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Meta-analysis

Efficacy of topical recombinant human platelet-derived growth factor for treatment of diabetic lower-extremity ulcers: Systematic review and meta-analysis

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ABSTRACT

Objective. Recombinant human platelet-derived growth factor (rhPDGF) is used topically in the treatment of diabetic lower-extremity ulcers. There have been few meta-analyses of the efficacy of rhPDGF in this treatment context. The aim of this study was to perform an updated systematic review and meta-analysis to assess the clinical efficacy of rhPDGF in the treatment of diabetic lower-extremity ulcers.

Methods. We searched the MEDLINE, Cochrane Library, EMBASE and Web of Knowledge databases up to April 30, 2014. Studies were identified and selected, and data were extracted by two independent reviewers. The primary efficacy outcome was complete healing rate. Adverse events were also assessed. The studies were evaluated for quality and publication bias.

Results. A total of 6 randomized controlled trials including 992 patients were selected from 173 identified studies. The studies compared rhPDGF treatment in the context of standard of care (SOC) to placebo or SOC alone. In the absence of study heterogeneity, a fixed-effects model was performed, and the combined odds ratio (OR) indicated a significantly greater complete healing rate in patients treated with rhPDGF compared to placebo or SOC alone. The ORs ranged from 0.58 to 2.77, with a combined OR of 1.53 (95% CI = 1.14 to 2.04, p = 0.004). A sensitivity analysis (leave-one-out method) indicated good study reliability, and a funnel plot with Egger test showed no publication bias.

Conclusion. These results indicate that rhPDGF is efficacious in the treatment of diabetic lower-extremity ulcers.

Abbreviations: ABPI, ankle brachial pressure index; Ad5-PDGF-B, E1-deleted adenovirus serotype 5 encoding human platelet-derived growth factor-B; AE, adverse event; CFU, colony-forming unit; CI, confidence interval; GAM501, Gene Activated Matrix 501, a proprietary product; IAET, International Association for Enterostomal Therapy; NA, not available; OR, odds ratio; PDGF, platelet-derived growth factor; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial; rhPDGF, recombinant human platelet-derived growth factor; SAE, serious adverse event; SD, standard deviation; SOC, standard of care; $TcPO_2$, transcutaneous oxygen tension.

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1. Introduction

Diabetes mellitus is characterized by a high level of glucose in the blood as a result of impaired insulin production and/or action. As of 2000, the worldwide prevalence of diabetes was estimated to be 171 million, and it is projected that this will increase to 366 million by 2030 [1]. A common and serious complication of diabetes is the development of foot ulcerations. It is estimated that 15% to 25% of diabetic patients will develop a foot ulcer during their lifetime [reviewed in 2,3] and that up to 40% of these patients may require amputation [reviewed in 4]. The standard of care (SOC) for diabetic foot ulcers involves debridement, local wound care, infection control and off-loading of pressure [5]. Despite this, many diabetic foot ulcers fail to heal, resulting in increased risks for the development of infection and amputation.

The roles of growth factors, such as epidermal growth factor, platelet-derived growth factor (PDGF) and fibroblast growth factor, among others, in wound healing are becoming increasingly understood [6]. Recombinant human PDGF (rhPDGF) is used as an adjunct to good wound care/SOC. It was approved by the United States Food and Drug Administration in 1997 for the treatment of chronic, nonhealing diabetic ulcers of the lower extremities, and it remains the only growth factor approved for this indication [7].

Meta-analyses of randomized controlled trials (RCTs), which were published in 1999 and 2005 [8,9], found that topical treatment with rhPDGF along with SOC is effective and well tolerated for the treatment of diabetic foot ulcers. Comprehensive reviews and noncontrolled studies suggest similar findings [10–13]. The aim of the present study was to perform an updated systematic review and meta-analysis to assess the clinical efficacy of rhPDGF in the treatment of diabetic lower-extremity ulcers.

2. Methods

2.1. Search strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14] (www.prisma-statement.org) (Fig. 1). The databases searched included MEDLINE, the Cochrane Library, EMBASE and Web of Knowledge (up to April 30, 2014). The search terms were as follows: diabetic/diabetes, foot ulcer/leg ulcer/ulcer, platelet-derived growth factor/recombinant human platelet-derived growth factor/becaplermin/Regranex/PDGF/rhPDGF. Reference lists of relevant studies were searched by hand.

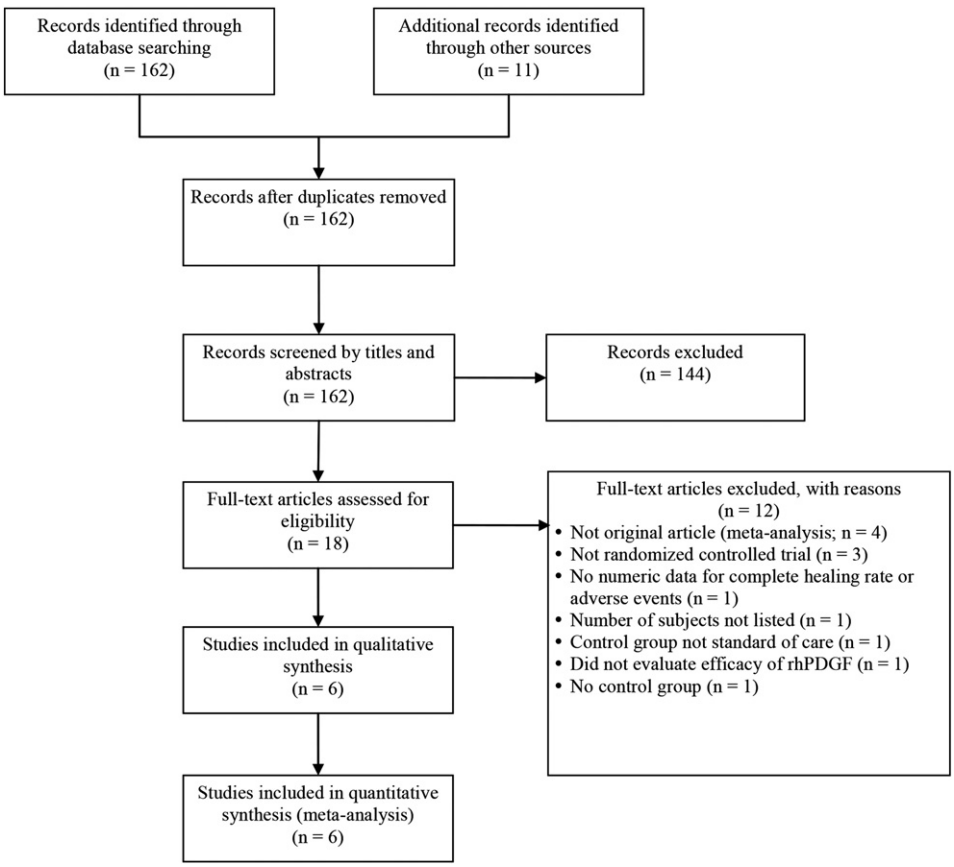

Fig. 1 – Flow diagram for identification of studies for inclusion in meta-analysis. rhPDGF: recombinant human platelet-derived growth factor.