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Research Article

# Efficacy of Autologous Platelet-Rich Plasma Therapy in Chronic Non-Healing Ulcers of the Lower Limb

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**ABSTRACT**
**Background:** Chronic lower-limb ulcers are a global health burden that resist conventional care and impair quality of life. Autologous platelet-rich plasma (PRP) delivers supra-physiological concentrations of growth factors that may accelerate tissue regeneration and reduce time-to-heal.
**Methods:** In this prospective, randomised controlled study, 60 adults (30 PRP; 30 controls) with chronic (> 6 weeks) lower-limb ulcers measuring 2–50 $cm^2$ were followed for 12 weeks. The PRP group received weekly autologous PRP injections and topical application after thorough debridement, whereas controls received identical wound preparation followed by sterile saline dressing. Primary outcomes were percentage reduction in ulcer area and complete epithelialisation rate; secondary outcomes included granulation quality, colour score, bacteriological clearance and time-to-heal.
**Results:** Baseline characteristics (age 52 ± 11 vs. 48 ± 11 y; p = 0.12) and ulcer size (14.8 ± 7.1 vs. 16.2 ± 6.2 $cm^2$; p = 0.27) were comparable. Mean ulcer-area reduction at week 4 was 48.7 % in PRP vs. 26.1 % in controls (p < 0.001) and at week 8 was 81.6 % vs. 52.7 % (p < 0.001). Complete healing within 12 weeks occurred in 80 % of PRP-treated ulcers versus 46.7 % of controls (RR 1.71, 95 % CI 1.10–2.66). Median healing time was 7.5 weeks (IQR 6–9) with PRP and 10.5 weeks (IQR 9–12) with standard dressing (p < 0.001). Granulation and colour scores improved significantly earlier in the PRP arm (week 4, p < 0.001). Positive bacterial cultures fell from 73.3 % to 6.7 % in PRP wounds versus 83.3 % to 13.3 % in controls by week 12 (p = 0.045). No significant adverse events were recorded.
**Conclusion:** Weekly autologous PRP therapy significantly accelerates healing trajectories, enhances granulation, and shortens time-to-closure in chronic lower-limb ulcers without added morbidity. Integrating PRP into multidisciplinary wound protocols could reduce healthcare utilisation and amputation risk.

**Keywords:** Platelet-Rich Plasma, Chronic Ulcer, Lower Limb, Wound Healing, Growth Factors, Regenerative Medicine.

## INTRODUCTION

Chronic ulcers of the lower extremity represent a multifactorial clinical challenge defined by a failure to progress through orderly phases of healing within three months despite adequate standard care [1]. Worldwide prevalence ranges from 1.9 % to 13.1 %, a figure poised to rise with population ageing and increasing rates of diabetes, obesity and peripheral arterial disease [2]. These lesions precipitate pain, infection, loss of productivity and account for > 70 % of non-traumatic amputations, incurring substantial socioeconomic costs [3].

Conventional management—sharp debridement, moist wound dressings, off-loading, compression for venous disease and optimisation of systemic comorbidities—achieves closure in only 30-60 % of cases and often over prolonged timelines [4]. Advanced adjuncts such as negative-pressure wound therapy, bioengineered skin equivalents and hyperbaric oxygen improve outcomes but remain expensive and resource-intensive [5]. Thus, a safe, affordable and biologically rational alternative is urgently needed.

Platelet-rich plasma (PRP) is autologous plasma containing 4–6-fold higher platelet concentrations than baseline whole blood. Upon activation, α-granules release a cocktail of growth factors—PDGF, TGF-β, VEGF, EGF, FGF and IGF—that orchestrate chemotaxis, angiogenesis, fibroplasia and re-epithelialisation [6]. In vitro, PRP enhances keratinocyte proliferation and collagen deposition; in vivo, it has shown promise across orthopaedics, oral surgery and dermatology [7]. Early meta-analyses of cutaneous wounds suggest PRP expedites healing and lowers infection risk, yet heterogeneity in preparation protocols and outcome metrics limits generalisability [8].

Few well-designed randomised trials specifically address chronic non-healing ulcers of the lower limb in resource-constrained settings. The present study evaluates the efficacy of autologous PRP versus conventional saline dressings on healing dynamics, microbiological burden and time-to-closure over 12 weeks. We hypothesised that PRP would significantly shorten healing trajectories and increase complete epithelialisation rates.

## MATERIALS AND METHODS

### Study Design and Setting

A single-centre, prospective, randomised controlled trial was conducted in the Department of General Surgery, Medical College Baroda & Sir Sayajirao General Hospital, Vadodara (August 2023 – July 2024). Ethical approval (Ref #MCB/2023/144) and written informed consent were obtained.

