Very early administration of progesterone for acute traumatic brain injury.

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BACKGROUND: Traumatic brain injury (TBI) is a major cause of death and disability worldwide. Progesterone has been shown to improve neurologic outcome in multiple experimental models and two early-phase trials involving patients with TBI.

METHODS: We conducted a double-blind, multicenter clinical trial in which patients with severe, moderate-to-severe, or moderate acute TBI (Glasgow Coma Scale score of 4 to 12, on a scale from 3 to 15, with lower scores indicating a lower level of consciousness) were randomly assigned to intravenous progesterone or placebo, with the study treatment initiated within 4 hours after injury and administered for a total of 96 hours. Efficacy was defined as an increase of 10 percentage points in the proportion of patients with a favorable outcome, as determined with the use of the stratified dichotomy of the Extended Glasgow Outcome Scale score at 6 months after injury. Secondary outcomes included mortality and the Disability Rating Scale score.

RESULTS: A total of 882 of the planned sample of 1140 patients underwent randomization before the trial was stopped for futility with respect to the primary outcome. The study groups were similar with regard to baseline characteristics; the median age of the patients was 35 years, 73.7% were men, 15.2% were black, and the mean Injury Severity Score was 24.4 (on a scale from 0 to 75, with higher scores indicating greater severity). The most frequent mechanism of injury was a motor vehicle accident. There was no significant difference between the progesterone group and the placebo group in the proportion of patients with a favorable outcome (relative benefit of progesterone, 0.95; 95% confidence interval [CI], 0.85 to 1.06; P=0.35). Phlebitis or thrombophlebitis was more frequent in the progesterone group than in the placebo group (relative risk, 3.03; CI, 1.96 to 4.66). There were no significant differences in the other prespecified safety outcomes.

CONCLUSIONS: This clinical trial did not show a benefit of progesterone over placebo in the improvement of outcomes in patients with acute TBI. ( Funded by the National Institute of Neurological Disorders and Stroke and others; PROTECT III ClinicalTrials.gov number, NCT00822900. ).

PMID: 25493974