

Meta-Analysis on the Efficacy and Safety of Platelet-Derived Growth Factor in Diabetic Foot Wound Healing

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Abstract: Background: Diabetic foot ulcers (DFUs) are a major complication of diabetes mellitus, posing significant challenges to wound healing and increasing the risk of lower limb amputations. Platelet-derived growth factor (PDGF) has shown potential as a therapeutic agent for DFUs due to its role in promoting cellular proliferation, angiogenesis, and tissue repair. However, the efficacy and safety of PDGF remain controversial, with mixed results from randomized controlled trials (RCTs).

Objective: This meta-analysis aims to evaluate the efficacy and safety of recombinant human platelet-derived growth factor (rhPDGF) in the treatment of DFUs, focusing on clinical outcomes such as healing rates, recurrence rates, healing time, and adverse event (AE) rates.

Methods: A systematic literature review was conducted across six databases (PubMed, Embase, Cochrane Library, Web of Science, CNKI, and WeiPu) to identify RCTs evaluating rhPDGF in DFU treatment. Inclusion criteria adhered to the PICOS framework. Data extraction and quality assessment were performed independently by two researchers. Meta-analysis was conducted using R software, with heterogeneity assessed via the I^2 statistic. Subgroup, sensitivity, and publication bias analyses were also performed.

Results: A total of 12 RCTs, involving 26,469 participants, were included. The meta-analysis demonstrated that rhPDGF significantly improved healing rates compared to control interventions (OR = 1.76, 95% CI: 1.37–2.27, $P < 0.01$). Subgroup analysis revealed that the 100 $\mu\text{g/g}$ rhPDGF concentration was more effective than 30 $\mu\text{g/g}$. No significant differences were found in recurrence rates (OR = 0.65, 95% CI: 0.36–1.17, $P = 0.15$), healing time (SMD = -0.46, 95% CI: -1.16–0.23, $P = 0.19$), or adverse event rates (OR = 0.84, 95% CI: 0.61–1.17, $P = 0.30$). Sensitivity analysis confirmed the stability of the results, and no publication bias was detected.

Conclusions: This meta-analysis provides robust evidence that rhPDGF, particularly at a concentration of 100 $\mu\text{g/g}$.

Introduction

Diabetic foot ulcers (DFU) are a serious health concern, with an estimated

prevalence of 2.1% to 12.4% in diabetic patients in India alone (Khandelwal et al., 2013). Diabetic foot complications globally are responsible for 40% to 90% of lower limb amputations, an indication of the necessity for effective management (Steed, 2006). The pathogenesis of DFU is multifactorial, most frequently the result of peripheral neuropathy, ischemia due to peripheral arterial disease (PAD), and impaired immune response (Khandelwal et al., 2013). Neuropathy causes insensitivity, with resultant insidious trauma, and ischemia compromises oxygenation, with impaired healing. Hyperglycemia hastens this process by inhibiting the function of leukocytes and sensitizing the patient to infection (Wieman et al., 1998, Paggiaro, et al., 2018).

Standard treatment for DFUs consists of infection management, debridement, offloading of the affected limb, and revascularization if there is ischemia. A large proportion of DFUs, despite these, fail to heal within a reasonable period, and adjuvant therapies like growth factors, bioengineered tissue substitutes, and hyperbaric oxygen have had to be tried (Steed et al., 1995; Margolis et al., 2005; Lavery et al., 2014). Of these, PDGF has received considerable attention for enhancing the process of wound healing.

PDGF is a growth factor that naturally occurs and plays a significant part in the cascade of wound healing by promoting fibroblast proliferation, inducing angiogenesis, and augmenting extracellular matrix deposition (Steed, 2006; Zelen et al., 2015). PDGF is a mitogen and chemoattractant for fibroblasts and smooth muscle cells that aids in the healing and regeneration of tissues (Steed et al., 1995; Abdo, 2016). Recombinant human PDGF-BB (rhPDGF-BB), which is marketed as Regranex (becaplermin), has been well researched in terms of its role in augmenting the healing of DFU as an adjunct to good wound care.

Multiple clinical trials have established that PDGF significantly increases the rate of complete wound closure and reduces healing time. In a seminal multicenter, randomized, placebo-controlled trial of 922 patients, PDGF treatment resulted in a 50% complete healing rate compared to 36% for placebo ($p = 0.007$) (Steed, 2006). PDGF also reduced the median time to complete healing by 30% (14 weeks vs. 20 weeks, $p < 0.01$), demonstrating that it can accelerate wound healing (Steed et al., 1995). Wieman et al. (1998) demonstrated in another study that PDGF treatment increased wound closure rates by 43% as compared to placebo.

PDGF has also been likened to other newer modalities of wound healing, including hyperbaric oxygen therapy (HBOT), antiseptic dressings, and dehydrated amniotic membrane dressings. Khandelwal et al. (2013) likened the effectiveness of antiseptic dressings, HBOT therapy, and PDGF in 60 patients with grade III and IV DFUs. While both HBOT therapy and PDGF were extremely effective in wound healing, PDGF was more cost-effective, easier to apply, and had fewer side effects. The authors believed that PDGF needs to be promoted for the healing of patients with chronic DFUs, particularly those who had not responded to standard therapy after 8 weeks.

Similarly, Tofigh and Tajik (2022) compared PDGF with dehydrated amniotic membrane dressings, indicating that while both treatments sped up healing considerably, amniotic membrane dressings were more effective in achieving faster wound closure. However, PDGF was a suitable alternative, especially where availability and affordability are taken into consideration.

