SCCM: Epoetin Alfa Reduces Death Risk For Critically Ill Trauma Patients

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The finding of the so-called EPO3 study -- the third randomized controlled trial to examine the role of the role of epoetin (Procrit, Epogen) -- was a surprise to investigators, said Howard Corwin, M.D., of Dartmouth Medical School in Hanover, N.H.

A similar result had been seen in a post-hoc subgroup analysis of the earlier EPO2 trial, published in 2002, but researchers thought it was just "noise," Dr. Corwin told a latebreaker session at the Critical Care Congress of the Society for Critical Care Medicine.

Now, he said, "I believe the finding is real. If someone in my family were in a car accident and came into the ICU, I would want them to have erythropoeitin."

However, the benefit was not seen in non-trauma patients, whether they were surgical or medical, Dr. Corwin said.

The earlier studies had concluded that treatment with epoetin reduced the need for red blood cell transfusions, but had no clinical benefit, Dr. Corwin said.

The placebo-controlled EPO3 study began in December 2003 and ended last June, It was intended to enroll more patients, have a longer safety follow-up, and prospectively revisit the subgroup effect.

A central difference was that the transfusion guidelines were changed to reflect today's more conservative approach, he said: as long as hemoglobin levels remained above 9 g/dL, transfusion would only take place if there was a clear indication for the procedure.

The primary endpoint was the percentage of patients transfused at day 29, Dr. Corwin said, and here there was -- again surprisingly -- no difference between the placebo and epoetin.

The finding is probably a function of the study size and more conservative modern transfusion guidelines, he said: "People are transfusing less, so the ability to see a difference is less."

A secondary endpoint was mortality at day 29 and overall, there was no difference between the arms.

But among trauma patients, 6.7% of placebo patients died, compared to 3.5% of those on epoetin. The odds ratio was 0.52, with a 95% confidence interval from 0.28 to 0.99.

By comparison, the odds ratio seen in the EPO2 study was 0.43, Dr. Corwin said.

The use of the cytokine, though, carries the risk of adverse cardiovascular events. Among the trauma patients, the researchers found a 40% increase in the risk of thrombotic events, which was statistically significant. On the other hand, Dr. Corwin said, trauma patients getting heparin at the same time did not have a significantly greater risk of thrombosis.

The researchers concluded that epoetin (along with heparin) should be given to trauma patients.
whose ICU stay was expected to be three days or more, but should not be used in surgical or medical non-trauma patients.

The finding that the cytokine had no effect on transfusions shouldn't be surprising, commented Clifford Deutschman, M.D., of the University of Pennsylvania Medical School in Philadelphia.

"We're transfusing much less often, so a difference might not show up," said Dr. Deutschman, who moderated the latebreaker session.

And the finding about mortality is a simple reminder that "nothing is as simple as we think it is," he said. "If there's a mortality benefit, it points to a biological effect (of epoetin) that we don't understand yet."

The study was sponsored by Johnson & Johnson, which sells recombinant erythropoietin alpha under the brand name Procrit. Dr. Corwin reported having received support from the company.

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