Beneficial Effect of Albumin Therapy Attributable to $\alpha_1$-Acid Glycoprotein?

To the Editor:

Belayev et al\textsuperscript{1} report that albumin therapy has the beneficial effect of reversing stagnation, thrombosis, and corpuscular adherence in the cortical venules of a rat model of middle cerebral artery occlusion. They cite further studies in which human serum albumin treatment conferred neurological and histological protection in rat stroke models of focal\textsuperscript{2–4} and global\textsuperscript{5} cerebral ischemia as well as traumatic brain injury.\textsuperscript{6}

We have previously shown\textsuperscript{7} that human $\alpha_1$-acid glycoprotein (orosomucoid), an acute phase protein, also has a beneficial effect in a rat model of global cerebral ischemia, even 30 minutes after reperfusion. In our study, human $\alpha_1$-acid glycoprotein was given IV in doses of 50, 200, and 600 mg/kg. Compared with control animals treated with placebo (albumin free of $\alpha_1$-acid glycoprotein), the doses of 200 and 600 mg/kg successfully mitigated brain edema.

The concentration of $\alpha_1$-acid glycoprotein in human plasma is about 0.2 to 1.4 mg/mL. One of its major physiological roles seems to be to maintain permeability of the capillary barrier,\textsuperscript{8} which is probably achieved by increasing the negative charge of the capillary endothelium\textsuperscript{9,10} and thus reducing the transvascular transport of polyanionic macromolecules. Increased vascular permeability is a common symptom in various kinds of shock, stroke, etc. A beneficial effect of $\alpha_1$-acid glycoprotein can therefore be anticipated under these pathophysiological conditions. Additionally, we have shown that resuscitation with human $\alpha_1$-acid glycoprotein effectively restores cardiac output and stroke volume in a rat model of hemorrhagic/hypovolemic shock\textsuperscript{11} by tightening the microvessel walls, thereby increasing the intravascular circulating volume.

During early postischemic reperfusion, there is a progressive accumulation of polymorphonuclear leukocytes in regions of low cerebral blood flow.\textsuperscript{12} It is known from in vitro studies with these leukocytes\textsuperscript{13,14} that $\alpha_1$-acid glycoprotein inhibits neutrophil aggregation and superoxide anion generation. Furthermore, $\alpha_1$-acid glycoprotein inhibits platelet aggregation\textsuperscript{15} and enables erythrocytes to pass through micropores,\textsuperscript{16} which probably improves altered rheologic conditions.

These studies in rat models of stroke point to the possibility that the beneficial effect of albumin treatment is attributable to the $\alpha_1$-acid glycoprotein content of albumin solution.

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