Traumatic Brain Injury

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Case Overview

Traumatic brain injury (TBI) is a leading cause of death and disability in the United States.[i] Each year, approximately 1.5 million Americans sustain a TBI; of these, 50,000 people die, 230,000 people are hospitalized and survive, and 80,000-90,000 people experience the onset of a long-term disability.1 While public health measures have succeeded in promoting brain injury prevention, there is little actual treatment of TBI available. Sex differences, however, may provide the basis for more effective future treatments.[ii] In animal models of brain injury, females tend to recover faster from a TBI than males.[iii] This clinical finding may be explained by the effect of progesterone, an endogenous steroid hormone with known neuroprotective properties that is present in higher levels in women than in men. Because administration of progesterone has also been demonstrated to aid in TBI recovery of animal models, it is now being considered as a possible treatment option for TBI. How well these findings translate to human populations remains to be fully examined; nevertheless, the study of progesterone provides an example of how an understanding of biologically-based differences may lead to novel medical treatments for challenging diseases.

Patient Profile

- Name: DD
- Age: 50 years
- Sex: Male

Medical History

- NIDDM
- Asthma
- Anxiety
- Depression
- Cigarette smoking
- Weekly binge alcohol use

Prescribed Medication: Unknown.

Presenting Complaint

DD was brought to the Emergency Department (ED) by ambulance after being assaulted while out drinking alcohol. He had been punched and kicked repeatedly to the head, chest, and abdomen, and experienced a loss of consciousness.

Assessment

Initial vital signs were blood pressure of 167/98, heart rate of 110, respiratory rate of 6, and oxygen saturation of 94%. On physical exam, DD had altered consciousness, opening his eyes and moving his body only to noxious stimuli, and confused as to time and location. His initial Glasgow Coma Scale (GCS) was calculated as 12 (classified as “moderate” brain injury). He had lacerations over the right eyebrow and left cheek, and had left periorbital tenderness with associated ecchymosis. Diffuse vertebral tenderness was noted on palpitation of the cervical, thoracic, and lumbar spine. CT scans of the brain, orbits, cervical spine, thoracic spine, and lumbosacral spine were obtained. DD was found to have small bilateral frontal subdural hematomas. He was intubated for airway protection and admitted to the trauma intensive care unit.

Diagnosis

DD was diagnosed with a moderate TBI based on his GCS and persistent mental status alteration.

Hospital Course

DD was extubated on hospital day two, when his alcohol level became undetectable but while he was still experiencing persistent decreased consciousness and confusion. An MRI of the brain on the second hospital day demonstrated structural damage to white matter consistent with diffuse axonal injury. Over the course of several days, DD gradually increased in alertness, although persistent diminished motor and cognitive function eventually required transfer to a rehabilitation facility.

Treatment

Persons with TBI do not have many treatment options. Little can be done to reverse initial brain damage from trauma, so medical personnel simply stabilize the patient, obtain imaging tests and follow the patient’s symptoms to determine the severity of the TBI, and aim to prevent further injury. Patients with mild to moderate TBI generally receive brain and spinal CT scans to check for intracranial bleeding and any fractures or spinal instability. For patients with signs of elevated intracranial pressure, short-term treatments include administration of hypertonic saline[iv], intravascular volume expansion, the administration of antidiuretics and vasopressor agents, or some combination thereof.[v] Long-term treatment for severe cases can involve a variety of rehabilitations services (physical therapy, physiatry, occupational therapy, etc.).

Discussion

TBI results from sudden trauma (an object hitting the head and/or piercing the skull) that causes damage to the brain.[vi] Symptoms range from mild to severe, depending on the extent of brain damage; a person with mild TBI may remain conscious or lose consciousness only for a few seconds. Other symptoms include headache, confusion, lightheadedness, dizziness, blurred vision, fatigue, and trouble with memory, concentration, or attention. Moderate to severe TBI symptoms include additional symptoms such as a severe, persistent headache that does not go

away, repeated vomiting, seizures, inability to wake from sleep, dilation of one or both pupils, slurred speech, weakness in the extremities, or loss of coordination.

Like others suffering TBI, DD received generalized treatment that does not acknowledge potential gender-related factors in TBI medical care. Research has found progesterone to have a neuroprotective quality; in a study measuring cerebral edema following cerebral contusion in rats, females showed significantly less edema than males, and this finding was linked to the increased presence of circulating progesterone in females. [vii] Therefore, it may be that progesterone directly and positively affects females' faster recovery to TBI. Whether progesterone has an effect in the acute phase only, or whether there is any role for progesterone therapy in the rehabilitation stage remains to be seen. Nevertheless, such studies suggest that gender plays an important role in TBI recovery and should be acknowledged when planning treatment.

The National Institute of Neurological Disorders and Stroke (NINDS) has conducted the Progesterone for the Treatment of Traumatic Brain Injury (ProTECT III), a research study to determine if progesterone is useful in limiting the amount of brain damage from TBI. If progesterone, coupled with standard medical care, is found to assist patients with brain injury in recovering more efficiently than standard medical care alone, the treatment of TBI would be greatly improved. A target sample size of 875 participants in hospitals around the United States has already been enrolled as part of the experimental clinical treatment phase. The ProTECT trial was recently halted after the independent Data and Safety Monitoring Board determined that it was unlikely progesterone treatment would demonstrate better outcomes compared to the control.

However, two factors may have limited the ProTECT study's ability to demonstrate an advantage in TBI patients. First, there was tremendous heterogeneity of patients enrolled in the study – including patients with severe non-brain trauma, leading to the consideration that the drug is better studied in a more narrowly defined patient population. Second, it may be that the location-specific nature of progesterone in the brain limited its apparent benefits. In animal models of brain injury, cortical lesion volume and neuronal loss in the medial and lateral ventroposterior thalamic nuclei were significantly less in the female mice than in the male mice. However, in CA3 of the hippocampus and laterodorsat thalamic nucleus, there were no gender differences in neuronal loss. Therefore, neuroprotection is likely to exhibit both regional and gender specificity.[viii]

Future research may find benefit in exploring the use of progesterone as a therapeutic treatment for male patients with moderate to severe TBI. Strong animal model research supports the use of progesterone as a neuroprotective agent. Further, the ProTECT III study demonstrates a model for turning a basic science observation into a potential clinical intervention by acknowledging, rather than ignoring, observed sex differences in animal models.

References:

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