Iron Contributes to Endothelial Dysfunction in Acute Ischemic Syndromes

To the Editor:

Congratulations to Duffy et al on their well-written article, “Iron Chelation Improves Endothelial Function in Patients With Coronary Disease.” We completely agree that increased body iron stores may be a risk factor for atherosclerosis and may accelerate endothelial dysfunction in acute ischemic syndromes. Hence, deferoxamine, an iron chelator, should prove useful both for preventing ischemia and improving endothelial function.

Our investigations into the efficacy of deferoxamine in acute ischemic syndromes and as a possible treatment for atherosclerosis, performed over the past 5 years, yielded the following corroborative findings:

(1) In vitro effect on fibroblasts, smooth muscle cells, and endothelial cells. To investigate deferoxamine’s in vitro effect on expression of basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF), we added it in different concentrations (10 μmol/L, 100 μmol/L, and 1 mmol/L) to 3 different cells. The highest concentration (1 mmol/L) increased the expression of bFGF in fibroblasts to 1054% and in smooth muscle cells to 532%, and increased the expression of VEGF to 651% in fibroblasts and to 589% in smooth muscle cells.

(2) Effect on revascularization of ischemic skeletal muscle. Conventional indirect immunofluorescent en-face staining showed that, at baseline, capillaries occupied 4.0±0.22% of the area in nonischemic skeletal muscle. After severe ischemic shock, capillaries occupied 3.0±0.46% of the area, indicating incomplete recovery even after 2 months. However, when deferoxamine (in fibrin sealant) was applied to ischemic muscle, the area occupied by capillaries increased to 9.6±0.8% (P<0.001). This data correlated well with results of blood flow investigation. In nonischemic muscle, blood flow was 0.36±0.04 mL/min/g, but decreased immediately after ischemic shock to 0.08±0.02 mL/min/g. Two months later, blood flow was only 0.29±0.04 mL/min/g, but increased to 0.44±0.06 mL/min/g with the application of deferoxamine.

(3) Effect on clinical indirect myocardial revascularization. In 7 patients whose coronary vessels were unsuitable for either bypass or endarterectomy, a modified Vineberg procedure was performed, then a special fibrin sealant with deferoxamine (100 mg) was injected into the myocardium surrounding the implant. Long term follow-up showed extensive neovascularization in the treated area.

Valeri S. Chekanov, MD, PhD
Victor Nikolaychik, MD, PhD
Heart Care Associates
Milwaukee Heart Institute of Aurora Sinai Medical Center
Milwaukee, Wis

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Valeri S. Chekanov and Victor Nikolaychik

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