Letter to the Editor

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Comment on the Paper Entitled 'Erythropoietin Ameliorates Oxidative Stress and Tissue Injury following Renal Ischemia/Reperfusion in Rat Kidney and Lung'

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Dear Editor,

We read with great interest the article by Ardalan et al. [1] that reported favorable effects of erythropoietin (Epo) on oxidative stress and tissue injury following renal ischemia/reperfusion in the rat kidney and lung. It is worth pointing out that the positive influence of Epo on cerebral injuries following perinatal asphyxia in newborns has also been shown [2]. Therefore, we would like to emphasize the clinical importance of Epo use in the treatment of patients with neonatal hypoxic ischemic encephalopathy.

Epo is a cytokine hormone with neuroprotective effects that decreases apoptosis, inflammation, and oxidative injury and promotes glial cell survival, angiogenesis, and neurogenesis [3]. Epo is reported to stimulate vascular endothelial growth factor secretion and angiogenesis via the PI3K/Akt and extracellular-signal-regulated kinase (ERK, also known as MAPK) signaling pathways. Other Epo effects are thought to be mediated through the Epo stimulation of brain-derived neurotrophic factor [4, 5]. McPherson and Juul [4] speculated that Epo neuroprotection includes systemic effects such as enhanced erythropoiesis, which increases the stabilization of oxygen availability and iron utilization, thereby decreasing the free iron and reducing the oxidative brain injury. Thus, it improves the long-term brain healing after an insult by providing an increased oxygen-carrying capacity through erythropoiesis and angiogenesis and by increasing neurogenesis. The net effect of the acute actions of Epo is a decrease in apoptosis. Schelshorn et al. [5] found that neurons could specifically express hemoglobin in response to either hypoxia or Epo, and that neuronal hemoglobin expression may be neuroprotective by facilitating oxygen uptake in neurons and serving as an oxygen capacitator molecule. Furthermore, it has been demonstrated that the combined use of hypothermia and Epo has more expressed neuroprotective effects than the sole use of hypothermia after perinatal asphyxia in newborns [3].

We therefore recommend that Epo be included in the treatment guidelines as an adjunctive therapy to therapeutic hypothermia for neuroprotection following a hypoxic-ischemic insult in newborn infants.

References

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4 McPherson RJ, Juul SE: Erythropoietin for infants with hypoxic-ischemic encephalopathy. Curr Opin Pediatr 2010;22:139–145.
5 Schelshorn DW, Schneider A, Kuschinsky W, et al: Expression of hemoglobin in rodent neurons. J Cereb Blood Flow Metab 2009;29:585–595.

Editor's Note: The authors of the paper 'Erythropoietin Ameliorates Oxidative Stress and Tissue Injury following Renal Ischemia/Reperfusion in Rat Kidney and Lung' were invited to respond to this letter, but no response was received from them.

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