds and demonstrated good clinical outcome in 26 patients.<sup>15</sup> Many studies are available with the direct application of PRP as gel form, but only few comprehensive studies exist with regard to the use of PRP in chronic non-healing ulcers as intralesional injection.

In the present study we demonstrated the outcome of intralesional autologous PRP injection in 34 patients with chronic non-healing cutaneous ulcers of various etiologies of more than 6 weeks duration who did not improve with standard wound care. PRP Injection was given weekly for 6 weeks and patients were followed till the wounds were healed.

Venous insufficiency is the most common cause of chronic non-healing wounds.<sup>16</sup> In our study of 34 patients, 18(58.8%) had venous ulcers which is similar to study by Bernuzzi et al (64.7%) and Suryanarayan et al (57.75%).<sup>9,17</sup>

In a study by Suryanarayanan et al with 33 ulcers treated for 6 weeks percentage improvement in area and volume were 91.7% and 95% respectively and is comparable with our study as shown in the Table 4.<sup>9</sup>

In the present study of 33 patients with a follow up period of 12 weeks we had mean duration of healing as  $7.67 \pm 2.314$  weeks. 49 patients were studied by Knighton et al in 1986 had mean duration of healing as  $7.5 \pm 6.5$  weeks.<sup>14</sup> 17 patients were included in a study by Bernuzzi et al with mean duration of healing 6.2 weeks.<sup>17</sup> Sakata et al conducted study on 40 wounds and had duration of healing as 4.83 weeks (Table 5).<sup>18</sup>

Many studies demonstrated that wounds with longer duration takes more time for healing as compared to wounds with shorter duration, but our study could not find any statistically significant relationship (p value 0.485) between the duration of ulcer and the duration of healing.<sup>19-25</sup>

In our study larger ulcers took longer duration to heal and smaller ones healed within shorter duration. This observation is significant (p value 0.006) and was also noted by Dionyssiou et al, hence we strongly recommend longer duration of PRP therapy in larger wounds.<sup>15</sup>

An accurate function of healing is denoted by percentage improvement, as opposed to absolute change in wound area and it denotes the efficacy of the therapy. The initial rate of healing can be utilized to distinguish between a healing and non-healing ulcer. A reduction in wound area of 30% within 4 weeks of treatment is a suitable predictor of healing and reflector of treatment efficacy.<sup>12,26</sup> It is recommended to discontinue the therapy if ulcer area is not reduced by 30% within 4 weeks.

#### ***Comparison of efficacy between PRP in gel form and as intralesional injection in chronic nonhealing ulcers***

PRP can be applied directly onto the wound either in the form of a gel or as intralesional injection to wound edges or wound bed. There are no studies comparing the effects of both methods. A gel formulation is easy to use but has certain disadvantages such as uneven distribution at movable body parts, possible loss, limited accessibility to the wound surface, limited duration of effect and high costs.



**Figure 4: Diabetic ulcer of 3 months duration after 6 sittings of PRP therapy and near total healing at 8<sup>th</sup> week: (A) Day 0; (B) 4th week; (C) 6th week; (D) 8th week.**

In study by Suryanarayanan et al where PRP gel was used weekly for 6 weeks percentage improvement in area was 91.7% and is comparable with our study in which intralesional injection is used (Table 4). Hence PRP as intralesional injection is a better option than platelet gel for non-healing ulcers in terms of efficacy and economic feasibility.

Photographs of the ulcers before and after PRP therapy are shown in Figures 4 and 5.



**Figure 5: Vasculitic ulcer of 2 months duration after 6 sittings of PRP therapy which completely healed at 8th week: (A) Day 0; (B) 3rd week; (C) 6th week; (D) 8th week.**

#### Limitations of the study

Transient pain during injection is the only side effect observed in our study. Because of small sample size and short duration of follow up, these results cannot be extrapolated to the community. While carrying out studies on treatment of chronic cutaneous ulcers, factors like aetiology of ulcers, ulcer durations, ulcer sizes and co morbidities which influence wound healing make randomization difficult. Standard operating procedure for PRP therapy should be developed using large randomized control trials in terms of method of PRP preparation, quantity of PRP to be injected and duration of injections.

#### CONCLUSION

Basic tenets of wound care are thorough assessment with medical and nutritional optimization, debridement, compression, management of ischemia, management of infection, and appropriate wound bed preparation. When the above principles are followed along with use of standard wound care guidelines most wounds will show a satisfactory healing response.

Non-healing cutaneous ulcers which do not heal within 4 weeks with conventional treatments may require advanced wound care therapies. Most of the advanced therapies require hospitalization and use of sophisticated equipments consuming time and resources, an alternative to this is PRP therapy.

Autologous PRP as weekly injections for 6 weeks is an effective therapy with significant reduction in the area and volume of the ulcer compared to the pretreatment

levels ( $p < 0.005$ ) and is comparable with the advanced modes of treatment. Larger ulcers take longer duration for healing, hence requires prolonged treatment for complete reepithelialisation. PRP is an effective, safe, readily available and cheap outpatient procedure for the treatment of chronic recalcitrant ulcers which improves the quality of life of patients and reduces their financial burden. Further research and controlled, randomized prospective clinical trials on larger population are necessary to validate the results.

