Acute Metabolic Encephalopathy

Essay

Submitted for partial fulfillment of master degree in Intensive care

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2011

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توطئة للحصول على درجة الماجستير
في العناية المركزة

مقدمة من

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2011

Summary

Encephalopathies defined as diffuse, multifocal and functional cerebral disturbances, Metabolic encephalopathies are disorders in which a disturbance of cerebral function results from failure of some other organ system (e.g., heart and circulation, lungs and respiration, kidneys, liver, pancreas or the endocrine glands); in fact in many cases they are multifactorial in origin

Metabolic encephalopathies are most common complications of many diseases in patients treated at intensive care units and their clinical manifestations can be taken as a warning of deterioration or beginning of organ dysfunction.

Most ME is reversible, making prompt recognition and treatment important. But there is certain metabolic encephalopathies result in permanent structural brain damage if untreated rapidly including those caused by sustained hypoglycemia and Wernicke's encephalopathy.

The patients who are most at risk for development of a metabolic encephalopathy are those with single or multiple organ failure, the elderly (older than 60 years of age), those receiving multiple central nervous system toxic agents, and those with severe nutritional deficiencies such as cancer patients and alcoholics. Other risk factors include infection, temperature dysregulation (hypothermia and fever), chronic degenerative neurologic or psychiatric diseases such as dementia or schizophrenia, and endocrine disorders.

Mechanism of metabolic encephalopathies has not been completely understood. The basic precondition is probably a disturbance of blood brain barrier(permeable to endotoxines

ACKNOWLEDGMENT

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

I would like to direct special thanks to prof. **Dr. Fekry Fouad Ahmed El Bokl,** *Professor of anesthesia and ICU, Faculty of Medicine, Ain Shams University, who was very helpful in managing this work and for his keen perception, continuous help, support, and meticulous guidance throughout this work.*

I would like to direct my special thanks and appreciation to prof. **Dr. Nevine Ahmed Hassan Kaschef,** *Assistant Professor of anesthesia and ICU, Faculty of Medicine, Ain Shams University, for his kind supervision, encouragement and moral support throughout this work.*

Also I would like to direct my special thanks and appreciation to **Dr. Amir Kamal Eshak Saleh,** *Lecturer of anesthesia and ICU, Faculty of Medicine, Ain Shams University, for his kind supervision, continuous encouragement and moral support throughout this work.*

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0.9NS	**0.9% sodium chloride in water**
ADH	**Antidiuretic hormone**
ADP	**Adenosine diphosphate**
AMP	**Adenosine monophosphate**
ARAS	**Ascending reticular activating system**
ARDS	**Acute Respiratory Distress Syndrome**
ARF	**Acute renal failure**
ASA	**American Society of Anesthesiologists**
ATP	**Adenosine triphosphate**
BBB	**Blood-brain barrier**
BUN	**Blood urea nitrogen**
Ca^{2+}	**Calcium ion**
CBF	**Cerebral blood flow**
CBV	**Cerebral blood volume**
CKD	**Chronic kidney disease**
CRF	**Chronic renal failure**
Cl^{-}	**Chloride ion**
CN	**Cranial nerves**
CNS	**Central nervous system**
Co_2	**Carbon dioxide**
CPM	**Central pontine myelinolysis**
CPP	**Cerebral perfusion pressure**
CRF	**Chronic renal failure**
CSF	**Cerebrospinal fluid**
CT	**Computed Tomography**
CVA	**Cerebrovascular accident**
CVP	**Central venous pressure**
D_5 W	**5% dextrose in water**
D_{50} W	**50% dextrose in water**
DIC	**Disseminated intravascular coagulation**
DKA	**Diabetic ketoacidosis**
DVT	**Deep venous thrombosis**
ECF	**Extracellular fluid**
ECG	**Electrocardiogram**
EEG	**Electroencephalogram**
EPSPS	**Excitatory post-synaptic potentials**
ETT	**Endotracheal tube**

FHF	**Fulminant hepatic failure**
FOUR	**Full Outline of UnResponsiveness**
GABA	**γ-amino-butyric acid**
GCS	**Glasgow Coma Score**
H^+	**Hydrogen ion**
HCO_3^-	**Bicarbonate ion**
HE	**Hepatic encephalopathy**
HNS	**Hyperosmolar nonketotic state**
ICF	**Intracellular fluid**
ICP	**Intracranial pressure**
ICU	**Intensive Care Unit**
IPSPS	**Inhibitory post-synaptic potentials**
K^+	**Potassium ion**
MAP	**Mean arterial pressure**
ME	**Metabolic encephalopathy**
Mg^{2+}	**Magnesium ion**
MI	**Myocardial infarction**
MRI	**Magnetic Resonance Imaging**
MRSA	**Methicillin-resistant Staph. aureus**
Na^+	**Sodium ion**
NMDA	**N-methyl-D-aspartate**
NMJ	**Neuromuscular junction**
O_2	**Oxygen**
ODS	**Osmotic demyelination syndrome**
PaCO2	**Partial pressure of carbon dioxide**
PaO2	**Partial pressure of oxygen**
PNS	**peripheral nervous system**
P_{osm}	**plasma osmolality**
PTH	**Parathyroid hormone**
RF	**Renal failure**
SIADH	**Syndrome of inappropriate antidiuretic hormone secretion**
TBW	**Total body water**
TSH	**Thyroid-stimulating hormone**
UE	**Uremic encephalopathy**
UOP	**Urine output**

Introduction

Encephalopathy literally means disorder or disease of the brain. In modern usage, encephalopathy does not refer to a single disease, but rather to a syndrome of global brain dysfunction; this syndrome can be caused by many different illnesses***(Supanc et al, 2003)***.

