Lithium in traumatic brain injury – A Literature Review

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INTRODUCTION

Consultation-liaison (CL) psychiatrists are frequently consulted to assist with the management of lithium in traumatic brain injury (TBI) patients. There are currently no clinical guidelines to help inform these decisions. This paper aims to provide a review of the existing literature on the use of lithium in the management of the neurocognitive and neuropsychiatric sequelae in TBI patients.

METHODS

The databases Ovid MEDLINE, EMBASE, APA PsychInfo, and CINAHL were searched for the 27 articles included in this review.

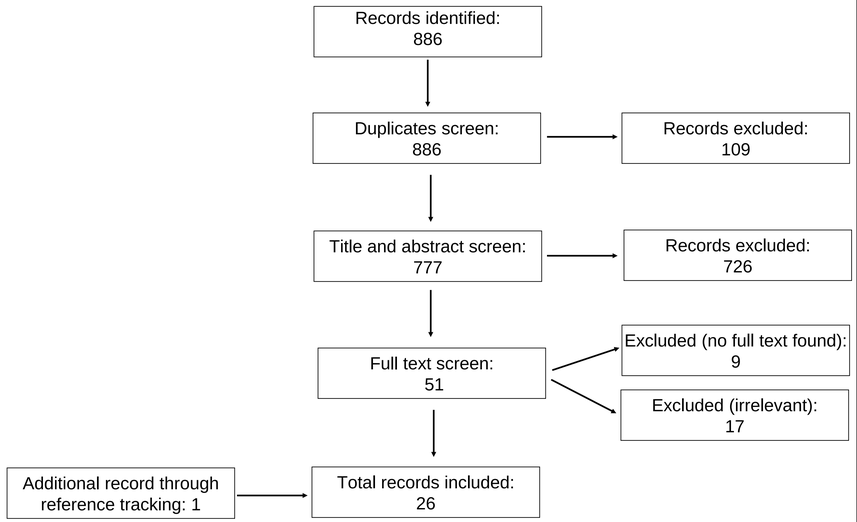

Figure 1: Study Selection

RESULTS

Treatment of neuropsychiatric sequelae of TBI with lithium:

- TBI treated with lithium showed a reduction in aggressive incidents, need for seclusion, and need for increased observation.
- Lithium's beneficial effects on neuroinflammation, neuronal protection, and functional recovery, raising the possibility of using it to treat the neuropathological processes associated with TBI.
- Lithium's use in management of impulse control disorders post-TBI. Adding lithium to medication regiments of TBI patients resulted in a significant reduction in agitation and behavioral issues.

Treatment of neurocognitive sequelae of TBI with lithium:

- Lithium has been found to be helpful in treating the neurocognitive sequelae of TBI. Combination of medications, including lithium and carbamazepine, showed improvement in the capability to semi-independently carry out daily activities.
- Lithium's mechanism of releasing norepinephrine and increasing serotonin turnover, impacting learning and behaviour.
- Animal studies - lithium treatment after the onset of post-TBI symptoms helped manage hyperlocomotor activity, anxiety-like behaviours, and impaired motor coordination, enhanced memory and spatial learning, alleviated of depressive symptoms. Chronic pre-treatment with lithium resulted in extensive neuroprotection, a decrease in lesion volume, neurodegeneration, and spatial learning and memory impairment post-TB. This could be due to reduction in interleukin-1β expression, brain oedema, hippocampal neurodegeneration, and loss of tissue in the hemispheres after lithium treatment. a significant increase in GSK-3β phosphorylation, followed by an increase in β-catenin and a decrease in neuronal loss in the hippocampus.
- The same model found a reduction in neuronal death and considerable mitigation of inflammation normally brought about by microglial activation, cyclooxygenase-2 induction, Aβ load, and metalloproteinase-9 expression. The blood-brain barrier's integrity was also protected.
- Improved neurotransmission of dopamine in the striatum post-TBI has also been shown after treatment with lithium. Also shown to inhibit 5-HT auto-receptors, suppress pro-apoptotic factors, enhance long-term potentiation, and enhance cytoprotective factor Bcl-2.
- Post-TBI calcium dysregulation can potentially be normalized using lithium, as it can prevent excess calcium release by suppressing IP3R activity and inhibit binding proteins that augment IP3R-mediated calcium release.

Increased toxicity risk:

- Close monitoring of lithium levels is necessary in TBI patients due to the risk of neurotoxicity and the difficulties in monitoring TBI patients' serum levels.
- Other therapeutic measures to be considered prior to using lithium in TBI patients – lithium's small therapeutic window and compliance issues.
- Significant lithium toxicity was observed when lithium was combined with carbamazepine, other anticonvulsants, and ECT. TBI- induced mania treated with ECT resulted in ECT-induced delirium.

Variable levels of effect:

- Varying levels of improvement in their post-TBI neuropsychiatric symptoms when treated with lithium. – transient, moderate, or marked improvement in their aggressive behaviour and affective instability
- A case report showed lithium was found to paradoxically increase aggression.
- Lithium's mechanism of inhibiting the release of norepinephrine and increasing serotonin turnover affected learning and behaviour and believed that removing it would account for behavioural gains.

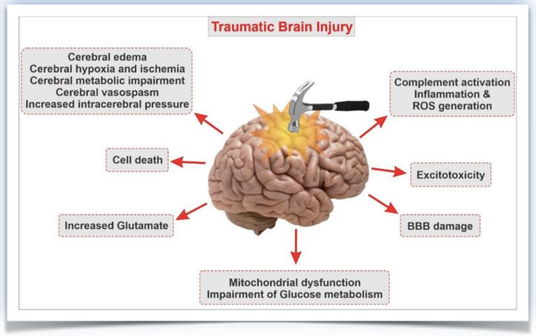

Figure 2: Effects of TBI

DISCUSSION

No clinical or dosing guideline could be established using the current body of literature, but some broad guidelines could be drawn. Patients may neurocognitively benefit from their lithium being maintained post-TBI, given the results of animal studies, and may benefit neuropsychiatrically from treatment with lithium post-TBI. A significant gap in the literature with regards to this subject was identified, and future research directions were identified.

CONCLUSION

The current body of literature pertaining to lithium and TBI is not sufficient to produce any sort of formal guideline around the use of lithium in patients pre-treated with that medication and currently admitted for TBI. However, we were able to examine lithium's use as an effective treatment for the neurocognitive and neuropsychiatric sequelae of TBI; and we were able to examine lithium's possible neuroprotective role in TBI. While we provided some broad guidelines using the existing evidence, more research around this question is essential for medical practitioners to be able to make safe decisions around this medication in their practice, and for the eventual establishment of clear practice guidelines.