

Pan-PPAR agonist, bezafibrate, restores angiogenesis in hindlimb ischemia in normal and diabetic rats

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Background and Aims: It is suggested that peroxisome proliferator-activated receptors (PPARs) may be involved in regulating angiogenesis. This study aimed to investigate the effect of bezafibrate as a pan-PPAR agonist on angiogenesis and serum nitrite, the main metabolite of nitric oxide (NO), vascular endothelial growth factor (VEGF) and VEGF receptor-2 (VEGFR-2) concentrations in hindlimb ischemia model of normal and type I diabetic rats.

Methods: 28 male Wistar rats were divided into control and diabetic groups. Diabetes was induced by intraperitoneal injection of streptozotocin (55mg/kg). Then, all rats underwent unilateral hindlimb ischemia. After recovery, they were randomly assigned to one of the following experimental groups: (1) control; (2) control+bezafibrate (400 mg/kg/day); (3) diabetic; (4) diabetic+bezafibrate. After three weeks, blood samples were taken and capillary density was evaluated in the gasterocnemius muscle of ischemic limb.

Results: results showed that bezafibrate increased capillary density and capillary/fiber ratio in ischemic leg of diabetic and control rats ($p < 0.05$). Serum VEGF and VEGFR-2 concentrations did not alter after bezafibrate administration, however, serum nitrite concentration was significantly higher in bezafibrate-treated groups than non-treated groups ($p < 0.05$).

Conclusions: Since diabetes is one of the most important risk factor for development of peripheral artery disease, it seems that bezafibrate, as a pan PPAR agonist, restores angiogenesis in hindlimb ischemic diabetic animals and is useful for prevention and/or treatment of peripheral artery disease in diabetic subjects.

Keywords: Angiogenesis; Diabetes; Hindlimb ischemia; Nitric oxide; Vascular endothelial growth factor