Despite its established benefits, PDGF therapy is not without problems. A meta-analysis of clinical trials raised doubts as to whether it could be linked to an increased risk of malignancy when used in large quantities over extended periods (Steed, 2006; Rangaswamy, Rubby & Prasanth, 2016). Subsequent research has not, however, found an association between PDGF and cancer risk, and the FDA continues to approve its use for DFUs with caution. Side effects most frequently reported in clinical trials include mild erythema, localized irritation, and transient pain at the application site (Wieman et al., 1998; Raghav et al., 2018).

With the inconsistency in reported outcomes between different clinical trials and the need for a collective evaluation of PDGF therapy, a meta-analysis is warranted. Although previous evaluations had been trial-based, a pooled analysis can provide more conclusive evidence on the overall effectiveness and safety of PDGF in the healing of DFU. The goal of this meta-analysis is to pool data from a number of studies to ascertain the size of PDGF benefit, compare its efficacy with other advanced wound care treatments, and evaluate its safety profile in general.

1. Materials and Methods

1.1 Search Strategy

In this study, we conducted a comprehensive literature search of several databases, including PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), and the WeiPu database. The literature search was conducted for records from the inception date of each database to December 2024 to include all the research on the application of PDGF in diabetic foot ulcer healing, and its efficacy and safety.

The search used a combination of controlled terms (subject headings) and free-text terms. The primary search terms utilized were: “platelet derived growth factor”, “recombinant human platelet derived growth factor”, “PDGF”, “rh-PDGF”, “diabetic foot”, “DFU”, and “diabetic ulcers”. This was done with the purpose of developing a sensitive search strategy with maximum recall of the studies of interest.

1.2 Inclusion and Exclusion Criteria

The selection of studies was based on the PICOS framework for methodological quality. Inclusion criteria: Participants (P): Studies involving patients with DFU. Intervention (I): The experimental group received PDGF with no restrictions for treatment duration and dose. Control (C): The control group received

either placebo treatment or standard wound dressings. Outcomes (O): Primary outcomes: Healing rate. Secondary outcomes: Recurrence rate, healing time, and adverse events (AEs) rate (AEs rate). Study Design (S): Randomized controlled trials (RCTs).

Research that met any of the subsequent exclusion criteria was not considered: (1) Non-randomized controlled trials (non-RCTs), review articles, conference presentations, case studies, and previous meta-analyses. (2) Publications not written in either Chinese or English. (3) Research lacking pertinent outcome measures, having incomplete datasets, or whose full texts were unavailable. (4) Instances of repeated publications.

These criteria for inclusion and exclusion were defined to ensure consistency and high-quality evidence among the selected studies.

1.3 Literature Screening and Data Extraction

We conducted the literature review with the help of two separate researchers. At first, papers that did not meet the inclusion criteria were removed from consideration based on their titles and abstracts. After that, we checked the admissibility of studies by reading their whole texts. We discussed it or brought in a third expert to help us settle any disputes. Both researchers used a standardized form to collect data separately. Important information about each study was recorded on this form, including the names of the authors, the year of publication, the interventions given to the control and experimental groups, the age and gender of the participants, the size of the sample, and the length of treatment. It also included both primary and secondary outcome results. Attempts were made to contact the original authors to retrieve missing data.

1.4 Quality Assessment of Included Studies

Methodological quality of included studies was ascertained through the use of the Cochrane Risk of Bias Tool (ROB1), following the criteria set out in version 5.1.0 of the Cochrane Handbook for Systematic Reviews of Interventions. Multiple important areas were evaluated, including: generating a random sequence; concealing allocations; blinding; using intention-to-treat analysis; dealing with inadequate outcome data; selectively presenting outcomes; and other potential sources of bias. The research was evaluated using R software. Two researchers independently scored each study and provided reasons for their ratings. When we couldn't agree on anything, we talked it out or brought in a third expert to help us choose the best course of action and ensure that our risk of bias assessments were accurate.

1.5 Statistical Analysis

The meta-analysis was executed using R software (version 4.2.0). The mean difference (MD) or standardized mean difference (SMD) was utilized to gauge the effect size for continuous variables, whereas the odds ratio (OR) was used for

dichotomous variables. Each effect size was accompanied by its 95% confidence intervals (CIs).

To assess study heterogeneity, the I^2 statistic was employed, ranging from 0% to 100%. An I^2 value between 0–25% suggested low heterogeneity, 25–50% indicated moderate, 50–75% denoted substantial, and 75–100% implied considerable heterogeneity. A common-effect model was applied if heterogeneity testing produced a P -value ≥ 0.1 and an $I^2 \leq 50\%$, suggesting homogeneity among the studies. In contrast, a random-effects model was utilized, and subgroup analysis was performed if needed, when $P < 0.1$ or $I^2 > 50\%$, to identify possible sources of heterogeneity and assess differences among subgroups.

We used a funnel plot to qualitatively analyze publication bias and Egger's test to quantitatively examine it when there were 10 or more studies in the analysis. The stability and reliability of the meta-analysis results were checked by sensitivity analysis, which was set at $P < 0.05$ for statistical significance.

2. Results

2.1 Literature Search Results

Figure 1 depicts the literature selection process. Initially, using a predefined search strategy, 503 studies were identified. There were 369 distinct research kept after duplication was eliminated. By going further into the titles and abstracts, we were able to weed out the irrelevant papers and keep 67 that were pertinent. Afterwards, 12 articles were included in the meta-analysis after 55 studies were excluded due to differences in article type, study design, or the lack of outcome data, as determined through full-text reviews.