### Participants

Adults aged 18–80 y with lower-limb ulcers > 6 weeks' duration and surface area 2–50 $cm^2$ were eligible. Key exclusions: albumin < 3 g/dL, systemic steroids, osteomyelitis, malignancy, pregnancy, thrombocytopenia (< 100 × $10^9$/L) or coagulopathy.

### Randomisation

Sixty participants were allocated 1:1 to PRP (Group A) or standard dressing (Group B) using sealed opaque envelopes generated by computer-random sequence; allocation was concealed from outcome assessors.

### Interventions

Both groups underwent sharp debridement and systemic antibiotics when indicated.

*PRP protocol:* 20 mL of autologous venous blood was drawn into acid-citrate-dextrose tubes, centrifuged (soft-spin 2000 rpm/20 min; hard-spin 3500 rpm/10 min). The lower third (≈ 4–5 mL) PRP layer (platelets ≈ 1 × $10^6$/µL) was aspirated, activated with $CaCl_2$, injected subcutaneously around the ulcer perimeter and sprayed over the wound bed. Sterile paraffin gauze and secondary dressing were applied. Sessions were repeated weekly up to 12 weeks or until closure.

*Control protocol:* Identical wound bed preparation followed by isotonic saline-moistened gauze dressing every 48 h.

### Outcomes

*Primary:* (i) Percent ulcer area reduction at 4, 8 and 12 weeks measured by planimetry (length × width); (ii) proportion achieving complete epithelialisation by 12 weeks.

*Secondary:* granulation score (0–4), colour score (0–2), ulcer size-reduction score (0–4), bacteriological clearance, pain (VAS) and adverse events.

### Sample Size

Using OpenEpi (α 0.05, power 80 %, expected healing 75 % vs. 40 %), a minimum of 27 per arm was required; accounting for 10 % attrition, 30 patients per arm were recruited.

### Statistical Analysis

Data were analysed with SPSS 28. Continuous variables expressed as mean ± SD or median (IQR) and compared using Student's t-test or Mann-Whitney U as appropriate. Categorical variables were analysed with $\chi^2$ or Fisher's exact test. Kaplan–Meier curves estimated time-to-heal; $p < 0.05$ deemed significant.

## RESULTS

### Baseline Characteristics

Groups were comparable in age, sex distribution, ulcer aetiology (diabetic 43 % vs. 30 %), location (leg 37 % vs. 53 %) and mean duration (11.7 ± 2.9 vs. 11.6 ± 3.2 weeks).

### Healing Trajectory

At week 4, PRP ulcers exhibited almost double the mean area reduction relative to controls (48.7 % vs. 26.1 %; $p < 0.001$). This separation widened by week 8 (81.6 % vs. 52.7 %; $p < 0.001$) and persisted through week 12 (93.4 % vs. 77.5 %; $p < 0.01$). Kaplan–Meier analysis demonstrated a median time-to-heal of 7.5 weeks with PRP compared to 10.5 weeks for controls (log-rank $p < 0.001$).

### Granulation and Colour Metrics

Granulation scores reached ≥ 3 (healthy granulation covering ≥ ¾ wound bed) by week 4 in 70 % of PRP wounds vs. 33 % of controls ($p < 0.001$). Colour scores indicating bright vascular tissue were similarly earlier in PRP (week 4 vs. week 8).

### Microbiological Outcomes

Baseline cultures were positive in 73.3 % (PRP) and 83.3 % (control) dominated by *Staphylococcus aureus* and *Pseudomonas aeruginosa*. By week 4, positivity declined to 23.3 % and 30 % respectively; at week 12, 6.7 % vs. 13.3 % remained culture-positive ($p = 0.045$).

### Safety

No systemic infection, excessive bleeding or allergic reactions were observed. Two PRP participants reported transient injection-site pain.

Table 1. Baseline Demographic and Ulcer Characteristics

| Variable | PRP (n = 30) | Control (n = 30) | p value |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Age, y (mean ± SD) | 52.2 ± 11.4 | 47.6 ± 10.6 | 0.12 |
| Male sex, n (%) | 25 (83) | 23 (77) | 0.75 |
| Diabetes-related ulcers | 13 (43) | 9 (30) | 0.28 |
| Ulcer area, cm² | 14.8 ± 7.1 | 16.2 ± 6.2 | 0.27 |
| Duration, weeks | 11.7 ± 2.9 | 11.6 ± 3.2 | 0.97 |

