Metabolic Encephalopathy in Intensive Care Unit

An essay
Submitted for fulfillment of master degree in **Critical Care**

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Ain Shams University
(2015)

سورة البقرة الآية: ٣٢

Acknowledgement

*First of all, all gratitude is due to **God** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

*Really I can hardly find the words to express my gratitude to **Prof. Dr./ Bahaa El-Din Ewees Hassan**, Professor of Anesthesia and Intensive care, faculty of medicine, Ain Shams University, for his supervision, continuous help, and encouragement throughout this work. It is a great honor to work under his guidance and supervision.*

*I would like also to express my sincere appreciation and gratitude to **Prof. Dr./ Rasha Samir Abd El-Wahab Bondok,** Professor of Anesthesia and Intensive care, faculty of medicine, Ain Shams University, for his continuous directions and support and effort he have done in the meticulous revision of the whole work.*

*I owe much to **Dr. Dina Salah El-Din Mahmoud,** Lecture of Anesthesia and Intensive care, Faculty of Medicine, Ain Shams University, for her continuous guidance, encouragement during the progress of this work and direct supervision.*

Last but not least, I dedicate this work to my family as well as my wife whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Mohammed Hosni Ahmed

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List of Abbreviations

AA	:	Arachidonic acid
AAA	:	Aromatic amino acids
ACA	:	Anterior cerebral artery
ACOM	:	Anterior communicating artery
ADH	:	Antidiuretic hormone
ATP	:	Adenosine triphosphate
BCAA	:	Branched-chain amino acids
CBF	:	Cerebral blood flow
CBV	:	Cerebral blood volume
CMRglu	:	Cerebral metabolic rate for glucose
CMRO2	:	Cerebral metabolic rate for oxygen
CNS	:	Central nervous system
CNS	:	Central nervous system
CO2	:	Carbon dioxide
CSF	:	Cerebrospinal fluid
EEG	:	Electroencephalogram
EET	:	Epoxyeicosatrienoic
EETs	:	Epoxyeicosatrienoic acids
eNOS	:	Endothelial nitric oxide synthase
G6P	:	Glucose-6-phosphate
GLUT-1	:	Glucose transporter-1
HE	:	Hepatic encephalopathy
HIF-1	:	Hypoxia-inducible factor-1
HK	:	Hexokinase
ICA	:	Internal Carotid Artery
IFNγ	:	Interferon-γ
IL	:	Interleukins
iNOS	:	Inducible nitric oxide synthase
LOLA	:	L-ornithine L-aspartate
MCA	:	Middle Cerebral Artery
MRI	:	Magnetic resonance imaging
NO	:	Nitric oxide
O2	:	Oxygen

List of Abbreviations (Cont.)

PCA	:	Posterior Cerebral Artery
PCOM	:	Posterior communicating
PDE	:	Progressive dialysis encephalopathy
PFK	:	Phosphofructokinase
PGE2	:	Prostaglandin E2
PLA2	:	Lipase and phospholipase A2
RAS	:	Reticular activating system
SAE	:	Sepsis associated encephalopathy
SE	:	Septic encephalopathy
TNF-α	:	Tumor necrosis factor-α
TPN	:	Total parenteral nutrition
UE	:	Uremic encephalopathy
WE	:	Wernicke's encephalopathy

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Introduction

The term encephalopathy is derived from the Greek encephalos (brain) and pathos (suffering or experience). In current times, acute encephalopathy is synonymous with acute confusional state, acute organic brain syndrome or delirium ***(Panayiotis and Carmelo, 2013)***. Encephalopathy is a broad term used for brain dysfunction of varying causes. It manifests as altered mental state, myoclonus tremor, asterexis, seizures, hallucinations, altered sleep wake cycle, delusions, manic behavior and coma which if not treated can lead to decorticate or decerebrate posture and permanent structural change in the brain. Often eye movements are impaired but pupil is normal ***(Chandra et al., 2012)***.

