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MONOTEMÁTICO SOBRE TRAUMA CRANEOENCEFÁLICO

Pathophysiology of severe traumatic brain injury

Fisiopatología de la lesión cerebral traumática severa

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KEY POINTS

- Primary Injury: injury for the traumatic event itself, the direct impact in the neural tissue with ischemia, contusion and hemorrhage.
- Secondary Injury: occurs after the primary injury that starts secondary cellular phenomena in the neural tissue:
  Early Phase: interruption of the blood flow with hypoxia
  Intermediary Phase: neuroinflammation, activation of the microglia
  Late Phase: regeneration and self-repair
- Cerebral blood flow auto regulation, primary measures to treat ICP elevation and ICP monitoring in severe TBI are also described.

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INTRODUCTION

Traumatic brain injury (TBI) is a complex entity involving a group of organs disorders who start with a brain injury. It can be caused by many different etiologies, such as traffic accidents, fire gun shots, falls (more commonly seen in pediatric and elderly people), among many other.

Despite several improvements in traffic legislation, such as helmets obligation for motorcycles, seatbelts for all passenger and also advances in neuro critical care, traumatic brain injuries still cause a lot of victims. It accounts for approximately 40% of all deaths from acute traumatic injury in the United States. Annually, 200,000 victims of TBI require medical attention. By this reason, it is an economic and social problem involving a large amount of money for prevention, assistance and rehabilitation.

TBI can be classified by its severity according to the Glasgow Coma Score (Table 1).

Other forms of classification TBI is according to its causative mechanisms

(penetrating versus non penetrating) or extension (focal or diffuse) (Table 2).

PATHOPHYSIOLOGY

TBI is divided in two events, primary and secondary injuries. Primary injury results from the trauma event itself caused by physical mechanisms like a direct collision of the brain tissue against the skull base and or vault at a tangible speed submitting brain tissue into different kinds of deformation: compressive, tensile (tissue stretching) and shear (tissue distortion produced as a result of sliding over other tissue). These lesions lead to neurons, glial cells and vessels damage, giving rise to hematoma, brain swelling and also traumatic axonal lesions.

Secondary injury occurs due to cellular phenomenon that occurred after primary injury and can be divided in three phases: early; intermediary and later phase.

Early phase of the secondary injury starts from the ischemic cascade initiated by interruption of normal blood flow. Reduced blood flow and oxygen metabolism cause a disruption of normal energy processes by switching usually aerobic process to anaerobic pathway. The decrease of glucose metabolism and the lactic acid accumulation cause reduction on ATP levels and lead to ATP-powered pump failure. There is a Ca^{++} influx and mitochondrial disorder. This ischemic cascade results in excitotoxicity, induced apoptosis process and cellular death.

Intermediary phase is characterized by neuro inflammation. TBI compromises the selective blood-brain-barrier (BBB) characteristics, allowing flow of chemical messengers and immune cells to brain tissue.

There are many triggers to start the TBI-Inflammation such as cellular debris, complement fragments, prostaglandins and reactive oxygen and nitrogen species. The inflammation response produces two effects on brain tissue: damage and regeneration. The activation of microglia results in recovery by phagocytosis of debris. However, production of pro-inflammatory of cytokines (IL1-β, IL-6, TNF-α) and chemokines encourage the expression of adhesion molecules on blood vessels which allows migration of leukocytes into brain tissue and continue with inflammatory process progression.

In a late phase, a modified neural circuitry is formed due to a regeneration tissue and self- repair process.

In this zones, epileptic focus can be seen as a result of an imbalance between excitatory potentials and inhibitory which affects the synchronous entrainment of neuronal nets.

Cerebral blood flow autoregulation

In the context of severe TBI, all of these events mentioned above induce both cytotoxic and vasogenic edemas, which will lead to a disruption of the intracranial components volume equilibrium according to Monro- Kellie doctrine. This hypothesis suggested that the cranial compartment volume is constant and its main contents (blood, brain tissue and cerebral spinal fluid) are incompressible.

These three main contents are in equilibrium, and an increase of one requires compensation by decreasing the volume of the other, what is called a compensatory mechanism.