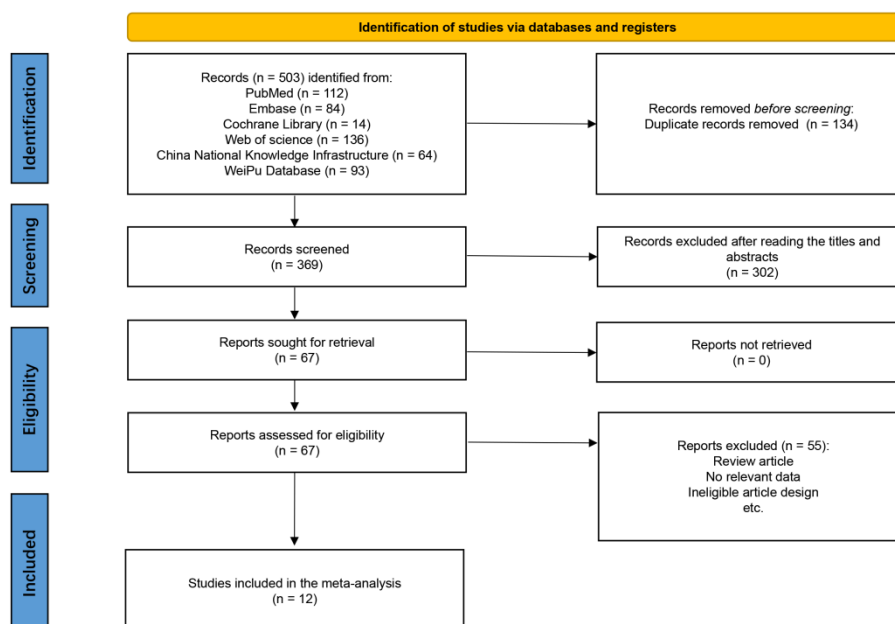


Figure 1. PRISMA Flow Chart

2.2 Basic Characteristics of Included Studies

Based on the search technique, a total of 12 RCTs were considered, including 26,469 patients with DFU. The number of patients in each group was as follows: 3,214 in the experiment and 23,255 in the control. Table 1 summarizes the main features of the research that were considered. Research with sample sizes ranging from twenty to twenty-four thousand, eight hundred and ninety-two people were published between 1998 and 2022.

In the experimental group, the intervention comprised recombinant human platelet-derived growth factor (rhPDGF) at concentrations of 100 µg/g and 30 µg/g. The control group received various interventions, including placebos, antiseptic and surgical dressings, and standard care, with treatment durations ranging from 4 days to 20 week.

Table 1. Basic Characteristics of Included Studies

Study	Country	Intervention		Duration	Sample size (n)		Age (years)		Gender (M/F)	
		E group	C group		E group	C group	E group	C group	E group	C group
Dong 2020	China	100 µg/g rhPDGF	Placebo	20 weeks	36	36	66±1.49	66±1.49	NR	NR
		30 µg/g rhPDGF	Placebo	20 weeks	36	36	66±1.49	66±1.49	NR	NR
Steed 2006	USA	100 µg/g rhPDGF	Placebo	20 weeks	61	57	NR	NR	43/18	46/11
Khandelwal 2013	India	100 µg/g rhPDGF	Antiseptic dressings	10 weeks	20	20	43.35±8.1	45±7.574	11/9	11/9
Tofigh 2022	Iran	100 µg/g rhPDGF	Surgical dressings	12 weeks	81	80	55.8±5.6	60.2±5.2	52/29	46/35
Margolis 2005	USA	rhPDGF	Nonusers	20 weeks	2394	22502	61.6±13.09	63.8±14.07	1463/931	12106/10396
Yuan 2015	China	100 µg/g rhPDGF	Placebo	20 weeks	70	70	61.38±9.65	58.91±11.03	42/27	44/25
		30 µg/g rhPDGF	Placebo	20 weeks	73	70	59.93±9.65	58.91±11.03	46/27	44/25
Jaiswal 2010	India	100 µg/g rhPDGF	Placebo	10 weeks	25	25	56.20±11.34	49.92±18.89	19/6	23/2
Blume 2011	USA	rhPDGF	Standard of care	4 weeks	72	19	57.9±10.9	54.8±12.3	50/22	15/4
Ma 2015	USA	rhPDGF	Placebo	16 weeks	23	23	59.3±6.7	60.1±9.2	NR	NR
Bhansali 2009	India	100 µg/g rhPDGF	Standard of care	20 weeks	10	10	51.7±13.6	49.5±8.8	7/3	5/5
Hardikar 2005	India	100 µg/g rhPDGF	Placebo	20 weeks	58	53	NR	NR	40/18	39/14
Wieman 1998	USA	100 µg/g rhPDGF	Placebo	20 weeks	123	127	57±11.5	58±11.8	82/41	91/36
		30 µg/g rhPDGF	Placebo	20 weeks	132	127	58±11.3	58±11.8	82/50	91/36

2.3 Quality Assessment of Included Studies

The quality assessment of the included studies is summarized in **Figure 2**. In the domain of “random sequence generation,” seven studies mentioned the use of randomization but did not specify the method, leading to an assessment of

“unclear risk.” One study used treatment plans for grouping and was therefore classified as “high risk,” while the remaining studies explicitly employed random number methods and were assessed as “low risk.” For “allocation concealment,” none of the studies provided relevant details, resulting in an “unclear risk” assessment across all studies. Regarding “blinding of participants and personnel,” five studies reported the use of either single-blinding or double-blinding methods and were rated as “low risk,” whereas the rest did not mention blinding and were classified as “unclear risk.” In the domain of “incomplete outcome data,” four studies reported loss to follow-up during the study period and were assessed as “unclear risk,” while the others were categorized as “low risk.” In contrast, for “blinding of outcome assessment,” “selective reporting,” and “other bias,” all included studies were rated as “low risk.” Overall, the quality of the included studies was evaluated as relatively good.

