Preventive hemophilia A treatment reduces annual bleeding events and frequency of infusions

January 9 2012

A Rush University Medical Center led international research team has announced that a treatment to prevent bleeding episodes in children with hemophilia A also is effective for adolescents and adults.

The preventive therapy will "optimize care for hemophilia patients of all ages by stopping unexpected bleeding events that can have a detrimental impact on the lives of patients," said Dr. Leonard Valentino, director of the Rush Hemophilia and Thrombophilia Center and principal investigator on the study. The study results appeared in the January online version of the *Journal of Thrombosis and Haemostasis*. Valentino is associate professor of Pediatrics at Rush University's Rush Medical College.

The study, sponsored by Baxter Healthcare Corporation, was conducted as part of a comprehensive clinical study of ADVATE Antihemophilic Factor (Recombinant), Plasma/Albumin Free Method (rAHF-PFM) to compare the effectiveness of two prophylactic treatment regimens, as well as between on-demand and prophylaxis treatments, in preventing bleeding in previously treated patients with severe or moderately severe hemophilia A. It is the first study designed to generate prospective data for stringent comparisons of bleeding rates.

Hemophilia A is a rare, inherited, potentially deadly blood clotting disorder that affects 400,000 people worldwide, most of them males.

Approximately one in 5,000 individuals is born with hemophilia annually.

In people with hemophilia A, a protein called clotting factor VIII is either absent or present at low levels. Factor VIII replacement, such as rAHF-PFM, is considered the treatment of choice for managing hemophilia A patients who lack inhibitors (antibodies) of factor VIII.

About 90 percent of people who have hemophilia have type A. Of these, 70 percent have the severe form of the disorder, indicated by a factor VIII level of less than 1 percent of normal.

Patients with severe disease are at particular risk for spontaneous bleeding into joints, muscles and internal organs, as well as trauma-induced bleeding following injury and surgery. Joint bleeding may occur as frequently as 20 to 30 times a year, resulting in clinically significant hemophilia-related arthritis. "The main goal of replacement therapy is to prevent this pathology," Valentino said.

Primary prophylaxis is already the standard of care for children with hemophilia A. It is believed that the early initiation of prophylaxis may confer a protective effect against factor VIII inhibitor, the most serious complication associated with replacement therapy. Adult hemophilia patients are treated either in response to bleeding (on demand) or with regular infusion of clotting factor to prevent bleeding and further joint damage. However, while on-demand treatment can slow the progression of hemophilia-related arthritis, it does not seem to prevent the condition.

In the Rush study, one regimen was based on common practice with every-other-day dosing. The other was customized for each individual based on the drug's activity in the body (pharmacokinetics, or PK) with every-third-day dosing. PK-tailored prophylaxis offers an alternative to standard prophylaxis for the prevention of bleeding.

Study participants aged 7 to 65 years received six months of on-demand treatment with dosing dependent on the severity and type of bleeding episode. After completing the on-demand treatment period, subjects were randomized to receive 12 months of either standard or PK-tailored prophylaxis treatment. Once the prophylaxis period began, factor VIII levels were assessed every three months.

Of the 66 subjects in the study, 22 (33.3 percent) who received prophylaxis had no bleeding episodes, in contrast to the patients treated on demand. No subject developed factor VIII inhibitors. The patients who achieved these results were adherent to the prescribed number of prophylactic infusions.

Compared with on-demand treatment, both prophylaxis regimens significantly reduced bleeding, including spontaneous and traumatic hemorrhaging, and improved the quality of life for adolescent and adults patients. Results of the study suggest that prophylaxis is the optimal treatment for patients with severe hemophilia. Data from the study also confirm and extend the safety and effectiveness of rAHF-PFM for controlling and preventing bleeding in the management of hemophilia A.

The study findings suggest that the PK-tailored prophylaxis regimen, which used similar amounts of rAHF-PFM and one fewer infusion per week, is a viable treatment alternative to standard prophylaxis. The availability of this option could increase treatment adherence, particularly in children and adolescents, for whom compliance with long-term medical regimens is especially challenging. Additionally, the study confirms and extends the safety and effectiveness of rAHF-PFM for controlling and preventing bleeding in the management of hemophilia A.

Provided by Rush University Medical Center