U.S. Department of Health and Human Services
NIH News
National Institutes of Health

National Heart, Lung, and Blood Institute

http://www.nhlbi.nih.gov

For Release
March 26, 2009

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The NHLBI Halts Study of Concentrated Saline for Patients with Shock Due to Lack of Survival Benefit

The National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health has stopped a clinical trial studying the benefits and safety of administering a highly concentrated form of saline solution in the ambulance (before hospital arrival) to trauma patients suffering from shock due to severe bleeding. The trial was stopped because patients who received the concentrated saline solutions were no more likely to survive than those who received a normal saline solution. A parallel study of concentrated saline for traumatic brain injury without shock continues.

Typically, in the crucial early minutes before blood transfusions can be safely administered in the hospital, trauma patients receive normal saline solution intravenously in the field to compensate for blood loss and buy time. Concentrated saline solution is believed to compensate for blood loss more effectively, lessen excessive inflammatory responses, and prevent brain swelling.

The trials of concentrated saline solutions are conducted through a network of clinical research sites in the United States and Canada called the Resuscitation Outcomes Consortium (ROC). A major focus of the ROC is to conduct randomized trials of promising new treatments for severe traumatic injury in real-world settings.

“Survival from traumatic injury is a critical public health issue and the large clinical trials under way in this effort are needed to improve the treatment of patients. Of course, it is always disappointing when new therapies, such as concentrated saline for shock, fail to offer added benefit to patients. However, we look forward to results from the other ongoing studies that are part of this important research consortium,” said Elizabeth G. Nabel, M.D., director of the NHLBI, the lead federal sponsor of the research effort.

The NHLBI suspended enrollment into the concentrated saline (hypertonic) shock study on Aug. 25, 2008, due to concerns raised by ROC’s Data and Safey Monitoring Board (DSMB), an independent group monitoring the study. In the shock trial, the DSMB observed no difference among the treatment groups in 28-day mortality. However, more of the patients receiving hypertonic saline died before reaching the hospital or in the

emergency department, while more of the patients receiving normal saline died during the remainder of the 28-day follow-up period.

The DSMB requested further analysis of these observations. The additional analysis looked at in-hospital data (following saline administration in the field) from 545 patients in the largest enrolling hospital from each site. The results, presented to the DSMB on Feb. 25, 2009, confirmed the previous findings that deaths occurred earlier in patients who received hypertonic saline and that there was no significant difference in cumulative mortality between the hypertonic and normal saline groups at 28 days. However, the new analysis did not fully explain the mortality findings. The investigators are completing analyses of these results and will submit them for publication in a peer-reviewed scientific journal.

Although there were no similar concerns about earlier mortality in the traumatic brain injury trial, this trial was also temporarily and voluntarily suspended last August so that emergency medical service (EMS) personnel could be retrained to enroll only brain injury patients, not those who would have been eligible for the shock study. The traumatic brain injury study resumed in late November 2008.

ROC is a research network of nine major regional clinical centers in the United States and Canada focusing on treating patients who collapse with cardiac arrest or with life-threatening traumatic injury before they reach the hospital. Under the various research protocols, participating EMS providers give standard emergency care to all patients, with some patients eligible to receive the experimental treatment in addition to usual care. The clinical trials are conducted under strict FDA and well defined Canadian guidelines that allow for patients in life-threatening situations to participate in research under an exception to informed consent, according to U.S. and Canadian law.

In both the shock and traumatic brain injury ROC hypertonic saline trials, patients were randomly selected to receive either approximately 8 ounces of intravenous normal saline, which has nearly the same concentration of salt as blood and is considered standard care; approximately 8 ounces of hypertonic saline, which has a higher salt concentration; or about 8 ounces of hypertonic saline with dextran, a carbohydrate which can prolong the effect of the hypertonic saline. The stopped trauma shock study tested whether hypertonic solutions improve survival by 28 days after injury, compared to usual care with normal saline.

The now-resumed trial of brain- injured patients continues to investigate whether the hypertonic solutions improve both survival and brain function in patients 6 months after traumatic injury. As the traumatic brain injury study continues, ROC investigators hope that hypertonic saline will prove beneficial for this application. “Patients with traumatic brain injury have significant swelling of the brain, and hypertonic fluids are known to be very effective at reducing this swelling, which may improve recovery,” said Eileen Bulger, M.D., the University of Washington, Seattle, and co-principal investigator of the hypertonic saline studies.

“Hypertonic saline has also been shown to improve blood flow to the brain after injury and to protect nerve cells from increased intracranial pressure,” added David Hoyt, M.D.,

University of California, Irvine, the other co-principal investigator of the hypertonic saline studies.

The NHLBI is the lead sponsor of the ROC studies with additional funding provided by the NIH's National Institute of Neurological Disorders and Stroke, the Institute of Circulatory and Respiratory Health of the Canadian Institutes of Health Research, U.S. Army Medical Research & Materiel Command, American Heart Association, Defence Research and Development Canada, and the Heart and Stroke Foundation of Canada.

For additional information about ROC, see: https://roc.uwctc.org/tiki/tiki-index.php. To interview an NHLBI spokesperson, contact the NHLBI Communications Office at 301-496-4236 or at nhlbi news@nhlbi.nih.gov. To interview Dr. Bulger, contact Susan Gregg-Hanson at 206-616-6730; to interview Dr. Hoyt, contact John Murray/Tom Vasich at 714-456-7759.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at www.nhlbi.nih.gov.

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