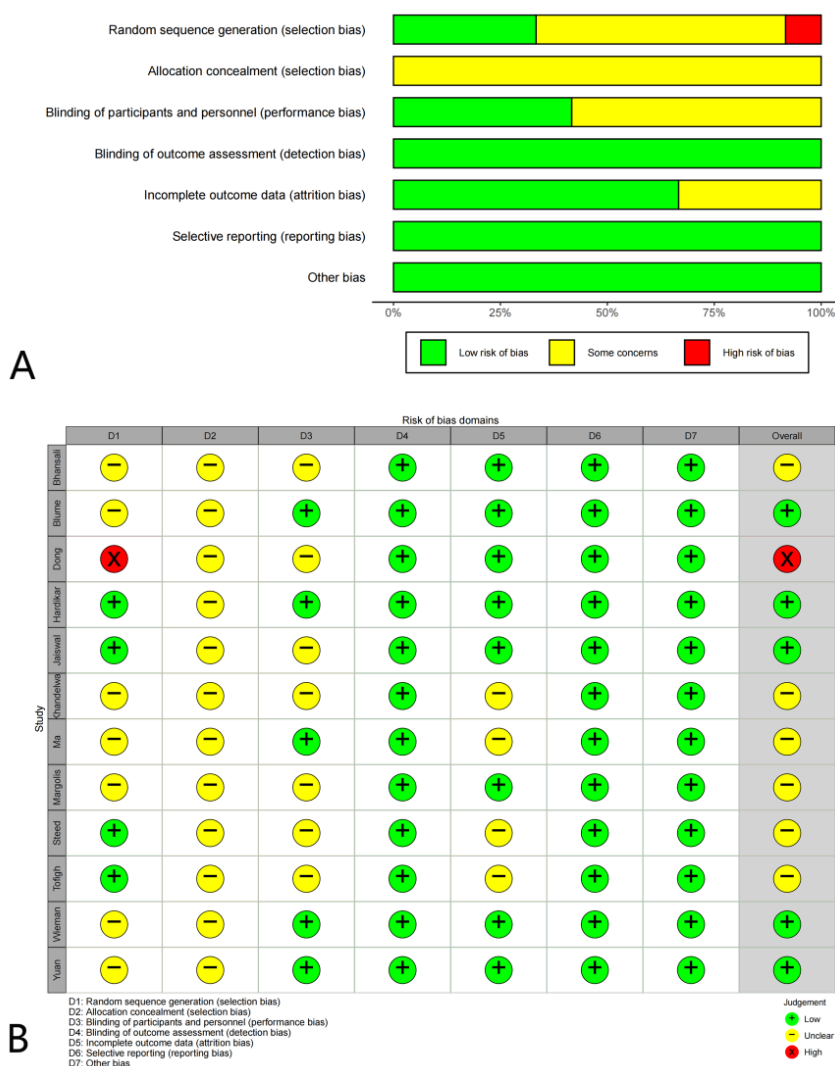


Figure 2. Quality Assessment of Included Studies
(A: Overview of Risk of Bias B: Detailed Results of Risk of Bias)

2.4 Meta-Analysis Results

2.4.1 Primary Outcome: Healing Rate

All included studies reported healing rates. Moderate heterogeneity was observed ($P = 0.02$, $I^2 = 48\%$), necessitating the use of a random-effects model for the analysis of pooled effect sizes. The meta-analysis (**Figure 3**), indicated a significantly higher healing rate in the experimental group (OR = 1.76, 95% CI (1.37, 2.27), $P < 0.01$).

Subgroup analysis, categorized by rhPDGF concentrations, demonstrated a significantly enhanced healing rate at 100 $\mu\text{g/g}$ ($P < 0.01$). Conversely, the healing rate at 30 $\mu\text{g/g}$ showed no significant difference from the control ($P > 0.05$).

