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Autologous Granulocyte Colony-Stimulating Factor-Mobilized Peripheral Blood CD34 Positive Cell Transplantation for Hemodialysis Patients with Critical Limb Ischemia: A Prospective Phase II Clinical Trial

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ABSTRACT

Critical limb ischemia (CLI) is a devastating disease in patients undergoing hemodialysis (HD). Based on the unsatisfactory results of autologous mononuclear cell transplantation for patients with CLI undergoing HD, we conducted a phase II clinical trial to evaluate the safety and efficacy of granulocyte colony-stimulating factor (G-CSF)-mobilized peripheral blood-derived autologous purified CD34 positive (CD34+) cell transplantation for CLI in patients undergoing HD. Six patients with CLI (two with Rutherford category 4 and four with Rutherford category 5) were enrolled. As for primary endpoint, there were no major adverse events related to this therapy. As for efficacy, the amputation-free survival rate was 100% at 1 year after cell therapy. Both rest pain scale and ulcer size were significantly improved as early as 4 weeks after therapy compared with baseline ($p < .01$), and three out of five ulcers completely healed within 12 weeks after cell transplantation. Clinical severity, including Fontaine scale and Rutherford category, significantly improved at 24 weeks after cell transplantation ($p < .05$), and further improved at 52 weeks ($p < .01$) compared with baseline. The improvement rate from CLI stage to non-CLI stage was 83.3% at 52 weeks. Toe skin perfusion pressure and absolute claudication distance were also significantly improved. In conclusion, G-CSF-mobilized peripheral blood CD34+ cell transplantation was safe, feasible, and effective for patients with CLI undergoing HD. STEM CELLS TRANSLATIONAL MEDICINE *2018;7:1–9*

SIGNIFICANCE STATEMENT

Improvement of critical limb ischemia (CLI) is often very difficult. Because outcome in CLI patients, especially in hemodialysis (HD) patients, is very poor, effective treatment is urgently needed. CD34 positive cells have potential to vascular regeneration. However, number of peripheral blood CD34 positive cells is severely decreased in HD patients with CLI due to uremic condition and inflammation. Mobilization by granulocyte colony-stimulating factor (G-CSF) significantly increased the number of CD34 positive cells in peripheral blood, and potential of CD34 positive cells was also confirmed in this study. Although this is a small study, regenerative therapy using autologous G-CSF-mobilized peripheral blood CD34 positive cell transplantation was highly effective in HD patients with CLI. This result may encourage novel cell-based therapy for patients with CLI requiring HD.

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INTRODUCTION

The prognosis of patients with critical limb ischemia (CLI) undergoing hemodialysis (HD) is poor [1, 2]. In patients with CLI, revascularization therapy, including bypass surgery or endovascular therapy (EVT), is an essential treatment strategy. However, revascularization therapy still has significant limitations in patients with HD. Infrapopliteal arteries are the most frequent affected sites for CLI in patients undergoing HD, and these arteries usually show extensive vascular calcification [3]. A