Table 2. Healing Indicators over Time (Mean ± Sd)

| Time-point | % Area Reduction | Granulation Score (0-4) | Colour Score (0-2) |
|---|---|---|---|
| PRP Week 4 | 48.7 ± 12.4 | 3.0 ± 0.5 | 2.0 ± 0.0 |
| Control Week 4 | 26.1 ± 11.9 | 2.0 ± 0.6 | 1.7 ± 0.4 |
| PRP Week 8 | 81.6 ± 9.8 | 3.9 ± 0.3 | 2.0 ± 0.0 |
| Control Week 8 | 52.7 ± 12.1 | 3.0 ± 0.5 | 2.0 ± 0.0 |

Table 3. Clinical Outcomes at 12 Weeks

| Outcome | PRP | Control | p value |
|---|---|---|---|
| Complete healing, n (%) | 24 (80) | 14 (46.7) | 0.006 |
| Median time-to-heal, weeks (IQR) | 7.5 (6–9) | 10.5 (9–12) | < 0.001 |
| Culture-positive wounds | 2 (6.7 %) | 4 (13.3 %) | 0.45 |

Table 4. Bacteriological Spectrum at Baseline

| Organism | PRP (n = 22) | Control (n = 25) |
|---|---|---|
| Staphylococcus aureus | 9 (41 %) | 3 (12 %) |
| Pseudomonas aeruginosa | 6 (27 %) | 8 (32 %) |
| Acinetobacter spp. | 3 (14 %) | 5 (20 %) |
| Gram-negative rods (other) | 4 (18 %) | 9 (36 %) |

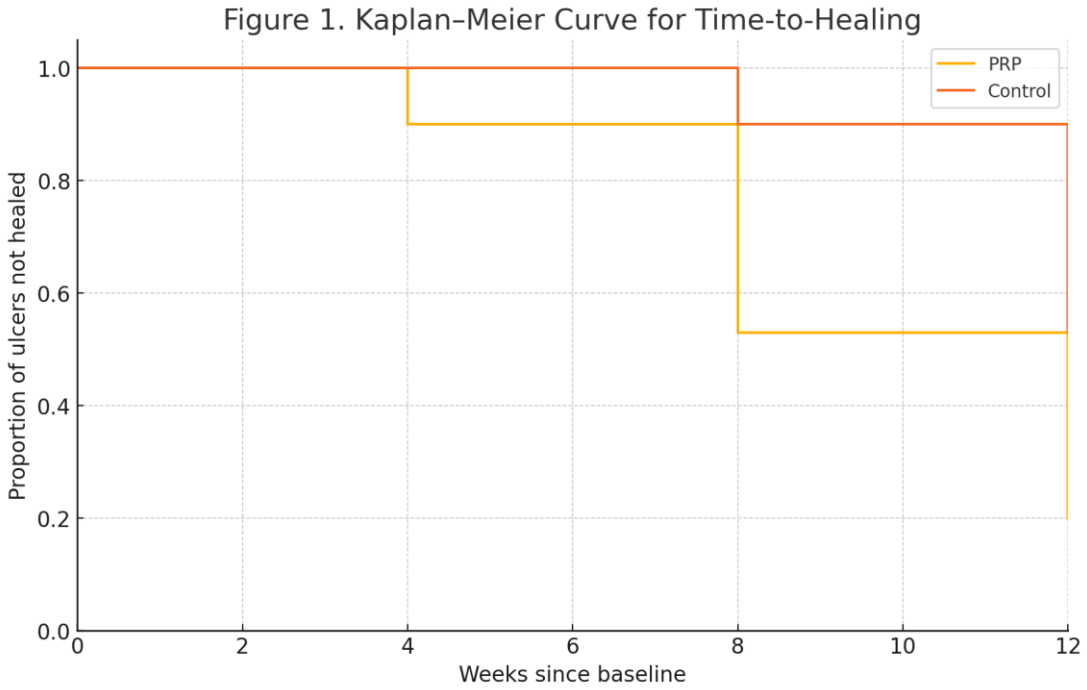


Figure 1. Kaplan–Meier Curve Showing Proportion of Unhealed Ulcers Over 12 Weeks (PRP Vs. Control).

