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Novel Modalities in Management of Acute Brain Injury in Critically Ill patients

An Essay
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Mohammed Mamdouh Hassan El-Hofy

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List of Abbreviations

AA	:	Arachidonic Acid
ABI	:	Acute brain injury
ABP	:	Arterial Blood Pressure
ACE	:	Angiotensin Converting Enzyme
AMPA	:	1-Amino-3-hydroxy-5-Methyl-4-isoxazole Propionic Acid
aPTT	:	activated Partial Thromboplastin Time
ARAS	:	Ascending Reticular Activating System
ATP	:	Adenosine Tri Phosphate
BBB	:	Blood Brain Barrier
CA	:	Cerebral Aneurysm
CAA	:	Cerebral Amyloid Angiopathy
CAT	:	Catalase
CBF	:	Cerebral Blood Flow
CBV	:	Cerebral Blood Volume
$CMRO_2$	:	Cerebral Metabolic Rate of Oxygen
CN	:	Cranial Nerve
CNS	:	Central Nervous System
CPP	:	Cerebral Perfusion Pressure
CSD	:	Cortical Spreading Depolarization
CSF	:	Cerebrospinal fluid
CT	:	Computed Tomography
CVP	:	Central venous pressure
DCI	:	Delayed Cerebral Ischemia
DNA	:	Deoxyribonucleic acid
DTI	:	Diffusion Tenson Imaging
DWI	:	Diffusion Weighted Imaging
EBI	:	Early Brain Injury
ECG	:	Electrocardiogram
EEG	:	Electroencephalogram
ER	:	Extended Release
EVD	:	Extraventricular device
FFP	:	Fresh Frozen Plasma
FOUR	:	Full Outline of Un Responsiveness

List of Abbreviations (Cont.)

GABA	:	Gamma Amino Butyric Acid
GCS	:	Glasgow Coma Scale
GPX	:	Glutathione Pedroxidase
H_2O_2	:	Hydrogen Peroxide
Hb	:	Hemoglobin
HE	:	Hepatic Encephalopathy
HIE	:	Hypoxic Ischemic Encephalopathy
HMG-CoA	:	Hydroxy Methyl Glutaryl Coenzyme A
HSE	:	Herpes simplex encephalitis
Ht	:	Hematocrit
ICH	:	Intracerebral hemorrhage
ICHTN	:	Intracranial Hypertension
ICP	:	Intracranial pressure
IJV	:	Internal Jugular Vein
IL-1	:	Interleukin-1
IL-8	:	Interleukin-8
IL-IB	:	Intrleukin-1B
INR	:	International Normalized Ratio
IVH	:	Intraventricular hemorrhage
MAP	:	Mean Arterial Pressure
MCA	:	Middle Cerebral Artery
MCP-1	:	Monocyte Chemotactic Protein 1
MMP	:	Matrix metaloproteinase
MRI	:	Magnetic Resonance Imaging
NIRS	:	Near Infrared Spectroscopy
NMDA	:	N-Methyl-D-Aspartic Acid
NO	:	Nitric Oxide
NOS	:	Nitric Oxide Synthase
O_2^-	:	Superoxide Anion
OH^-	:	Hydroxyl radical
$ONOO^-$	:	Peroxynitrite

List of Abbreviations (Cont.)

$PaCo_2$	:	Partial Pressure of Carbon Dioxide in arterial blood
PaO_2	:	Partial Pressure of Oxygen in Arterial Blood
$PbtO_2$	:	Brain Tissue Oxygen Tension
PCC	:	Prothrombin complex Concentrates
PEEP	:	Positive End-Expiratory Pressure
pH	:	Power of Hydrogen
Posm	:	Plasma Osmolality
PRES	:	Posterior Reversible Encephalopathy Syndrome
PT	:	Prothrombin Time
ROSC	:	Return of Spontaneous Circulation
rtPA	:	recombinant tissue type Plasminogen Activator
SAE	:	Sepsis associated encephalopathy
SAH	:	Subarachnoid hemorrhage
SBP	:	Systolic Blood Pressure
$SjvO_2$	:	Jugular Venous Oxygen Saturation
SOD	:	SuperOxide Dismutase
SpO_2	:	Peripheral capillary Oxygen Saturation
SSPE	:	Subacute Sclerosing Panencephalitis
TBI	:	Traumatic Brain Injury
TGFb1	:	Transforming Growth Factor beta1
TNF-α	:	Tumor Necrosis Factor-alpha
TTM	:	Target Temperature Management
XO	:	Xanthine Oxidase

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Abstract

Traumatic brain injury (TBI) may be blunt head injuries, penetrating head injuries, and blast head injuries. Also, traumatic brain injury may be mild, moderate, or severe. A Glasgow Coma Score (GCS) of 13 to 15 is considered mild, 9 to 12 moderate, and GCS of 8 or less severe.