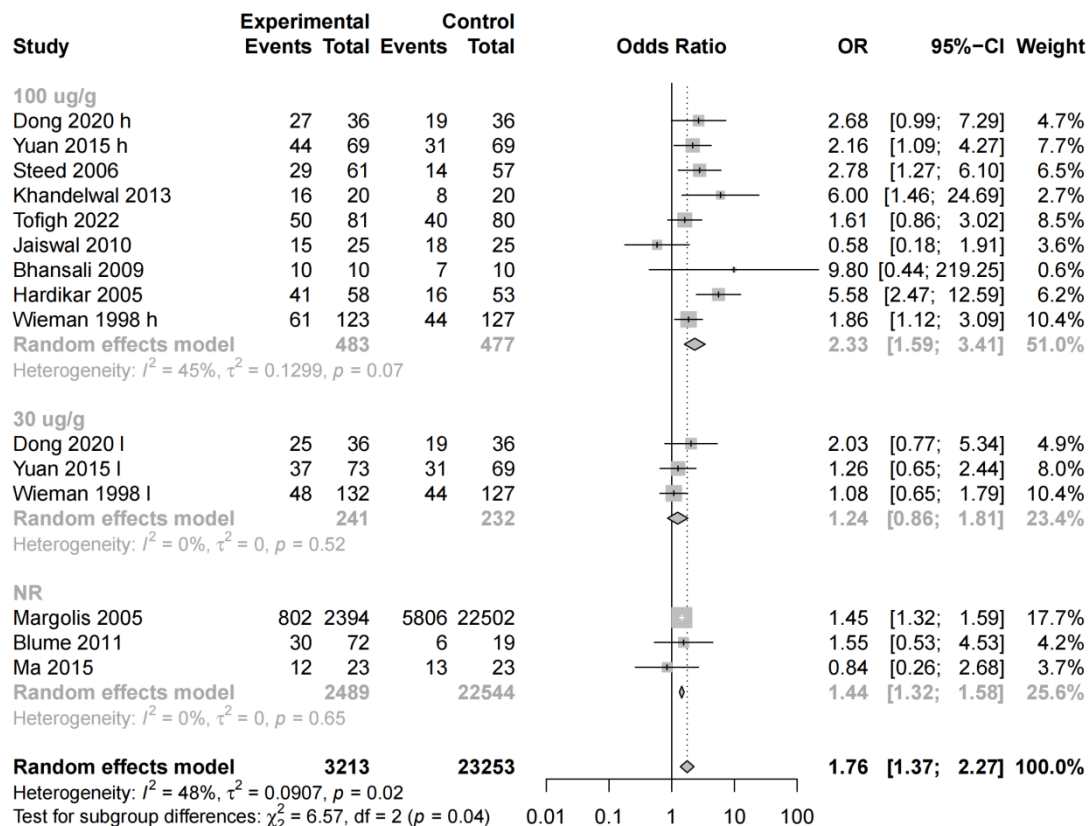


Figure 3. Forest plot comparing healing rates after treatment. NR, not reported.

2.4.2 Secondary Outcome

2.4.2.1 Recurrence Rate

Four studies yielded data regarding recurrence rates. Due to the minimal heterogeneity observed in these studies ($P = 0.54$, $I^2 = 0\%$), a common-effect model was utilized. The findings illustrated in **Figure 4** indicate that there was no notable disparity in recurrence rates following treatment when comparing the experimental and control groups [OR = 0.65, 95% CI (0.36, 1.17), $P = 0.15$].

A subgroup analysis based on rhPDGF concentrations revealed that neither

100 µg/g rhPDGF nor 30 µg/g rhPDGF showed significant differences in recurrence rates ($P > 0.05$).

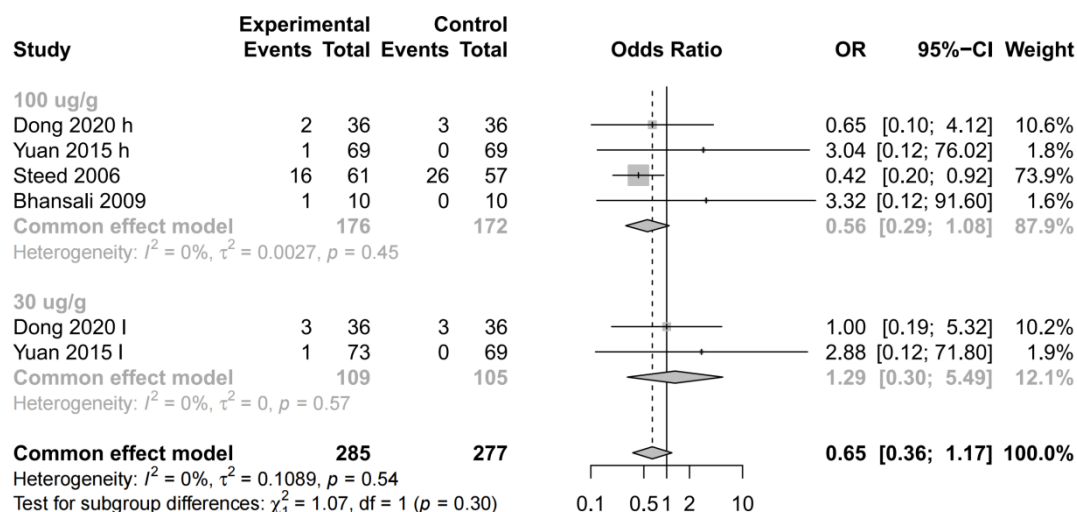


Figure 4. Forest plot comparing recurrence rates after treatment.

2.4.2.2 Healing Time

Three studies centered on the duration of healing, revealing significant variability ($P < 0.01$, $I^2 = 80\%$). A random-effects model was utilized, and the findings, illustrated in **Figure 5**, revealed no notable difference in healing time between the experimental and control groups following treatment [SMD = -0.46, 95% CI (-1.16, 0.23), $P = 0.19$] (**Figure 5**).

Due to the limited number of included studies, no subgroup analysis was conducted for healing time.

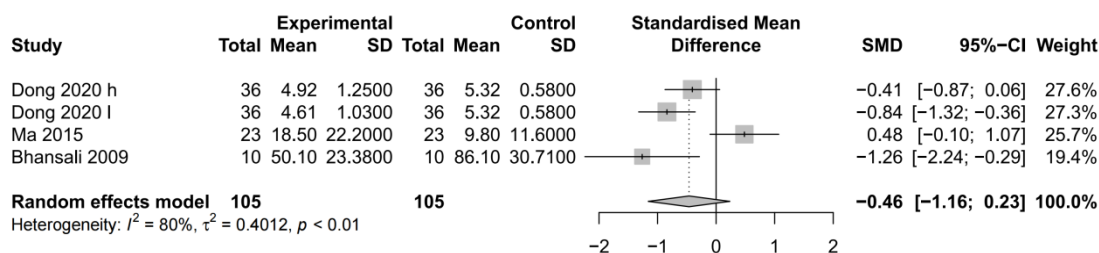


Figure 5. Forest plot comparing healing time after treatment.

2.4.2.3 AEs Rate

AE rates were documented in four studies. Minimal heterogeneity was noted among these studies ($P = 0.85$, $I^2 = 0\%$), leading to the utilization of a common-effect model for the analysis of the pooled effect size. The meta-analysis revealed that there was no statistically significant difference in AE rates between the experimental and control groups following treatment [OR = 0.84, 95% CI (0.61, 1.17), $P = 0.30$] (**Figure 6**).

