

Barbiturate coma treatment in children with refractory intracranial hypertension due to traumatic brain injury; is it useful?

Abstract

In pediatric severe Traumatic Brain Injury (TBI) the appearance of refractory intracranial hypertension is related to an unfavourable prognosis. Severe TBI (ECG <8) is present in 60% of polytrauma children and is associated with high morbidity and mortality. The monitoring of intracranial pressure (ICP) and the treatment of intracranial hypertension have been subjects of attention in neurotrauma for years in the evidence-based guidelines currently being a topic of discussion.

Currently the guides based on evidence showing acceptance of some guidelines for the management of intracranial hypertension, within the most accepted of sedatives/analgesics, hyperosmolar agents (hypertonic saline solution HTS and mannitol) and barbiturates, although the level of evidence of these recommendations is insufficient to standardize such management in the centers of attention.

Keywords: pediatrics, brain injury, traumatic brain, intracranial hypertension, barbiturates

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Irina Suley Tirado Pérez,¹ Andrea Carolina Zárate Vergara²

¹Medical Epidemiologist, Pediatric student, Corporación Universitaria Remington (CUR)

²Medical Epidemiologist, Pediatric Intensive Care, Universidad de Santander (UDES) – Clinic Specialist The Concepcion, Colombia

Correspondence: Andrea Carolina Zárate Vergara, Medical epidemiologist, Pediatric Intensive Care, Universidad de Santander (UDES) – Colombia,
Email andreacarolinazaratevergar@gmail.com

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Introduction

The intracranial vault is composed of three elements: brain (80%), cerebrospinal fluid (CSF) (10%) and cerebral blood volume (CBV) (10%). When thinking about the physiology of the brain, it is essential to consider the Monro-Kellie doctrine that states any individual component of the intracranial vault can suffer alterations, but the total volume remains fixed as space within the skull is fixed. Therefore, any increase in one of these components will cause a change outside the box or increase the pressure inside the box. The brain has certain normal compensatory mechanisms to maintain normal (intracranial pressure) ICP. Once these compensatory mechanisms are exhausted, a small increase in the volume will result in a large increase in the ICP.^{1,2}

Review

Intracranial pressure monitoring can be used as a guide for treatment. Current guidelines suggest:

- ICP monitoring can be considered in infants and children with severe ECT (Glasgow com scale: 3–8)
- ICP monitoring is not routinely indicated in patients with mild or moderate head injury; The clinician may choose to monitor ICP in certain conscious patients with massive traumatic injuries who are at relative risk of neurological impairment or in whom the serial neurological examination is prevented by sedation, neuromuscular blockage or anaesthesia.

The elevated ICP in pediatric TEC or causes a secondary brain injury. ICP monitoring is the important and established method of management after trauma. The range should be considered according to the patient's age, Table 1. Supporting circulation, airways and breathing are the basis of therapy. Head lift, sedation, analgesia, or therapy and hyperventilation can rapidly decrease ICP.²

In cases of refractory HIC, the protocols indicate the following forms of treatment: less and less controversial hyperventilation, hyperosmolar therapy or high dose barbituric richand decompressive craniectomy. Among mechanical therapies, one should think about

the elevation of the child's head, keeping the cervical spine stable (excluding trauma and / or cervical injuries). The head in elevation of 30° compared to the rest of the body can help in the drainage of blood by decreasing volumes and ICP.^{1,2}

Table 1 Normal intracranial pressure (ICP)

Normal ICP for age	
Age	Normal range (mmHg)
Adult	<10-15
Children	7-15
Term infants	1.5-6

Adapted from reference.²

There is evidence of several drugs used in this scenario for example, the evidence that the continuous infusion of Propofol <4mg/kg/h for periods >48 h can be considered, however, still not being approved by the FDA at which recommends handle with caution the continuous infusion of propofol in Pediatric Severe Traumatic Brain Injury. As for bolus medication, propofol is sometimes used briefly as an adjuvant for procedural sedation. In however, it considers that the use of Propofol after trauma may be associated with the induction of apoptosis due to the expression of the receptor increase neurotrophin P75, sensitizing the brain neurotoxic effects in young neurons.^{3,4}

