A Comparison of Therapeutic Agents Used for the Reduction of Intracranial Pressure Following Traumatic Brain Injury

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Introduction

In neurotrauma care, a better understanding of treatments following traumatic brain injury (TBI) has led to a significant decrease in morbidity and mortality in this population. TBI represents a significant medical problem, and complications following TBI are associated with the initial injury and post-event intracranial processes such as elevated intracranial pressure (ICP) and brain edema. Consequently, appropriate therapeutic interventions are required to reduce brain tissue damage and improve cerebral perfusion. We present a contemporary review of literature on the use of pharmacologic therapies to reduce intracranial pressure following TBI and a comparison of their efficacy.

Methods

This review was conducted by PubMed query. Only studies discussing pharmacologic management of patients following TBI were included. This review includes prospective and retrospective studies and includes randomized controlled trials as well as cohort, case-control, observational and database studies. Systematic literature reviews, metanalyses, and studies that considered conditions other than TBI or pediatric populations were not included.

Results

Review of the literature describing the current pharmacological treatment for intracranial hypertension following TBI most often discussed the use of hyperosmolar agents such as hypertonic saline (HTS) and mannitol, sedatives such as fentanyl and propofol, benzodiazepines, and barbiturates.

Results

Hypertonic saline is associated with faster resolution of intracranial hypertension and restoration of optimal cerebral hemodynamics, although these advantages did not translate into long term benefits in morbidity or mortality. In patients refractory to treatment with hyperosmolar therapy, induction of a barbiturate coma can reduce ICP, although requires close monitoring to prevent adverse events.

Table 1. Summary of Literature Findings

Therapy	Dosing Modality	ICP Reduction within 1 Hour (range)	Notes
HTS (3-30%)	Bolus	7.1 - 24.5 mmHg	
Mannitol (20%)	Bolus	0 - 7 mmHg	
Barbiturates (Pentobarbitol, Thiopental)	Bolus Loading dose followed by maintenance	0 - 14.9 mmHg No change	
Propofol	Continuous	7.3 mmHg	
Fentanyl	Continuous	8.22 mmHg	
Midazolam	Continuous	No change	When comparing midazolam to propofol, equivalent effect on ICP reduction and similar value for cerebral perfusion pressure; propofol associated with increase in serum triglyceride levels, not observed with midazolam
Dexmedetomidine	Continuous	No change	Reduced need for bolus mannitol/HTS in patients with refractory ICP elevation
Sufentanil	Bolus	No change	
Cistracurium	Bolus	No change	Safe for use in patients with elevated ICP for neuromuscular blockade

Most common administration of each of the treatments included in the study with a range of reduction of ICP within 1 hour following administration, if available.

Learning Objectives

1.Discuss the intracranial pressure (ICP) and brain edema following TBI.

2.Identify the different therapeutic agents used for the reduction of intracranial pressure following traumatic brain injury.

3.Compare therapeutic agents used for the reduction of intracranial pressure following traumatic brain injury.

Conclusion

HTS exhibits beneficial advantages compared to the other medications as a first line treatment of intracranial hypertension in patients with severe TBI. It is associated with a higher efficacy, improved treatment outcomes, and reduced mortality rates as compared to mannitol, sedatives and barbiturates. The current guidelines do not support the use of HTS as an official recommendation due to a lack of formal comparative studies, and suggest that further investigation is still required (1). In patients refractory to treatment with hyperosmotic agents, induction of a barbiturate coma can help to reduce ICP and exert neuroprotective effects. Induction of barbiturate coma is a level II recommendation by the Brain Trauma Foundation for patients refractory to maximal surgical and primary medical interventions (1).

References

1. Carney N TA, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery 2016; 80(1): 6-15.