Subgroup analysis examining the impact of different concentrations of rh-PDGF revealed that neither the 100 µg/g nor the 30 µg/g concentrations significantly altered AE rates ($P > 0.05$).

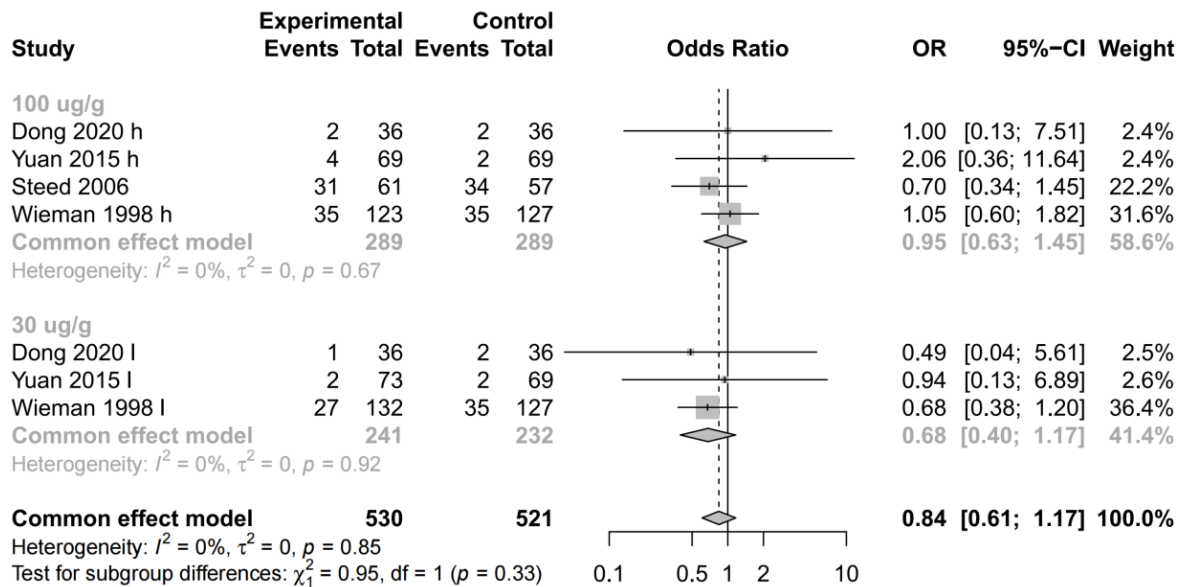


Figure 6. Forest plot comparing adverse event (AEs) rates after treatment.

2.5 Sensitivity Analysis

Sensitivity analysis was performed using the leave-one-out approach to assess the robustness and reliability of the results. The outcomes of this analysis for the evaluated variables are depicted in Figures S1–S3. The limited availability of studies precluded the possibility of conducting a sensitivity analysis for healing time. The results indicated that the exclusion of any individual study did not markedly alter the overall findings, thereby reinforcing their robustness.

2.6 Publication Bias

The rate of healing emerged as the sole outcome variable with over 10 studies, facilitating the evaluation of publication bias via a funnel plot and Egger's test. The funnel plot exhibited a fairly symmetrical distribution of points (**Figure 7**), and Egger's test yielded a P-value of 0.11, suggesting an absence of significant publication bias among the studies analyzed.

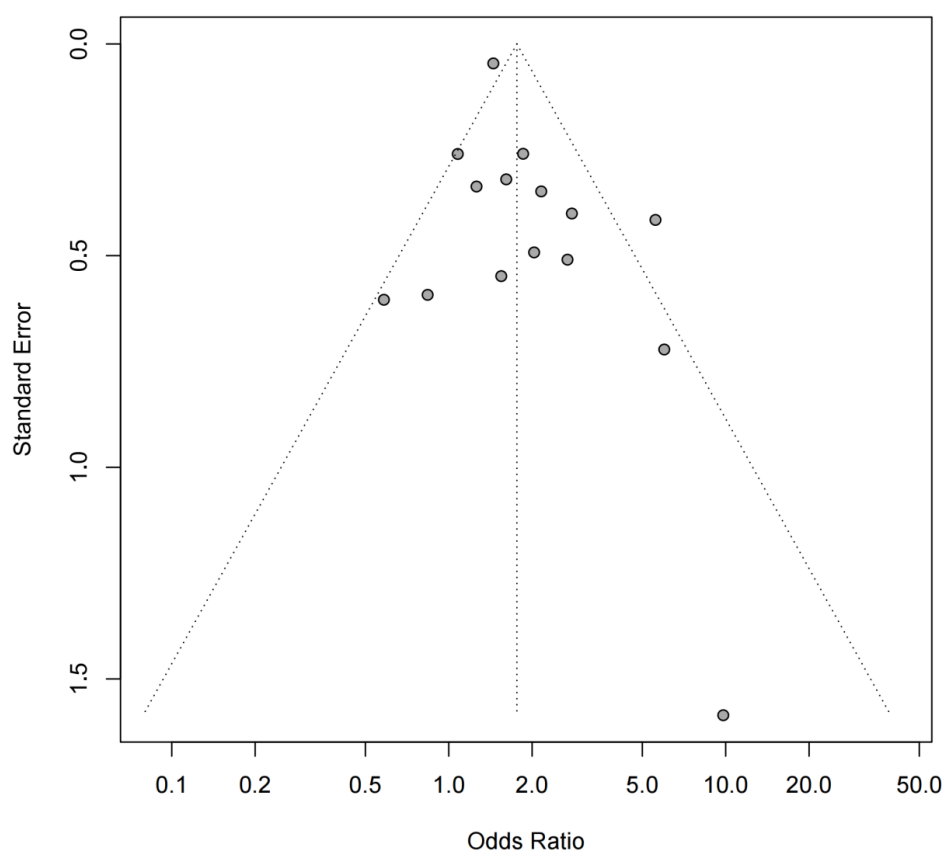


Figure 7. Funnel plot of publication bias.

