Variations in Antithrombotic Use Affect Bleeding Risk in Hemodialysis

The data from a large international study of patients receiving hemodialysis showed a wide variation in antithrombotic therapy, along with an increased risk of bleeding among patients receiving oral anticoagulants (OACs), reports Kidney International.

In more than 48,000 patients enrolled in nine clinical trials and five observational studies and prospective patterns study, the researchers assessed variations in antithrombotic therapy and major bleeding events. The study also sought to identify risk factors for stroke and bleeding events in this very large and diverse patient population.

The use of all categories of antithrombotic agents varied widely among countries: from 0.3% to 18% for OACs, 3% to 25% for anti-platelet agents (APAs), and 8% to 36% for aspirin. The rates of major bleeding events also varied widely: from 0.05 to 0.22 events per year. In adjusted analyses, receiving OACs were at increased risk of all-cause and cardiovascular mortality as well as bleeding events requiring hospitalization. Antiplatelet agents were also associated with increased all-cause and cardiovascular mortality.

In patients with atrial fibrillation, the CHADS2 score was a significant predictor of stroke risk. Gastrointestinal bleeding within the past year was a strong predictor of bleeding risk: for patients with one such event the bleeding rate was at least twice as high as the stroke rate. This was so at all levels of CHADS2 score and among patients at high risk of stroke.

The results show a wide variation in the use of antithrombotic agents in patients receiving hemodialysis, with increased bleeding risk in patients receiving OACs. Both OACs and APAs are associated with increased mortality. “Appropriate risk stratification and a cautious approach should be considered before OAC use in the dialysis population,” the researchers conclude [Sood MM, et al. Major bleeding events and risk stratification of antithrombotic agents in hemodialysis: results from the DOPPS, Kidney Int 2013; 84:606-608].

Copper Deficiency Plays Role in Cysteine Toxicity

Patients with cystinosis and cysteine toxicity show evidence of copper deficiency—suggesting that copper supplementation might prevent cysteine toxicity, reports a study in the Journal of Pediatrics.

Laboratory tests for copper deficiency performed in 30 patients with cystinosis. Of these, 22 had renal Fanconi syndrome (FS), including seven with signs of cysteine toxicity, including bruise-like lesions and/or red skin striate. Twelve patients had undergone kidney transplantation, one was receiving hemodialysis, and one had oculocutaneous.

Cystinuria copper excretion was increased in all 22 patients with FS. Nine patients—including seven with cysteine toxicity—had decreased serum copper and ceruloplasmin levels, while one had normal copper levels. Ascorbic acid and vitamin C intake were similar in patients with and without cysteine toxicity.

Genetic testing, tests including the copper transporter, lipoyl, and type I procollagen genes, showed no specific variations associated with cysteine toxicity. There were no differences in fibroblast (procollagen) synthesis in a comparison of three patients with and two without cysteine toxicity.

Cysteine toxicity was recently described as a complication of high-dose cysteine therapy in patients with cystinosis. There are clues that cysteine may interfere with collagen synthesis.

The new study shows that cysteine toxicity is associated with copper deficiency, with no evidence of relevant genetic abnormalities. Copper deficiency may cause decreased activity of lipoamide, a low molecular weight critical regulator of collagen cross-linking. The researchers conclude, “[T]he administration of copper supplements should be considered in patients with cystinosis, especially in those with FS” [Bew MTP, et al. Copper deficiency in patients with cystinosis with cysteine toxicity. J Pediatr 2013; 163:754-760].

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