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RESEARCH NEWS

The Risk of Hematopoietic Growth Factor Therapy in Newborn Infants

A review of: Casadevall N, Nataf J, Viron B *et al*. 2000 Pure red-cell aplasia and antierythropoietin antibodies in patients treated with recombinant erythropoietin. New Engl J Med 346:469–475

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THE HEMATOPOIETIC GROWTH factors, erythropoietin (Epo), (Tpo), granulocyte macrophage colony-stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) have been used or suggested for use for the treatment of anemia, thrombocytopenia or neutropenia in newborn infants.

Are they needed and are they safe? Epo is the most commonly used of these factors. I have discussed previously (1) the current status of Epo therapy for newborns concluding that there is neither or only rarely an indication for its use and that its safety in newborns remains to be established. Noted also were the side effects of slow weight gain, thrombocytosis, and neutropenia along with the potential toxicity of the accompanying iron therapy.

A recent report suggests that a more serious side effect of Epo could develop, specifically pure red cell aplasia. Casadevall *et al*. (2) described severe transfusion-dependent anemia in 13 adults who had been treated with Epo for the anemia of renal disease. The anemia was caused by a failure of erythrocyte production, and bone marrow aspirates revealed an absence of red cell precursors. These are the features of pure red cell aplasia. This disorder occurs as a result of tumors or parvovirus infection, as a congenital failure of red cell production (Blackfan-Diamond syndrome), or as an autoimmune disease. In the latter instance antibodies or cytotoxic lymphocytes are directed against red cell precursors.

In the studies reported by Casadevall *et al*., all the patients had formed IgG antibodies directed against Epo. *In vitro*, the antibodies reacted with a variety of forms of recombinant Epo. In severe anemia Epo levels are raised however in these patients Epo was undetectable in 10 and normal (but not elevated) in three. This indicated that the antibody had reacted with the patients' Epo, lowering its level and thereby interfering with the production of red blood cells. The authors refer to three previously reported cases and, as an addendum to their article, nine additional cases. To date, there are no reported instances of anti-Epo antibodies and/or pure red cell aplasia in newborn infants who had received Epo. Nevertheless, because of the potential for inducing severe disease, Epo therapy in the newborn must be considered only when there is incontrovertible evidence of need and effectiveness.

This consideration should apply to the use of other hematopoietic growth factors in newborn infants. G-CSF and GM-CSF has been used for the treatment of neutropenia associated with severe neonatal infections. The existing evidence suggests that neither of these agents has been definitively proven to be effective in the newborn and antibodies against these factors have developed in humans following treatment (3, 4). The anti-GM-CSF antibody inhibits the action of GM-CSF, whereas the anti-G-CSF antibody does not inhibit G-CSF. Tpo has not been used in the newborn; however, it has been proposed for the treatment of thrombocytopenia (5). A recent report describes three adults who received Tpo and developed persistent thrombocytopenia, secondary to the development of anti-Tpo antibodies (6).

At present there is little or no convincing evidence for the use of hematopoietic growth factors in newborn infants. Indeed the evidence suggests that great caution should be exercised in their use because of the potential for harm.

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