

Adoptive Autologous Vascular Stem Cell Therapy for Diabetic Foot Patients

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Ischemic diabetic foot patients with peripheral vascular disease are difficult to cure once all conventional treatment modalities are exhausted, amputation is the final solution. The major concern for diabetic foot amputation is that five year mortality rates after lower extremity amputation for diabetics, critical limb ischemia and peripheral artery disease range from 39% to 68% [1]. Furthermore, the economic burden of diabetic foot ulcer is estimated to be 98 billion per year [2]. In order to overcome these difficulties, many researchers and clinicians have been looking into an alternative new therapy to successfully cure these patients. After the discovery of endothelial progenitor cells (EPCs) by Asahara's group in 1997, these vascular stem cells became the subject of intense experimental and clinical investigation for angiogenesis and wound healing [3]. Preliminary studies supports the potential of stem/progenitor cells for angiogenesis and wound and its cell based therapy has become an alternative therapeutic option for peripheral vascular disease and diabetic ulcers [4]. Clinical studies involving patients with diabetic ulcer and peripheral vascular disease with application of bone marrow or peripheral blood EPCs have started world-wide. However, ours and reports from other researchers have demonstrated the limitations of autologous diabetic EPC therapy [5].

First study on relation between EPC and diabetic was done by Tepper et al. demonstrating that diabetic patients exhibit significant decrease in number of peripheral blood EPCs and impaired EPCs function in mobilization, proliferation, adhesion and tubulization [6,7]. Supporting this we demonstrated that EPCs dysfunction is seen not only in the peripheral blood but also in the bone marrow in response to flap injury and that diabetic EPC dysfunction lies mainly on differentiation [8]. Since diabetic patients have low number and function of EPCs, autologous EPC therapy is thought to be less effective compared to non-diabetic patients.

In order to overcome these issues, we have established a newly developed quantity and quality control culture (QQc) system to potentiate the vasculogenic property of EPCs for tissue repair [9]. One week of QQc culture significantly increased murine diabetic EPCs and diabetic EPC vasculogenic potential with significant enhancement in wound closure. Recently, we are now investigating the efficacy of QQc using human peripheral blood EPCs preparing clinical trial of peripheral blood QQc autologous EPC therapy for diabetic foot patients. Since QQc is serum-free and it rapidly expands the number of diabetic EPCs, this system may facilitate cell-based therapies for DM patients. We believe that his study can be stated to be the first step in establishing an ideal cell based therapy for diabetic patients. Moreover, the rapidly expanded post-QQc EPC population could be aliquoted, cryopreserved, and used again for metachronous wounds or other ischemic conditions (e.g. myocardial ischemia).

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