In one article of *New concepts in treatment of pediatric traumatic brain injury* published in the American journal Anesthesiology Clinics, in the treatment of hypertension intracranial refractory can also be used hyperosmolar solutions it is that they are hypertonic saline to the 3% in doses of 0.1 to 1 ml /kg/hour or mannitol in doses of 0.25 to 1 g /kg. It is important to remember that the serum osmolarity must be less than 320mOsm/L for the use of hypertonic saline. Although mannitol has been traditionally administered, hypertonic saline solution at 3% is gaining place as a therapy for HIC.^{3,6}

Etomidate could be useful as therapy of bolus episodes intracranial hypertension because of their profile hemodynamic; however, its use is often limited at the time of intubation. It has been linked to effects such as adrenal insufficiency.^{5,6}

Thiopental can cause life-threatening hydroelectrolytic disorders, especially about potassium. Dexmedetomidine has been reported to induce hypertension at high infusion doses ($> 4 \mu\text{g}/\text{kg}/\text{h}$) for several hours. Other reports have indicated the appearance of bradycardia, which is more evident when this agent is combined with another drug that produces a negative chronotropic effect.^{3,4,6,7}

Metamizole is often used, as an analgesic first non-opioid line for adults in many countries, but its use in controversial pediatrics even in most developed countries is contraindicated in children.³

Discussion

It is known that barbiturate coma therapy is a useful method to control the increase in intracranial pressure to refract medical and surgical treatments. Its effect in decrease ICP for effect of decreasing cerebral metabolic rate but may cause hemodynamic instability significant. The pentobarbital to the most barbiturate used. Its use is considered when osmotherapy and hyperventilation does not maintain an ICP of less than 25 mmHg, which may be more frequent than the four-hour dose of osmotic diuretics or hypertonic saline solution or induced hypocapnia. If the infusion of barbiturates cannot control ICP, as defined by persistent ICP greater than 25 mm Hg, decompressive craniotomy or one of the other second level therapies, it should be considered, recognizing once again that the order of use of second level therapies are at the discretion of the clinician and often vary from center. In patients with ICP maintained less than 20 mm Hg for 24 hours while receiving a stable dose of pentobarbital infusion, the infusion may decrease and then withdrawn for 24-96 hours.

During barbiturate infusion therapy, close attention should be paid to the state of cerebral perfusion and volume, as well as MAP (mean arterial pressure) and CPP (cerebral perfusion pressure). Vasopressors are often necessary to maintain adequate CPP. There are limited pediatric studies to show the effectiveness of barbiturate, some studies have shown an improved ICP with good results. Similarly, studies in adults also reported that pentobarbital is an effective treatment to decrease ICP. However, some studies have shown no benefit in the outcome or even a worse neurological outcome. Barbiturates produce cardiac suppression, which may cause hypotension, therefore, adequate hemodynamic monitoring and inotropic support should be provided during barbiturate therapy. The possible negative effects of common use of barbiturates can be divided into short or long term. Short-term difficulties relate mainly to undesirable hemodynamic side effects, that is, a decrease in MAP resulting in a decrease in CPP that may further exacerbate the brain damage caused. Continuous propofol infusion is associated with Propofol Infusion Syndrome (PRIS), which is characterized by the appearance of metabolic acidosis, rhabdomyolysis, acute renal failure, cardiac dysrhythmias and hyperlipidemia.^{1,9-11}

Furthermore should bear in mind what's effects side as disorders electrolyte mainly alteration potassium either hypokalemia which is related phosphofructokinase inhibition results in a shift of potassium into intracellular compartment to hyperkalemia rebound which is believed is related to the reduction of those induced by barbiturates. Activity of $\text{Na}^+ - \text{K}^+ - \text{ATPase}$ in addition to the replacement of potassium to correct hypokalemia, these are managed according to the guidelines of critical care in pediatrics.^{9,10}

Conclusion

The ICP decreases using barbiturate coma for the management

of refractory intracranial hypertension. However, it cannot be recommended as a first-line drug for the treatment of intracranial hypertension in children with traumatic brain injury. Barbiturate coma determines arterial hypotension, with the consequent compromise of cerebral perfusion pressure, which is a factor of poor prognosis. Therapy with high doses of barbiturates may be considered in patients hemodynamically stable exhibiting HIC refractory, although after 1 drug or surgical treatment. It is recommended to maintain continuous monitoring of blood pressure and cardiovascular support to maintain cerebral perfusion pressure. More studies are needed for its recommendation in the neuro-monitoring guidelines worldwide in pediatrics.

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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