Standard aplastic anemia therapy improves patient outcomes better than newer version

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A comparison clinical study of two aplastic anemia treatments found that ATGAM, currently the only licensed aplastic anemia drug in the United States, improved blood cell counts and survival significantly more than did Thymoglobulin, a similar but reportedly more potent treatment. The research was funded by the National Heart, Lung, and Blood Institute (NHLBI), a part of the National Institutes of Health; the study participants were treated and then followed at the NIH Clinical Center in Bethesda, Maryland.

The study will appear in the August 4 New England Journal of Medicine.

"This important study compared the clinical effectiveness of two drugs with similar mechanisms of action. Doctors and patients need to know the most effective therapy for severe aplastic anemia, a rare life-threatening disorder," said Susan Shurin, M.D., acting director of NHLBI.

While Thymoglobulin is not licensed for aplastic anemia in the United States, it has been reported to be effective when used in patients who did not respond or who relapsed following ATGAM treatment. Thymoglobulin is the only aplastic anemia option available in Europe, Japan, and Latin America. Thus, the findings of this study have implications for management of this disorder internationally.

"This study suggests that ATGAM should remain the first-line regimen of choice in treating severe aplastic anemia," said NHLBI hematologist

Phillip Scheinberg, M.D., a lead author on the study.

Aplastic anemia is a rare blood disorder, newly diagnosed in approximately 600 patients in the United States every year. Most patients are children or young adults. The disease destroys bone marrow and lowers the number of functional blood cells in the body. Bone marrow failure can lead to anemia, hemorrhage, and increased risk of infections. In its severe form, aplastic anemia is often fatal if not treated. Aplastic anemia can occur for a number of reasons, including benzene exposure, radiation, hepatitis, or an inherited defect. In most cases, the patient's own immune system destroys the marrow.

ATGAM and Thymoglobulin are drugs known as antithymocyte globulins or ATGs. They work primarily by suppressing the immune system. ATGAM is derived from the blood of horses injected with human blood cells, while Thymoglobulin is derived from the blood of similarly immunized rabbits. Thymoglobulin's past positive results in relapsed patients, plus its preferred use in other clinical situations such as kidney transplants, suggested that it might be superior to ATGAM as a first therapy for aplastic anemia.

The NIH study was designed to compare the two ATG drug types as treatments for severe aplastic anemia. The research team enrolled 120 patients from 2 to 77 years of age, who were randomly assigned to either the horse or the rabbit ATG (60 participants in each group).

Six months after starting treatment, 68 percent of patients given ATGAM had improved blood cell counts, compared to 37 percent of patients given Thymoglobulin. After three years, survival was also significantly different. Ninety-six percent of ATGAM patients survived, compared to 76 percent of Thymoglobulin patients.

"It is difficult to do head-to-head studies in rare diseases such as aplastic

anemia," Scheinberg said. "Our ability to carry out this trial underscores the importance of having referral centers, such as the NIH Clinical Center, for rare diseases. We would like to recognize and honor the patients who came to Bethesda for the frequent treatments and follow-up visits. Their tremendous cooperation and participation was essential in carrying out this study."

Scheinberg added that this study also shows the need to conduct randomized clinical trials for all drugs and to not just rely on assumptions, even if they are based on seemingly solid evidence. "A stronger drug is not necessarily a better drug."

This important finding may affect the future treatment of aplastic anemia, particularly in places like Europe where ATGAM is not currently available. It may also inspire further studies that compare horse and rabbit ATG to better understand how ATG helps restore bone marrow.
Since some patients responded very well to Thymoglobulin and others responded poorly to ATGAM, future work might identify the optimal ATG treatment for specific patient subgroups.

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