Encephalopathy can result from hypoxia, hypoglycemia, electrolyte imbalance, nutritional, toxic, metabolic, vascular, demyelinating or infective factors ***(Chandra et al., 2012)***. Metabolic encephalopathy, particularly of septic aetiology, is the most common cause of altered mental status in the ICU setting ***(Balasubramanian, 2009)***. The list of causes of diffuse or metabolic encephalopathies is so lengthy that the problem of diagnosis must be resolved by a process of elimination. Drugs and toxins lead all other possible causes, with a frequency of approximately 50% .Hepatic, renal, or pulmonary failure is causative in another 12% and endocrine or electrolyte disturbances in approximately 8%. Other less common etiologies include thiamine deficiency (Wernicke's encephalopathy), cardiac bypass surgery, subacute bacterial endocarditis, and hyperthermia ***(Paula, 2008)***.

Arousal and awareness systems involved in higher cognitive functions suffer when the milieu is deranged. Clinical manifestation are non specific and do not always point to the etiology. However treatment depends on cause and prognosis depends on the cause, extent of damage, duration of

encephalopathy and presence of previous neurological illness. If proper treatment is not given permanent structural damage can occur, hence it is important to recognize and treat early ***(Chandra et al., 2012)***.

The incidence of delirium has been estimated between 5-40% for hospitalized patients in general and between 11-80% for critically ill patients. Other studies have reported a lower incidence of about 30%, after the exclusion of patients maintained in purposeful drug-induced sedation. Many etiologies of acute encephalopathy can be easily detected with neuroimaging as a well visualized structural lesion (ischemic stroke, intracerebral or subarachnoid hemorrhage, tumor etc). A frequent reason for a Neurological consultation, however, remains the non-structural, metabolic syndrome and its management considerations ***(Panayiotis and Carmelo, 2013)***.

Aim of the Essay

This essay will focus on the causes, pathophysiology and management of metabolic encephalopathy.

Physiology of the Brain

The brain tissue is the largest component in the skull. It has a mass of about 1400g and consists of supporting (glial) and neural elements, intracellular and extracellular water. The maintenance of an environment suitable for nerve cell function is achieved by the presence of the blood-brain barrier. The presence of the blood-brain barrier removes the need for lymphatic drainage of the brain. Pathological increase in brain tissue are the result of tumours, increased intracellular water (cytotoxic oedema) or extracellular water (vasogenic oedema) ***(Carl and Bhaskar, 2003).***

Cerebrospinal fluid (CSF) (Fig. 1):

CSF is produced by the choroid plexus in the lateral, third and fourth ventricles by both filtration and active transport (by Na^+/K^+-ATPase and carbonic anhydrase). In normal adults, approximately 20mL of CSF is produced each hour, at a rate of 0.3 ml/minute (500 ml/day), and the CSF volume is 125 to 150 ml. approximately 20 percent of the CSF is contained in the ventricles; the rest is contained in the subarachnoid space in the cranium and spinal cord ***(Whiteley et al., 2006)***.

The CSF has a variety of functions. It helps to ensure a constant supply of glucose and maintains a chemically stable environment, necessary for neurotransmission. It also effectively reduces the mass of the brain to about 50g, which reduces the inertia of the brain and allows rapid head movement without damage to the delicate neural structures (protect the brain from trauma). It also re-circulates interstitial proteins back to plasma (there are no brain lymphatics). It is iso-osmolar compared with plasma, but has a lower concentration of K^+, Ca^{2+}, HCO_3^-, H^+ (pH 7.33), protein and glucose, and a higher concentration of Na^+, Cl^-, Mg^{2+} and carbon dioxide ***(Menon and Summors, 2000)***.