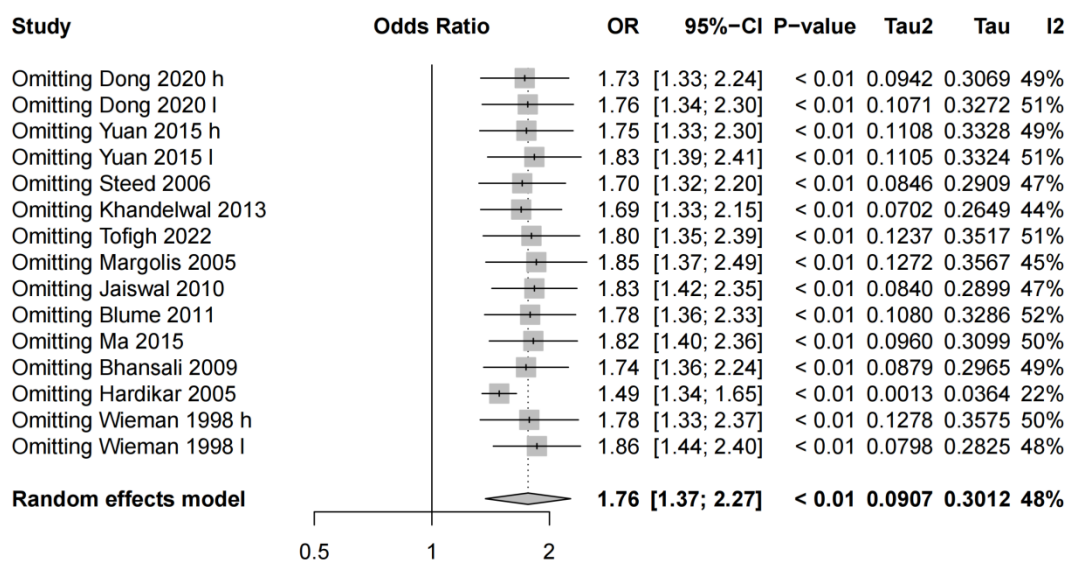


Figure S1. Sensitivity analysis comparing healing rates after treatment.

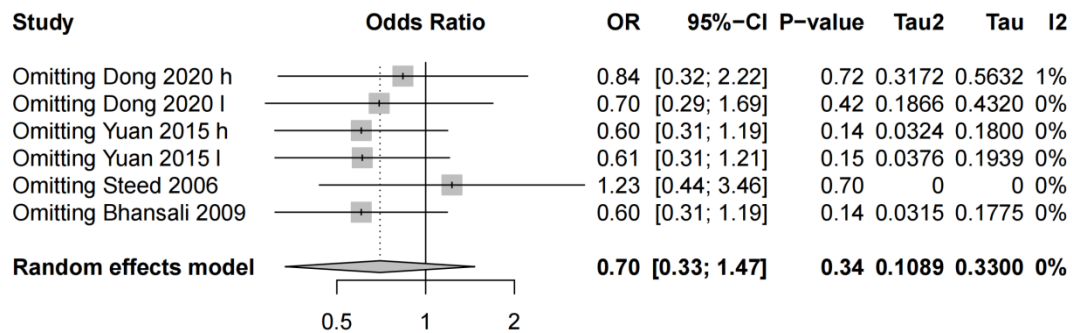


Figure S2. Sensitivity analysis comparing recurrence rates after treatment.

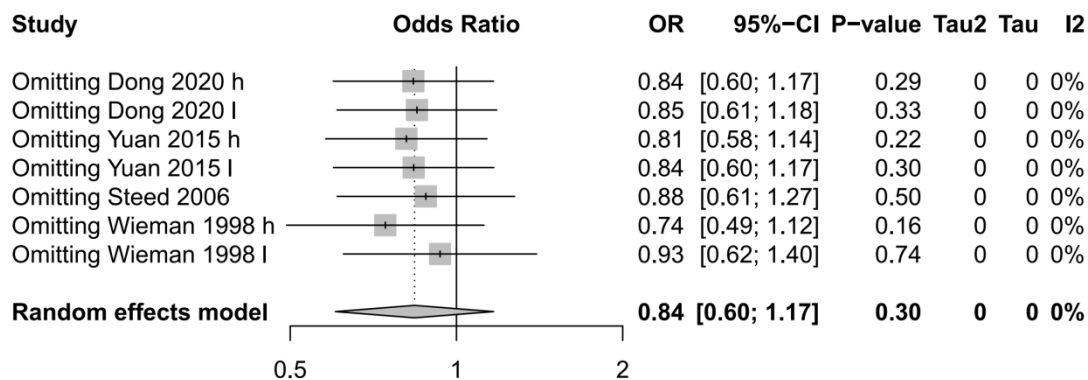


Figure S3. Sensitivity analysis comparing adverse event (AEs) rates after treatment.

Discussion

The effectiveness of rhPDGF-BB in treating DFU has been extensively investigated in various RCTs and observational studies. While numerous studies demonstrate a marked improvement in wound healing rates and a decrease in healing time with PDGF treatment, other research suggests that its efficacy is similar to that of standard wound care when optimal offloading measures are implemented.

