A blood substitute's effectiveness and safety addressed in large clinical trial

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A predicted shortfall of over 4 million units of blood worldwide is driving the need to develop an alternative to red blood cells.

Academic and industry researchers participated in a Phase III multi-center clinical trial and found that use of a blood substitute was relatively safe in patients under 80 years old who have a moderate need for transfusion, up to the equivalent of three units of regular blood.

Published in the June edition of the Journal of Trauma, this study is the first Phase III trial to compare a blood substitute to regular blood and was conducted at 46 sites in the United States, Europe and South Africa.

"The majority of patients who received the blood substitute did well," said Dr. Jonathan Jahr, study lead author and professor of clinical anesthesiology, David Geffen School of Medicine at UCLA.

The six-week study involved 688 patients, ages 18 and older, undergoing elective orthopedic surgery, since these procedures often have a high need for blood transfusions. Patients initially received either one unit of blood, which is about a pint, or received an equivalent one unit or 65 grams of a blood substitute product called HBOC-201, a hemoglobin-based oxygen carrier, manufactured by Biopure Corporation.

Made from a bovine source after multiple purifications, HBOC-201 can be kept at room temperature for up to three years and does not need to be matched to one's blood type.

Patients could receive up to 10 units of the blood substitute during a six-day period, or for those in the study group receiving regular blood, unlimited transfusions. Subjects were evaluated daily and six weeks post-operatively.

"We found that we eliminated the need for blood transfusions for 59 percent of the 350 patients who received the blood substitute," said Dr. Colin F. Mackenzie, study author, professor and former director, National Study Center for Trauma & EMS, University of Maryland School of Medicine. "The blood substitute worked best in those under 80 years old with a moderate transfusion need."

For those over age 80 with more acute health issues and higher transfusion needs, the blood substitute did not work as well as blood. As a result, many of these patients were crossed over into the group to receive regular blood.

A number of adverse events involving the cardiac and central nervous systems were found in 21 of these older patients who received the blood substitute. Analysis revealed that the issues were due to advanced age, heart failure or possibly under-treatment.

"For this specific older acute patient population, we suggest using a blood substitute only if blood is not available. These patients also need to be carefully monitored for vascular volume status and avoidance of fluid overload," said Dr. A. Gerson Greenburg, study author and vice president, medical affairs, Biopure Corporation.

Mortality rates in both study groups with moderate transfusion needs were low -- at one percent. The higher transfusion need groups reported a five percent mortality rate in the blood substitute group and a three percent rate in the group receiving regular blood, which are comparable according to researchers.

Many of the less serious adverse effects seen in the overall group receiving the blood substitute were due to temporary expected physiologic effects of this class of drugs which can include skin discoloration interpreted as jaundice, elevation of blood pressure and the rise of levels in the enzymes troponin and lipase.

"Although these temporary side effects didn't lead to any clinical problems in most patients, these should be studied in future trials," said Jahr.

The majority of the 350 patients in the study arm using the blood substitute received an average of five or less units. A total of 338 patients receiving blood were given less than 2 units on average.

"This product has a definite place where blood is not an option, such as in patients whose immune system attacks red blood cells or those whose religion forbids blood transfusions and in situations where blood is not available," said Mackenzie.

The next stage of research will include studies in military and trauma situations and further studies in anemia and ischemia.

Source: University of California - Los Angeles