Non traumatic brain injuries include vascular brain injuries (acute ischemic stroke, intracerebral hemorrhage and subarachinoid hemorrhage), hypoxic-ischemic brain injury, toxic-metabolic brain injury, inflammatory brain injury and Infectious brain injury (Infectious encephalitis)

The examination of brain injured patient should begin with an assessment of vital signs. Not only this allows evaluation of the stability of the patient, it also provides clues to the etiology of the patient's unresponsiveness e.g. hyperthermia can be seen in midbrain hemorrhage and infection. Similarly, hypertension can be secondary to increased intracranial pressure, or indicative of posterior reversible encephalopathy syndrome (PRES). Hypotension can point toward sepsis or progression to brain death.

The primary goal of the neurologic examination in brain injured patient is to localize the lesion and narrow the differential diagnosis. The examination should proceed in a stepwise fashion and be familiar to the neurologist because of constant repetition. In the process of the comprehensive neurologic examination, the depth of coma should be determined using a coma scale. The Glasgow Coma Scale (GCS) is the most common of such scales.

Head tomography is essential upon suspicion of brain injury and must be the first image requested. It is performed in a few seconds, is available in most emergency services and has good sensitivity to detect bleeding (subarachnoid hemorrhage, subdural hematoma, epidural hematoma, or intraparenchymal hematoma), hydrocephalus, tumors and extensive brain infarcts. On suspicion of meningitis, carry out head tomography whenever possible prior to performing lumbar puncture, since herniation of the brain stem is a real possibility in the presence of intracranial hypertension.

Conclusion

The brain can be injured in many different ways. The type of injury can affect just one or several parts of the brain which are responsible for different functions. Each brain injury is unique, so that symptoms can vary widely. Acute brain injury may be traumatic or non traumatic. Acute brain injury, whatever its cause, is associated with short- and long-term morbidity and mortality.

Keywords: Acute Brain Injury; Critically Ill patients

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Introduction

Acute brain injury (ABI) typically occurs as a result of road traffic accidents, assaults or falls (traumatic brain injury), problems in the supply of blood in the brain such as a bleed (hemorrhage) or blockage (stroke), problems in the supply of oxygen (hypoxia), inflammation or swelling of the brain (encephalitis) ***(Grace et al., 2015)***.

Acute brain injury is a complex disorder, with a wide spectrum of presentation, dependent on the mechanism of injury, ranging from transient alteration in brain function in concussion to coma or death. It can be viewed as a progressive disorder where the primary injury -in the form of hemorrhage, contusion, ischemia or diffuse axonal injury- can initiate a cascade of complex biochemical and metabolic sequences evoking both local and systemic responses ***(Williams et al., 2015)***.

Neurological injury progresses over hours and days, resulting in a secondary injury. Inflammatory and neurotoxic processes result in vasogenic fluid accumulation within the brain, contributing to raised intracranial pressure (ICP), hypoperfusion, and cerebral ischemia. Much of this secondary injury may be amenable to intervention.

Secondary injury also occurs as a result of further physiological insults. Hypoxia, hypotension, hyper- or hypocapnia, hyper- or hypoglycemia have all been shown to increase the risk of secondary brain injury. This is a crucial period when mortality and morbidity can be influenced by interventions to prevent secondary brain injury. Targeted resuscitation and early specialist management have resulted in a decline in mortality over the last few decades ***(Moppett, 2007)***.

Because of long term consequences and costs of acute brain injury from many different etiologies, novel monitoring tools and neuroprotective strategies that can limit secondary brain injury are of obvious importance ***(Stocchetti et al., 2015)***.

Aim of the Essay

The aim of this essay was to discuss pathophysiology of acute brain injury and updated strategies in its management in critically ill patients.

Anatomical and Physiological Aspects of The Brain

The brain lies entirely within the skull. It consists of three parts, that are common to all mammals: the cerebrum, the cerebellum, and the brain stem ***(Bear et al., 2016)***.

