Progesterone for traumatic brain injury tested in phase III clinical trial

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Researchers at 17 medical centers across the country soon will begin using the hormone progesterone to treat patients who experience traumatic brain injury (TBI). The treatment is part of a randomized, double-blind Phase III clinical trial that will enroll approximately 1,140 people over a three- to six-year period beginning in March, 2010. The trial is funded by a grant to Emory University from the National Institutes of Health.

The clinical trial is led by David Wright, MD, associate professor of emergency medicine at Emory University School of Medicine. Atlanta's Grady Memorial Hospital will serve as the lead center, with faculty from Emory School of Medicine and Morehouse School of Medicine.

Wright will discuss progress in clinical trials using progesterone for TBI at the American Association for the Advancement of Science (AAAS) Annual Meeting in San Diego.

Emory researchers concluded in an earlier three-year clinical trial conducted in 100 patients that giving progesterone to trauma victims shortly after a brain injury appears to be safe and may reduce the risk of death and long-term disability. That clinical trial was called ProTECT I (Progesterone for Traumatic brain injury - Experimental Clinical Treatment). The current trial is named ProTECT III.

The earlier trial found evidence that progesterone is safe for use in patients suffering from traumatic brain injuries. Results also showed a

50 percent reduction in mortality in those patients treated with progesterone. The treatment improved functional outcomes and reduced disability in patients with moderate brain injury.

Progesterone is naturally present in small but measurable amounts in the brains of males and females. Human brain tissue is loaded with progesterone receptors. Laboratory studies suggest that progesterone is critical for the normal development of neurons in the brain and exerts protective effects on damaged brain tissue.

Donald G. Stein, PhD, Asa G. Candler Professor of Emergency Medicine, Emory School of Medicine, and director of Emory's Department of Emergency Medicine Brain Research Laboratory, pioneered discoveries regarding the effect of progesterone following traumatic brain injury - first discovering the neuro-protective properties of progesterone in the laboratory more than 25 years ago.

Every 15 seconds, someone in the United States sustains a significant traumatic brain injury. Approximately 2 million adults and children in the United States suffer from traumatic brain injuries each year - leading to 50,000 deaths and 80,000 new cases of long-term disability, according to the Centers for Disease Control and Prevention. Despite the enormity of the problem, scientists have failed to identify effective medications to improve outcomes following a traumatic brain injury.

"No new treatment for severe TBI has been approved in over 30 years," says Wright. "With such promising success in laboratory testing and in our previous clinical trial, we hope to conclude in this national trial that progesterone-along with standard medical trauma care-works better than standard medical care alone in reducing brain damage caused from a TBI."
Site principal investigators for the proTECT III trial at Grady Memorial Hospital in Atlanta will be Michael Frankel, MD, Emory professor of

neurology, and Jeffrey Salomone, MD, Emory associate professor of surgery. The trial will be conducted through the Neurological Emergencies Treatment Trial (NETT) network coordinated by the University of Michigan. Data analysis will occur at the Medical University of South Carolina.

Exception from Informed Consent (EFIC)

As part of the trial, patients who are enrolled in the study may be provided the progesterone hormone without consent of family members or next-of-kin, in large part because success of the drug is highly dependent on its being administered to the patient as quickly as possible after sustaining a brain injury.

According to Wright, researchers normally get permission (consent) before a person participates in a clinical study. If that person is unconscious, such as in a traumatic brain injury (TBI), they will be unable to consent for themselves. In these cases researchers will ask for permission from a person's legal guardian (usually next of kin). However, since TBI must be treated quickly, there might not be enough time to locate and talk to someone about the study before the medication is started.

"In ProTECT III, a person might very well be enrolled in the study without a legal guardian's or family member's consent," explains Wright. "The U.S. Food and Drug Administration (FDA) has, in fact, created a set of special rules, called "Exception from Informed Consent" (EFIC). These rules allow research studies in certain emergency situations to be conducted without consent."

EFIC applies only when all of the following apply: A. The person is in a life-threatening situation; B. Current treatments are unproven or unsatisfactory; C. The study might provide direct benefit to the person;

D. It is not possible to obtain informed consent from: 1) the person because of his or her medical condition or 2) the person's guardian because there is a very short amount of time required to treat the medical condition.

Provided by Emory University