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**Progesterone does not significantly improve outcome after traumatic brain injury**

*NIH-funded study reveals treatment does not show benefit over placebo following head injury*

Results of a phase 3 randomized, placebo-controlled clinical trial suggest that progesterone may not significantly improve outcomes in patients who have suffered a moderate to severe traumatic brain injury. The study was funded by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health, and the findings were published in the Dec. 11 issue of the New England Journal of Medicine.

"The trial results were not what we had hoped. Scientists must now redouble their efforts to develop treatments that protect the brain and enhance its natural recovery mechanisms. Most importantly we need to aggressively pursue whether or not the drugs showing promise in animal studies indeed achieve the desired biologic effect in people before moving to late stage trials. Without such indicators we never learn whether we chose the right dose, duration or even the right drug." said Walter Koroshetz, M.D., acting director of NINDS.

The Progesterone for Traumatic Brain Injury, Experimental Clinical Treatment trial (ProTECT- III) study took place at 49 trauma centers across the United States. Eight hundred and eighty two patients were randomized to receive progesterone or placebo within four hours of sustaining head injury. Patients were treated for 96 hours and then closely followed by researchers for six months. The main outcome of this study was recovery at six months after head injury.

The researchers had originally planned to enroll 1140 subjects, but the trial was stopped for futility during a safety review. Based on the data analyzed at that point, the researchers concluded there was no sense in continuing the study because early results suggested no benefit to administering progesterone treatment after head injury.

When researchers compared the treatments, they found that favorable outcomes occurred in 51 percent of patients who received progesterone and 56 percent of patients who received placebo, suggesting that progesterone did not significantly improve outcome after head injury.

“The results are a wakeup call to our current approach to drug development and translation of preclinical evidence of neuroprotection and TBI. This study should lead to intense introspection as to how we are conducting both preclinical drug development studies and clinical trial validation studies for head injury,” said David W. Wright, M.D., Director of Emergency Neurosciences at Emory University School of Medicine in Atlanta, Georgia and lead author of this study.

Progesterone is a hormone that is associated with pregnancy but is also found in the brains of males and females. Animal studies have shown that progesterone may help improve recovery and reduce the extent of brain damage following traumatic head injury. In addition, small clinical trials have suggested that progesterone may be beneficial following head injury.

Progesterone was well tolerated by the subjects in the ProTECT study and was not associated with serious side effects.

Dr. Wright and his colleagues suggest that in order to improve results of clinical trials, cutting-edge research techniques need to be developed, including animal studies that will better predict outcomes of human trials.

“As we move forward, we need to completely overhaul of the process of clinical trial design. We need a radically new approach for reviewing how drugs are assessed in animals, how drugs are prepared for human trials and how trials themselves are designed,” said Dr. Wright.

This study was supported by grants from NINDS (NS062778, NS059032, NS056975).

**Article:**

Wright et al. “Very Early Administration of Progesterone for Acute Traumatic Brain Injury,” *New England Journal of Medicine*, December 11, 2014

For more information about traumatic brain injury, please visit: <http://www.ninds.nih.gov/disorders/tbi/tbi.htm>

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NINDS (<http://www.ninds.nih.gov>) is the nation’s leading funder of research on the brain and nervous system. The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

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