Boosting Red Cell Production Helps in Brain Injury

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Giving erythropoiesis-stimulating agents (ESAs) after traumatic brain injury (TBI) may improve survival without increasing comorbidities, researchers found.

Despite longer hospital and intensive care unit stays, patients in a prospective study who were given the red cell production stimulants after TBI had a 75% lower mortality risk than those not given the agents, Peep Talving, MD, PhD, of the University of Southern California, and colleagues reported in the March issue of *Archives of Surgery*.

In animal models, ESAs given after TBI offered neuroprotective effects by decreasing secondary neuronal damage and improving neurological outcomes. Also, Talving and colleagues had conducted an earlier retrospective analysis of 89 TBI patients given ESAs and found a significant survival benefit.

To validate those findings, they conducted a prospective, observational study of patients with severe TBI who were admitted to the surgical intensive care unit at Los Angeles County and University of Southern California Medical Center between Jan. 1, 2009 and Dec. 31, 2010.

Of 566 patients, 75 were given ESAs, and these patients were compared with matched controls not given the agents.

All ESAs were given within the first two weeks of hospital admission, and administration lasted two weeks.

There were no baseline differences between cases and controls in terms of demographics, injury severity, or any other variable, the researchers said.

They found that those given ESAs had significantly lower inhospital mortality than those not given the agents (9.3% versus 25.3%, OR 0.25, 95% CI 0.08 to 0.75, P=0.012).

At the same time, there were no differences in any major inhospital complications, including deep vein thrombosis and pulmonary embolism (1.3% of ESA patients versus 0% of controls for both), acute respiratory distress syndrome, acute renal failure, or pneumonia.

ESA patients did, however, have significantly longer lengths of stay in the surgical ICU (mean 16.1 days versus 8.6 days, P<0.001) and in the hospital overall (22.2 days versus 12.9 days P<0.001). There also was a trend toward increased anemia severity in the ESA group, with significant differences on hospital days zero, five, and 10, but the researchers noted that there was no overall difference in transfusion of blood products.

Talving and colleagues explained that in TBI, ESAs may mediate anti-inflammatory and anti-apoptotic responses, and also may enhance angiogenic properties by recruiting endothelial progenitor cells in brain tissue.

This is possible because erythropoietin is present in the central nervous system, because erythropoiesis-secreting tissues are widely distributed in humans, and because erythropoiesis receptors are expressed in human neurons, glia cells, astrocytes, and cerebral endothelial cells, they wrote.

The study was limited because patients weren't randomized to receive ESAs, but rather were given the agents at the discretion of their treating physician.

Talving and colleagues called for a large randomized controlled trial to validate their findings before it can be concluded that ESAs offer a survival edge for TBI patients.