

Effect and Safety of Adipose Tissue-derived Stem Cell Implantation in Critical Limb Ischemia

[Purpose] Treatment of critical limb ischemia (CLI) by bypass operation or percutaneous vascular intervention is difficult. The safety and efficacy of multiple intramuscular adipose tissue-derived mesenchymal stem cells (ADSCs) injections was evaluated in CLI patients. [Methods] 15 male patients with ischemic resting pain in one limb with or without non-healing ulcers and necrotic foot were enrolled. ADSCs were isolated from adipose tissue of thromboangiitis obliterans (TAO) patients, diabetes patients (D-ADSCs), and healthy donors. In a colony forming unit assay, the stromal vascular fractions of TAO and diabetic patients yielded lesser colony than those of healthy donors. D-ADSCs showed lower proliferation and osteogenic differentiation and higher adipogenic differentiation than others. Multiple intramuscular ADSCs injections at ischemic area cause no complications. [Results] At 6 months, significant clinical improvement was noted on pain rating scales in eleven (73.3%, $p=0.032$) patients, and claudication walking distance ($p=0.046$). Digital subtraction angiography (DSA) before and at 6 months after ADSCs implantation showed formation of numerous vascular collateral networks across affected arteries in 11 of 13 patients. 5 (33.3%) patients required minor amputation during follow-up, and all amputation sites healed completely. 3 patients agreed clinical follow workup at 24 months. We could observe good maintenance of collateral networks on DSA at 24 months. There were no differences of pain scale rate, and claudication walking distance between 6 months and 24 months. [Conclusion] ADSCs implantation may be a safe, alternative method to achieve angiogenesis in patients with CLI who are refractory to other treatment modalities. And, collateral networks developed maintained after 24 months.