Cerebral spinal fluid (CSF) dislocation to the spinal canal, decrease and increase on CSF production and absorption respectively, vasoconstriction are all examples of compensatory mechanisms to decrease intracranial pressure (ICP). In pathological context of imbalance, when compensatory mechanisms start to failure, ICP tends to

increase and sustained values above 20 mmHg are considered pathologic. Under pathological conditions, increased ICP decrease cerebral perfusion pressure (CPP = MAP - PIC, where MAP is the mean arterial pressure).

Under physiological conditions, mechanisms of auto regulation are capable to keep cerebral blood flow (CBF) constant with MAP values between 60-160 mmHg. This constant CBF is necessary to allow adequate cerebral perfusion and oxygenation. TBI severely affects the auto regulation and consequently CBF, leading to low perfusion brain areas and potential isquemia. Situations of high ICP or low MAP prejudice CBF even more leading to low CPP, that is associated with a higher mortality rate.

PRIMARY MEASURES TO TREAT AN ELEVATE INTRACRANIAL PRESSURE

Initial management of patients requires basic life support based on ABC algorithm. Hemodynamic support is mandatory, hypotension is common after TBI and should be aggressively treated, but the use of vasopressors or excessive fluid resuscitation can also increase the cerebral edema, requiring caution in the traumatic scene.

Ventilatory support is also mandatory, especially in patients with severe TBI injury who are comatose.

Blood concentration of CO2 influences significantly ICP. Higher PaCO2 results in dilated cerebral vessels and increase blood volume in the intracranial compartment, increasing ICP. Values above 40mmHg can substantially raise ICP. Hyperventilation is described as a transitory treatment in such cases, but, on the other hand, it may also result in vasoconstriction and consequently reduction of CBF and hypoxia.

Others important measures for control ICP includes neutral neck and head positioning, elevation of patient's bed at 30 degrees (to improve venous return), avoidance of hyperthermia and hyperglycemia, recognition and treatment of early seizures.

Fever is common in TBI patients and is associated with a worse outcome and accelerated neuronal damage. The exact mechanism of hyperglycemia harmful effect is not completely elucidated. Some authors have reported that hyperglycemia leads to endothelial dysfunction.

It induces an augmentation of the inflammatory activity.

Intracranial pressure monitoring in severe traumatic brain injury

ICP monitoring is important for treatment and outcome of TBI patients. There are different modalities of ICP monitoring. The most common ones are subdural, intra-ventricular and intra-cerebral catheter. Some international guidelines recommend monitoring of ICP in all patients with severe TBI and abnormalities on computed tomography (CT) obtained at the time of hospital admission, as well as in selected patients (those who are over the age of 40 years with hypotension or abnormal flexion or extension in response to pain) with a normal CT scan.

As mentioned before, ICP sustained values above 20 mmHg should be treated. Treatment of ICP depends on the causative reason of elevation. A CT scan is necessary to exclude surgical lesions, such as focal hematomas or brain contusions.

Additional therapies for ICP control includes induced hypertension (for improve CPP), osmotic therapy (with mannitol or hypertonic saline solution to improve red blood cells rheological properties allowing better oxygen offer to

tissues, less need of blood flow and consequently vasoconstriction), cerebral fluid drainage (with an external shunt, for instance, that may also be used for ICP monitoring), metabolic suppression (coma induced by barbiturates for decrease neural tissue consumption of oxygen) or even surgical treatment (consisted in decompressive craniotomy to decrease ICP and improves cerebral perfusion) All these procedures are considered second tier therapies and are controversial, once they may decrease mortality but at cost increased morbidity, and should be used in selected cases.

Table 1: Classification according to Glasgow coma score

Traumatic brain injury - Classification by Glasgow coma score	
Classification	**Glasgow Coma Scale(GCS)**
Mild	13-15
Moderate	9-12
Severe	3-8

Table 2: Classification according to injury type (focal or diffuse)

Traumatic brain injury - Classification by extension of lesions	
Classification	**Lesions**
Focal	Epidural hematoma
	Subdural hematoma
	Traumatic subarachnoid hemorrhage
	Contusions
Diffuse	Difuse axonal lesion
	Difuse microvascular lesion
	Hypoperfusion induced lesion
	Brain swelling

RECOMMENDED LECTURES

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Conflictos de intereses

Los autores declaran no tener conflictos de intereses.

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