

The Effect of Intensive Glycemic Control on Endothelial Progenitor Cells Level and Function in Patients with Diabetes

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Background: Vascular injury has a central role in the pathogenesis of cardiovascular complications of diabetes. Recent evidence has shown that endothelial progenitor cells (EPCs) have an important role in the repair process following vascular injury. However, in patients (pts) with diabetes EPC number and function are significantly reduced. Intensive glycemic control can reduce diabetic complications, but it is not known how such management affects EPC number and function. We aimed to examine whether intensive glycemic control can improve EPC number and function in pts with uncontrolled diabetes.

Methods: Fifteen pts with treated diabetes and HgA1c level $\geq 8.5\%$ were included. Pts were tested at baseline and after 3 months of intensive glycemic control. The treatment goal was to reach HgA1c level of 7%. Circulating EPC levels were assessed by flow cytometry as the proportion of peripheral mononuclear cells co-expressing VEGFR2, CD133 and CD34. The capacity of the cells to form colony forming units (CFUs) was quantified after 1 week of culture on fibronectin-coated plates. Functional properties of the cultured cells were evaluated by the MTT proliferation assay, and migration assay.

Results: Pts (n=15) had a mean age of 59.5 ± 10 years, 16 ± 9 years from diagnosis, BMI of 31 ± 7 , 18% were women. All pts were treated with aspirin, and statins. Baseline HgA1c was $9.5 \pm 1\%$. After 3 months of intensive control HgA1c decreased to $8.2 \pm 1\%$. Circulating EPC levels increased after the intensive control period (VEGFR2+CD34+: $0.45 \pm 0.6\%$ at baseline vs. $1.3 \pm 0.8\%$ post, $P=0.02$; VEGFR2+CD133+: $0.4 \pm 0.6\%$ at baseline vs. $0.9 \pm 0.7\%$ post, $P=0.06$). The number of CFUs (mean 2.5-2.6 CFUs per well) did not change significantly after the intensive control period, nor were there changes in the functional assays.

Conclusions: In this preliminary study, tight glycemic control was associated with an increase in the levels of circulating EPCs, without improvement in the functional properties of the cells