Synergistic Effect of Hyperglycemia and Ox-LDL in Type 2 Diabetes

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Background: Previous studies suggested negative effect of either hyperglycemia or oxidized low-density lipoprotein (OxLDL) on the functional activity of endothelial progenitor cells (EPCs). The present study was conducted to examine the effect of both factors simultaneously on EPCs.

Methods: EPC number and activity were studied in 55 patients divided into three groups: patients with type 2 diabetes (DM), patients with coronary artery disease (CAD), patients with DM/CAD, and 15 control subjects. All measurements were correlated with subject's serum OxLDL. EPCs from DM patients were incubated with OxLDL, and EPCs from CAD patients were incubated with high glucose (HG). EPCs incubated with combination of HG and OxLDL in the presence or absence of sodium nitroprusside (SNP). After incubation, EPC adherence to human umbilical vein endothelial cells (HUVECs) and NO bioavailability were evaluated. Western blot was performed to assess nitric oxide synthase (NOS) and Akt activity.

Results: EPC number, colonies and NO bioavailability were significantly reduced in DM and DM/CAD patients compared with controls ($p<0.01$). These parameters were inversely correlated with serum OxLDL ($r=-0.43$, $p=0.004$, $r=-0.63$, $p<0.001$, and $r=-0.65$, $p<0.001$; respectively). Incubations of DM-EPCs with OxLDL or CAD-EPCs with HG as well as incubation of controls-EPCs simultaneously with HG and OxLDL were associated with the most significant reduction in EPC adherence to HUVECs and NO bioavailability. These alterations were ameliorated by the presence of SNP.

Conclusions: Our findings suggest that combination of HG and OxLDL exerts a synergistic adverse effect on EPC functional activity through NO system modification. Avoiding this interaction in the future may provide a clinical approach to minimize vascular injury in diabetic patients.