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*Ethical approval: The study was approved by the institutional ethics committee*

#### REFERENCES

1. Kumar V, Abbas AK, Fausto N, Aster JC. Kumar: Robbins and Cotran Pathologic Basis of Disease, Professional Edition. 8th ed. 2009: 1464.
2. Schreml S, Szeimies R-M, Prantl L, Landthaler M, Babilas P. Wound healing in the 21st century. J Am Acad Dermatol. 2010;63(5):866–81.
3. Augustin M, Maier K. Psychosomatic Aspects of Chronic Wounds. Dermatology Psychosom/ Dermatologie und Psychosom. 2003;4(1):5–13.
4. Snyder RJ. Treatment of nonhealing ulcers with allografts. Clin Dermatol. 2005;23:388–95.
5. Taylor JE, Laity PR, Hicks J, Wong SS, Norris K, Khunkamchoo P, et al. Extent of iron pick-up in deferoxamine-coupled polyurethane materials for therapy of chronic wounds. Biomaterials. 2005;26(30):6024–33.
6. Gist S, Tio-Matos I, Falzgraf S, Cameron S, Beebe M. Wound care in the geriatric client. Clin Interventions Aging. 2009;4:269–87.
7. Edwards JV, Howley P, Cohen IK. In vitro inhibition of human neutrophil elastase by oleic acid albumin formulations from derivatized cotton wound dressings. Int J Pharm. 2004;284(1–2):1–12.
8. Schönfelder U, Abel M, Wiegand C, Klemm D, Elsner P, Hipler UC. Influence of selected wound dressings on PMN elastase in chronic wound fluid and their antioxidative potential in vitro. Biomaterials. 2005;26(33):6664–73.
9. Suryanarayan S, Budamakuntala L, Sarvajnamurthy S. Efficacy of autologous platelet-rich plasma in the treatment of chronic nonhealing leg ulcers. J Plastic Aesthetic Res. 2014;1(2):65–9.
10. Lacci KM, Dardik A. Platelet-rich plasma: support for its use in wound healing. Yale J Biol Med. 2010;83(1):1–9.
11. Bhanot S, Alex JC. Current Applications of Platelet Gels in Facial Plastic Surgery. Facial Plast Surg. 2002;18(1):27–34.
12. Arnold T, Stanley J, Fellowes EP, Moncada GA, Allen R, Hutchinson JJ, et al. Prospective, multicenter study of managing lower extremity venous ulcers. Ann Vasc Surg. 1994;8(4):356–62.

13. Blume PA, Walters J, Payne W, Ayala J, Lantis J. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. *Diabetes Care*. 2008;31:631-6.
14. Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic nonhealing wounds. Successful treatment with autologous platelet-derived wound healing factors (PDWHF). *Ann Surg*. 1986;204:322-30.
15. Dionyssiou D, Demiri E, Foroglou P, Cheva A, Saratzis N, Aivazidis C, et al. The effectiveness of intralesional injection of platelet-rich plasma in accelerating the healing of chronic ulcers. An experimental and clinical study. *Int Wound J*. 2013;10(4):397-406.
16. Kumar SA, Binitha MP, Sarita S. A clinical and aetiological study of chronic leg ulcers. *IJCMR*. 2016;3(12):3438-40.
17. Bernuzzi G, Tardito S, Bussolati O, Adorni D, Cantarelli S, Fagnoni F, et al. Platelet gel in the treatment of cutaneous ulcers: The experience of the Immunohaematology and Transfusion Centre of Parma. *Blood Transfus*. 2010;8(4):237-47.
18. Sakata JI, Sasaki S, Handa K, Uchino T, Sasaki T, Higashita R, et al. A retrospective, longitudinal study to evaluate healing lower extremity wounds in patients with diabetes mellitus and ischemia using standard protocols of care and platelet-rich plasma gel in a Japanese wound care program. *Ostomy Wound Manag*. 2012;58(4):36-49.
19. Jones JE, Nelson EA. Skin grafting for venous leg ulcers. Update in *Cochrane Database Syst Rev*. 2013;1:CD001737;23440784.
20. Wiechula R. The use of moist wound-healing dressings in the management of split-thickness skin graft donor sites: a systematic review. *Int J Nurs Pract*. 2003;9(2):9-17.
21. Fu X, Li X, Cheng B, Chen W, Sheng Z. Engineered growth factors and cutaneous wound healing: Success and possible questions in the past 10 years. *Wound Repair Regeneration*. 2005;13:122-30.
22. Hong JP, Kim YW, Jung HD, Jung K II. The effect of various concentrations of human recombinant epidermal growth factor on split-thickness skin wounds. *Int Wound J*. 2006;3(2):123-30.
23. Nanney LB, Paulsen S, Davidson MK, Cardwell NL, Whitsitt JS, Davidson JM. Boosting epidermal growth factor receptor expression by gene gun transfection stimulates epidermal growth in vivo. *Wound Repair Regen*. 2000;8(2):117-27.
24. Jones V, Grey J, Harding K. ABC of wound healing: Wound dressings. *Br Med J*. 2006;332:777-80.
25. Cutting KF. Wound dressings: 21st century performance requirements. *J Wound Care*. 2010;19(1):4-9.
26. Van Rijswijk L. Full thickness leg ulcers: Patient demographics and predictors of healing. Multi-center Leg ulcer study Group. *J Fam Pract*. 1993;36(6):625-32.
27. Crovetti G, Martinelli G, Issi M, Barone M, Guizzardi M, Campanati B, et al. Platelet gel for healing cutaneous chronic wounds. *Transfus Apher Sci*. 2004;30(2):145-51.
28. Steenvoorde P, van Doorn LP, Naves C, Oskam J. Use of autologous platelet-rich fibrin on hard-to-heal wounds. *J Wound Care*. 2008;17(2):60-3.

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