**Synergistic vasculogenic effects of systemically infused AMD3100 and locally injected SDF-1α in sciatic nerve vasa nervorum of diabetic peripheral neuropathy mice**

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**Introduction**

Autologous endothelial progenitor cell (EPC) transplantation may have several limitations especially in diabetes complication, because normal functions of the EPC is impaired in diabetes. Hence, it should be considered ex vivo EPC therapy or another approaches in diabetes condition. An alternative approach of stem cell therapy is stimulation of endogenous bone marrow derived EPCs recruitment into ischemic lesion by administration of stem cell mobilization agents or chemokines. The aim of the present study was therefore to examine whether pharmacological activation of the impaired EPC function restore the sciatic nerve vasa nervorum and the nerve conduction velocity in diabetic neuropathy (DN) mice model.

**Materials and Methods**

Before the main experiment, it was tested EPC mobilization effect of vascular endothelial growth factor (VEGF) and AMD3100 in diabetic mice. AMD3100 was administrated systemetically to stimulate EPC mobilization and SDF-1α was injected locally to enhance its migration in streptozotocin-induced DN mice model.

**Results**

We found that AMD3100 was effective EPC mobilization agent but VEGF did not increased circulating EPCs in diabetic condition. Notably, the combination therapy of systemic AMD3100 and local SDF-1α increased expression levels of vasculogenesis associated factors and new born endothelial cells in sciatic nerve, resulting in restoration of sciatic vasa nervorum. Finally, it enhanced the impaired sciatic nerve conduction velocity in DN mice.

**Discussion and Conclusions**

The decreased vascularity in vasa nervorum has been therapeutic target of diabetic peripheral neuropathy. For example, local gene delivery of angiogenic factors or EPC transplantation restores the vasa nervorum, resulting in enhanced sciatic nerve conduction velocity in experimental DN animal models [1]. In present study, we show another novel approach for restoration sciatic nerve vasa nervorum in DN. It is new therapeutic strategy for DN that AMD3100 induced EPC mobilization and local injected SDF-1α can restore the vasa nervorum. However, the effect was not long-lasting up to 3 weeks. In previous studies, transplanting stem cells in DN animal model, the therapeutic effect is lasted over 4 weeks based on nerve conduction velocity. Though our therapeutic strategy is less long-lasted than exogenous stem cell transplantation, this approach is more convenient and economical, thus it might be easy to treat multiply. Also, in this concept, another EPC mobilization of migration agents could be studied to treat diabetic complications including DN.

**Reference**


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