Physiological findings of CSF are summarized in the following tables:

Table (1): Physiological findings of CSF**.**

1) Ions

Substance	Value	% of plasmatic value
pH	7,28-7,32	
Osmolarity	285 mosm/l	
Specific weight	1003-1008	
Na+	135-150 mmol/l	
K+	2,0-3,0 mmol/l	
Ca2+	1,1-1,25 mmol/l	~50 %
Cl-	115-130 mmol/l	>100 %

(Menon and Summors, 2000)

2) Nutrients and proteins

Substance	Value	% of plasmatic value
Glucose (glycorrhachia)	2,2-4,2 mmol/l	~60 %
Proteins (proteinorrhachia)	0,1-0,40 g/l	~1 % (small proteins mostly, immunoglobulins – IgG, IgM)
Lactate	1,1-2,0 mmol/l	
Urea	3-6,5 mmol/l	
Lipids	10-30 mg/l	

(Menon and Summors, 2000)

3) Cells

Type	Value
Erythrocytes	0 / mm3
Lymphocytes	0-5 / mm3
Bacteria	0 / mm3

(Menon and Summors, 2000)

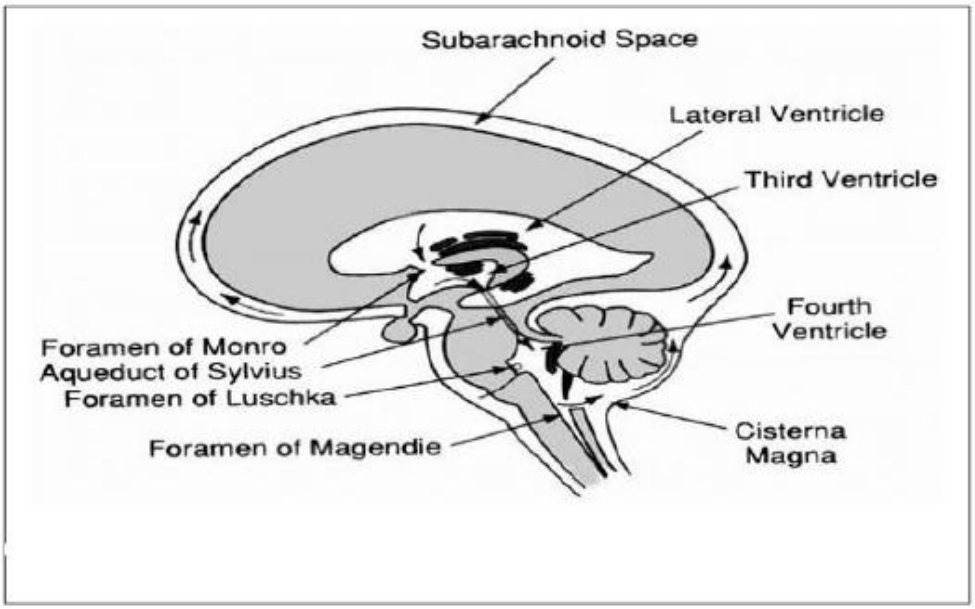

Fig. (1): Cerebrospinal *fluid circulation* ***(Stoelting and Hillier, 2006).***

The Blood-Brain Barrier

The term "blood-brain barrier" is used to describe barrier systems that separate the brain and the CSF from the blood and prevent entry by simple diffusion of fluids, electrolytes, and other substances from blood into the CSF or brain. There are actually two barriers: a blood-brain barrier, and a blood-CSF barrier. Both barriers separate the central nervous system (CNS) from systemic immune responses and affect the composition of the brain interstitial fluid and CSF. The blood-brain and the blood-CSF barriers are not precisely equivalent ***(Paulson, 2002).***

Both brain barrier systems are dynamic. Endothelial cells and astrocytes that compose the blood-brain barrier and cells forming the blood-CSF barrier are capable of producing cytokines such as tumor necrosis factor and interleukins. In addition, astrocytes can act as antigen-presenting cells that modulate the immunologic response to CNS infections. Release of cytokines from endothelial cells and astrocytes