A notable multicenter, double-blind, placebo-controlled study conducted by Wieman et al. (1998) demonstrated that the application of topical becaplermin (rhPDGF-BB) gel at a concentration of 100 µg/g significantly enhanced complete wound closure rates by 43% (50% vs. 35%, $p = 0.007$) and decreased the time required for closure by 32% (86 vs. 127 days, $p = 0.013$). The research highlighted the essential functions of sharp debridement, offloading, and infection management alongside PDGF therapy. Steed et al. (2006) supported these findings through a meta-analysis of five clinical trials, revealing that PDGF treatment notably accelerated the healing process in chronic diabetic neuropathic ulcers, resulting in a 30% decrease in healing duration (14 weeks vs. 20 weeks, $p < 0.01$) (Steed, 2006).

However, not all studies have demonstrated a statistically significant benefit of PDGF. Jaiswal et al. (2010) conducted a randomized controlled study in India on 50 patients and stated that while 60% of ulcers treated with PDGF healed compared to 72% in the control group, the difference was not significant ($p > 0.05$) (Jaiswal et al., 2010). The authors attributed this finding on the grounds of small sample size, brief application duration, and potential multifactorial deficiencies in chronic wounds that PDGF alone was not in a position to overcome.

One of the critical issues in PDGF therapy for DFUs is the effect of offloading on wound healing outcomes. Ma et al. (2015) randomized patients with Wagner grade I ulcers to PDGF therapy or placebo, with offloading being achieved by windowed short leg walking casts. There was no difference between the PDGF and placebo groups in healing rates (57% vs. 52%, $p = 0.77$), suggesting that proper offloading alone might be sufficient for ulcer healing and reduce the added value of PDGF (Ma et al., 2015). Bhansali et al. (2009) also observed that when total contact casts (TCCs) were used, PDGF accelerated healing but did not significantly alter overall healing incidence because all the ulcers healed during the study duration (Bhansali et al., 2009). These studies emphasize the important role of offloading in the healing of DFU, which may reduce the independent role of PDGF when used in combination with optimal modalities of offloading.

Several studies have compared PDGF with other wound therapies, including dehydrated amniotic membrane (DAM), HBOT, and antiseptic dressings. Tofigh and Tajik (2022) conducted a randomized clinical trial on 243 patients that compared PDGF, DAM, and routine surgical debridement. They found that DAM resulted in the highest percentage area reduction (PAR) in wound size (87.6%) compared to PDGF (61.7%) and surgical debridement (50%) at 10 weeks ($p < 0.05$) (Tofigh & Tajik, 2022). While PDGF was superior to routine debridement, DAM appeared to offer superior healing rates, potentially due to its anti-inflammatory, antimicrobial, and regenerative properties.

Similarly, Khandelwal et al. (2013) compared PDGF, HBOT, and antiseptic dressings in Grade III and IV DFUs. In this trial, both PDGF and HBOT were effective with 80% and 60% complete healing rates, respectively, compared with 40% for antiseptic dressings ($p = 0.0348$) (Khandelwal et al., 2013). They did state, however, that HBOT required more infrastructure and patient compliance, and therefore PDGF was more readily available and less expensive.

While RCTs provide strong evidence of PDGF effectiveness in a controlled environment, effectiveness in everyday clinical practice is also required. Margolis et al. (2005) conducted an enormous retrospective cohort study of 24,898 DFU patients to determine the effect of PDGF in the real world. They demonstrated that PDGF-treated patients were 32% more likely to heal ($RR = 1.32$, 95% CI: 1.22–1.38) and 35% less likely to undergo amputation ($RR = 0.65$, 95% CI: 0.54–0.78) compared to standard therapy (Margolis et al., 2005). These results are consistent with RCTs, validating the effectiveness of PDGF in the clinic, although patient selection, compliance, and variations in wound care practice may

moderate outcomes.

Safety of PDGF therapy has been a concern, in particular for potential carcinogenicity. The Food and Drug Administration (FDA) post-marketing surveillance study suggested a potential association between long-term use of PDGF (>45 g) and death from malignancies (Steed, 2006; Haugh et al., 2017). However, subsequent analyses have not demonstrated a statistically significant increased risk of cancer (Ma et al., 2015; Zaitseva et al., 2017). Most common AEs reported are local irritation, mild erythema, and transient pain on application, with no differences in significant AEs such as infection or osteomyelitis between PDGF and placebo groups (Wieman et al., 1998; Bhansali et al., 2009; Rahbar et al., 2020).

While PDGF has shown significant efficacy in wound healing acceleration and amputation risk reduction, several limitations must be considered. First, a major limitation is the heterogeneity in study designs, such as the use of different wound classification systems (e.g., Wagner vs. IAET), offloading modalities, and follow-up durations, which makes between-study comparisons difficult. Moreover, most of the studies, including those of Jaiswal et al. (2010) and Bhansali et al. (2009), had modest sample sizes, which could diminish the statistical power of these studies in detecting a significant difference between the groups. Another drawback is the lack of long-term follow-up data because, in the majority of the studies, short-term healing alone was considered as the primary outcome measure with limited data on ulcer recurrence and long-term functional improvement. Lastly, since PDGF has the potential to promote cellular proliferation, future studies must assess its potential synergistic effects when used in combination with advanced wound care therapies like negative pressure wound therapy (NPWT) and bioengineered skin substitutes to maximize treatment outcomes.

Conclusion

The collective findings from RCTs, observational studies, and meta-analyses suggest that PDGF is an effective and safe therapeutic option for DFU, particularly when used in conjunction with good wound care, debridement, and offloading techniques. While its efficacy is comparable to HBOT and superior to antiseptic dressings, dehydrated amniotic membrane therapy may offer additional advantages. The real-world effectiveness of PDGF aligns with controlled trial outcomes, reinforcing its role in clinical practice. However, further large-scale, long-term studies are needed to evaluate its optimal use, cost-effectiveness, and potential benefits in combination with other advanced wound care modalities.

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