Editorial

Steroids and Traumatic Brain Injury: Time to Revisit?

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Secondary insults such as brain edema are an important and relatively common event occurring after traumatic brain injury (TBI), leading to consequences such as raised intracranial pressure and cerebral herniation. Further, posttraumatic inflammatory changes are known to significantly contribute to neuronal dysfunction.

Pre-2000 Era: Waxing and Waning

Steroids have been used in head injuries since the 1970s. However, "steroids and traumatic brain injuries" can be seen as a multiphase process in its history, starting with a rise, then moving into mixed patterns and then the fall.

Before 2000, many studies were published of which some demonstrated the beneficial role of steroids in head injuries while others concluded against steroid use. Due to these disparities in the outcomes, the evidence provided remained inconclusive. This was mainly thought to be because of the smaller sample size in the majority of the studies, thus leading to great variations in use of corticosteroids in TBI.[1,2]

Renewed Interest

With the promising results of National Acute Spinal Cord Injury Study (NASCIS-2) trial conducted in acute spinal cord injury patients, there was a renewed interest in the role of steroids in head injuries. They showed that high-dose methylprednisolone administered in the early period improves neurologic recovery.[3]

2005: Nail in the Coffin

To provide conclusive evidence regarding the justification of usage of steroids in TBI, the multicentric placebo-controlled randomized Medical Research Council–Corticosteroid Randomisation After Significant Head injury (MRC-CRASH) trial was conducted.[4] The researchers recruited 10,008 TBI patients across 49 countries and patients were given 48-hour methylprednisolone infusion similar to NASCIS-2 trial protocol. They found that steroids were associated with significant increase in risk of death within 2 weeks and concluded that steroids should not be used routinely in TBI. Very soon, based on this level 1 evidence, the Brain Trauma Foundation guidelines also recommended against using steroids in TBI. Thereafter, without any further clinical studies, the research topic of "steroids and head injuries" became archaic and obsolete.

2021: Resurgence?

Recently, Prasad published a retrospective study in which steroids were prescribed to a specific group of TBI patients. In that study, corticosteroids were given in minor TBI cases with contusions and pericontusional edema after 4 to 5 days of trauma.[5] Few studies were quoted which showed that brain edema is biphasic with an initial cytotoxic type and a later vasogenic type. Furthermore, studies have demonstrated that many inflammatory mediators are released after TBI and these may play an important in the development of edema.[6–8] In that study, dexamethasone was prescribed at a mean interval of 7 days after the trauma and the mean duration of treatment was 6.3 days. The authors concluded that the timing of steroid usage and dose of steroids is important key aspects that might determine its efficacy in TBI.[5] Simultaneously, results of a prospective observational diffusion tensor imaging-magnetic resonance imaging-based study (including only brain contusions) were published wherein the authors actually demonstrated that edema around brain contusions is very similar to edema around lesions such as brain tumors which is vasogenic type. They observed that there was reduction in edema volume, a decrease in the apparent diffusion coefficient value, and an increase in the fractional anisotropy values after treatment with dexamethasone in their subjects.[9]

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Future

Looking into these studies, we may note that the results of the CRASH trial may not be applicable uniformly to all cases of TBI and there may be a certain subset of patients who may actually benefit from corticosteroids.

There may be few reasons for the gross discrepancy in the observations between CRASH trial and the recent two studies:

First, steroids were given within 8 hours in the CRASH trial, during which the edema is actually cytotoxic and steroids have no role in cytotoxic edema.

Second, TBI is a heterogeneous entity with respect to the radiological appearance. There may be subarachnoid hemorrhage, subdural hematoma (SDH), diffuse axonal injury, etc. and it is probably unwise to categorize all of them into one common entity of TBI. The CRASH trial included all types of severe head injuries such as diffuse edema, acute SDH, contusions, whereas the latter included only mild TBI cases with contusions with pericontusional edema.

Third, the dosage of steroids used in the CRASH trial was similar to the NASCIS trial that was high-dose methylprednisolone. Spinal cord and head injuries are different entities and hence, similar dose steroids may not be effective or rather harmful in TBI.

In the latter two studies, both the dose and formulation were different, wherein low-dose dexamethasone was prescribed to their patients

Looking into these recent observations, is it the time to revisit the role of steroids in TBI? The phrase "one size doesn't fit all" aptly fits into this context. Prospective, multicentric studies can probably provide definite answers to this enigmatic question.

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G. Lakshmi Prasad designed and drafted the manuscript. Deepak Agarwal revised the manuscript and gave final approval.

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Conflicts of Interest
None declared.

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