The cerebral hemispheres make up the largest portion of the human brain. Each hemisphere consists of 4 lobes: frontal, parietal, occipital and temporal ***(Fig. 1)***. The surfaces of the cerebral hemispheres contain many fissures and sulci that separate the lobes from each other. The sylvian fissure separates the temporal lobe from the frontal and parietal lobes. The insula, a portion of cortex that did not grow much during development, lies deep within the fissure. The circuminsular fissure surrounds the insula and separates it from the adjacent frontal, parietal, and temporal lobes. The central sulcus separates the frontal lobe from the parietal lobe. The parieto-occipital fissure separates the parietal lobe from the occipital lobe. Each lobe has its specialized cortical areas ***(Table 1)***. The hemispheres are separated by a deep median fissure, the longitudinal cerebral fissure. The corpus callosum is a large bundle of myelinated and non myelinated fibers, the great white commissure that crosses the longitudinal cerebral fissure and interconnects the hemispheres ***(Waxman, 2013)***.

The frontal lobe includes not only the motor cortex but also frontal association areas responsible for initiative, judgment, abstract reasoning, creativity, and socially

appropriate behavior (inhibition of socially inappropriate behavior). These latter parts of the cortex are the phylogenetically newest and the most uniquely "human" ***(Waxman, 2013).***

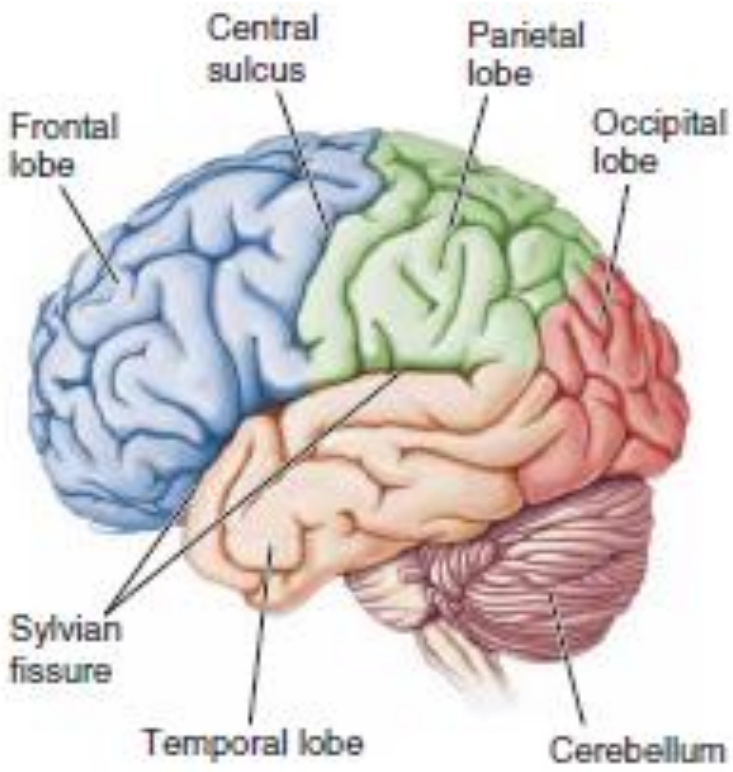

Fig. 1: The lobes of the cerebrum ***(Bear et al., 2016)***

In general, the right cerebral hemisphere receives sensations from, and controls movements of, the left side of the body. Similarly, the left cerebral hemisphere is concerned with sensations and movements on the right side of the body ***(Bear et al., 2016)***.

Table 1: Specialized cortical areas.

	Brodmann's Area	Name	Function
Parietal lobe:	3,1,2	Primary sensory cortex	Somatosensory
Frontal lobe:	4	Primary motor cortex	Voluntary muscle activation
	6	Premotor cortex	
	8	Frontal eye field	Eye movements
	44, 45	Broca's area	Motor aspects of speech
Occipital lobe:	17	Striate cortex = primary visual cortex	Processing of visual stimuli
	18,19	Extrastriate = visual association cortex	Processing of visual stimuli
Temporal lobe:	41	Primary auditory cortex	Processing of auditory stimuli
	42	Associative auditory cortex	
	22	Wernicke's area	Language comprehension

(Waxman, 2013)

The cerebellum is located behind the dorsal aspect of the pons and the medulla. It is separated from the occipital lobe by the tentorium and fills most of the posterior fossa. A thinner midline portion, the vermis, separates the two cerebellar hemispheres. It is concerned with equilibrium and connects with the vestibular system. The paleocerebellum (the anterior portions of the hemispheres and the anterior and