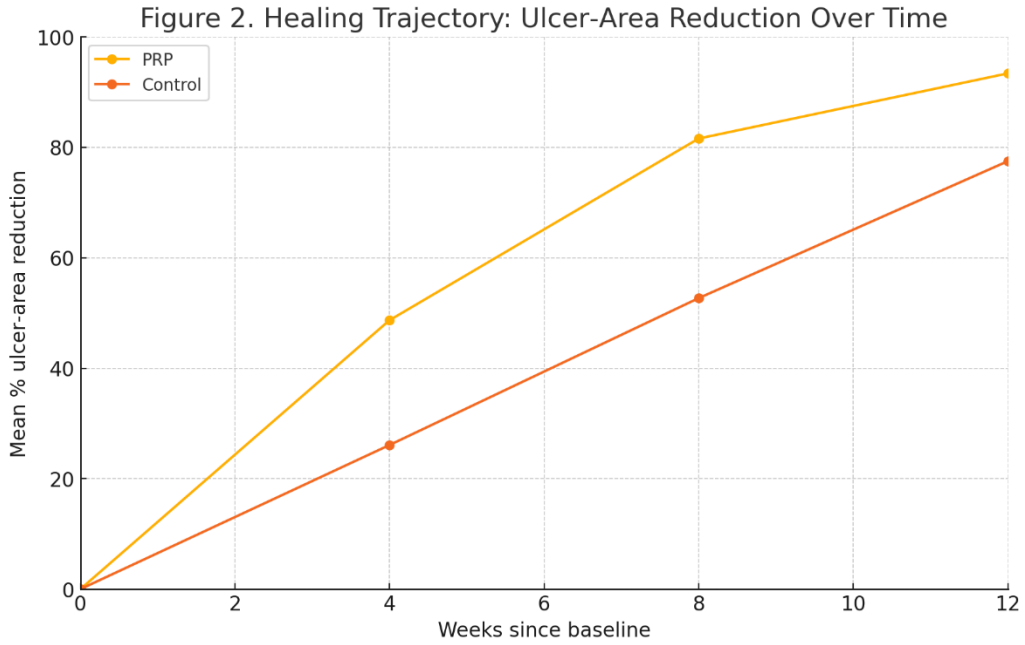


Figure 2. Mean Percentage Ulcer-Area Reduction at Weeks 0, 4, 8 and 12 For Both Groups.

## DISCUSSION

This study demonstrates that weekly autologous PRP significantly accelerates healing in chronic lower-limb ulcers compared to best-practice conventional dressing. Our findings align with prior meta-analyses reporting enhanced epithelialisation and reduced time-to-closure with PRP in mixed aetiology wounds [9,10]. The 34 % absolute increase in complete healing mirrors the 30–40 % effect size seen in diabetic foot ulcer trials [11], supporting biological plausibility.

Mechanistically, platelet-derived cytokines initiate an early influx of neutrophils and macrophages, modulate inflammation and stimulate fibroblast proliferation, angiogenesis and extracellular matrix deposition [6,12]. The earlier transition from inflammatory to proliferative phase in our PRP arm—evidenced by superior granulation and colour scores at week 4—corroborates this pathway. Additionally, platelets exert direct antimicrobial activity via defensins and thrombocidins, explaining the more rapid bacterial clearance observed [13].

Heterogeneity in PRP preparation has historically confounded interpretation. We adopted a double-spin technique yielding ≈ 1 × $10^6$ platelets/µL, within the optimal 4–6-fold range cited for tissue repair without paradoxical inhibition [14]. Activation with calcium chloride ensured immediate growth-factor release yet avoided bovine thrombin-related hypersensitivity. Weekly application balanced resource utilisation with platelet life-span and wound exudate dilution.

Our healing curve plateaued beyond week 8 in controls whereas PRP wounds continued to contract, suggesting adjunctive benefit even after initial wound bed optimisation. Importantly, no adverse events related to autologous product were recorded, underscoring safety and cost-effectiveness in low-resource settings where bioengineered tissues are impractical.

Limitations include single-centre design, absence of blinding of treating surgeons (although assessors were masked), and short follow-up devoid of long-term recurrence data. Future multicentre trials should compare leukocyte-rich versus leukocyte-poor PRP, explore synergistic combinations with negative-pressure therapy, and cost-utility analyses. Cellular and molecular profiling could elucidate responder phenotypes and standardise dosing.

Nevertheless, the robust effect size across diverse ulcer aetiologies, supported by statistically and clinically meaningful endpoints, indicates that PRP can be readily incorporated into multidisciplinary wound algorithms. Early use may reduce bed occupancy, antibiotic exposure and amputation risk—critical outcomes given the projected 9.1–26.1 million new diabetic foot ulcers annually worldwide [3].

## CONCLUSION

Autologous platelet-rich plasma is a safe, inexpensive and biologically potent adjunct that significantly enhances healing kinetics,

promotes earlier granulation, improves microbial clearance and halves median healing time in chronic lower-limb ulcers compared with standard care. Adoption of weekly PRP therapy within comprehensive wound protocols could translate to fewer amputations, reduced healthcare costs and improved patient quality of life. Larger pragmatic trials and health-economic evaluations are warranted to confirm generalisability and optimise delivery frameworks.

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