Metabolic encephalopathies can be defined as diffuse, multifocal and functional cerebral disturbances, which are not caused by inflammation, in otherwords, it is not encephalitis, and, at least in the beginning, is not combined with morphologic changes ***(Supanc et al, 2003).***

It is the most common cause of altered mental status in the intensive care unit (ICU) setting, either medical or surgical, (it is most common complication of many diseases in patients treated at intensive care units and their clinical manifestation can be taken as a warning of deterioration or beginning of organ dysfunction), and is also one of the most treatable, so; Early recognition of it is critical to management of the ICU patient***(Supanc et al, 2003).***

Metabolic encephalopathy is always suspected when there is an altered cognitive status in the absence of focal neurologic signs or an obvious anatomic lesion such as an acute cerebrovascular accident or head injury. A patient may progress over days from intermittent agitation into depressed consciousness or quickly into coma without any antecedent signs (e.g., hypoglycemia). In mild cases, it is easily mistaken for fatigue or psychogenic depression, whereas more severe cases may develop into coma and are life threatening ***(Ravin, 2008).***

Patients who appear unconscious lie mostly motionless, usually with the eyes closed and seemingly unaware of their environment. The causes of this condition include normal sleep, depressed consciousness, psychogenic coma, locked-in state, and brain death ***(Lawrence et al, 2008)***.

Sleep

The normal unconsciousness of sleep is characterized by prompt reversibility on threshold sensory stimulation, and maintenance of wakefulness following arousal. The degree of stimulation required depends on the stage of sleep (stage IV non-rapid eye movement sleep is the deepest) and the sensory stimulation used ***(Lawrence et al, 2008)***.

Depressed Consciousness

Consciousness is deemed depressed when suprathreshold sensory stimulation is required for arousal and wakefulness cannot be maintained unless the stimulation is continuous.The spectrum of depressed states (lethargy, hypersomnolence, obtundation, stupor, and coma) is defined by the level of consciousness observed on examination. The degree of depression dependent on the nature of the insult, its duration, and the location and extent of the brain injury***(Lawrence et al, 2008)***.

The first signs of brain dysfunction may be mild and barely noticed. The patient may be described as lethargic or hypersomnolent before progressing to a more depressed state. Hypersomnolent patients maintain arousal only with vigorous and continuous sensory stimulation; while awake; however, they may be oriented and make appropriate responses.

Obtunded patients usually can be aroused by light stimuli but are mentally dulled and unable to maintain wakefulness. *Stuporous patients* can be aroused only with vigorous noxious stimulation. While *awake*, neither obtunded nor stuporous patients demonstrate a normal content of consciousness (if testable), but both may display purposeful movements, as in attempts to ward off painful stimuli or to remove catheters, endotracheal tubes, or intravenous lines ***(Lawrence et al, 2008)***.

Patients in coma are unarousably unresponsive to suprathreshold sensory stimulation, including noxious stimulation that is strong enough to arouse a deeply sleeping patient but not so strong as to cause physical injury. Although the patient usually lies motionless, movements such as stereotyped, inappropriate postures (decerebration and decortication) and spinal cord reflexes (triple flexion and Babinski responses) may occur. Whatever the etiology, the duration of coma is typically no longer than 2 to 4 weeks, after which one of three conditions supervenes: - arousal to full or partial recovery**,** persistent vegetative state **or** death ***(Lawrence et al, 2008)***.

Psychogenic Coma

Patients in psychogenic coma appear comatose but have clinical and laboratory evidence of wakefulness. Psychogenic unresponsiveness may be suggested by active resistance or rapid closure of the eyelids, pupillary constriction to visual threat, fast phase of nystagmus on oculovestibular and avoidance of self-injury***(Lawrence et al, 2008)***.

Locked-in State

In this state, patients have normal consciousness but complete body paralysis, except for vertical eye movements. These patients cannot move their limbs, grimace, or swallow but are able to look up and down and blink. The lesion is typically in the base of the pons but due to sparing of the ascending reticular formation, consciousness is not impaired and patients are fully alert ***(Smith et al, 2005).***

Brain Death

The term brain death refers to a determination of physical death by brain-based, rather than cardiopulmonary-based, criteria ***(Wijdicks, 2001).***

Brain death is the irreversible destruction of the brain, with the resulting total absence of all cortical and brainstem function, although spinal cord reflexes may remain**.** It is not to be confused with severe but incomplete brain damage with a poor prognosis or with a vegetative state, conditions in which some function of vital brain centers still remains ***(Ropper et al, 2004).***

Persistent Vegetative State

Patients in a persistent vegetative state are akinetic, mute and lack outward manifestations of any significant brain activity other than reflex responses. These may include decerebrate or decorticate posturing, deep tendon reflexes, Babinski or triple flexion reflexes, yawning, and so on. The term is usually reserved for the patient who has recovered only to this extent from coma due to a severe anoxic, metabolic, or traumatic brain injury***(Lawrence et al, 2008)***.

Physiology of the brain

The brain tissue is the largest component in the skull. It has a mass of about 1400 g 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 increases 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) (figures 1-1):-

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 20 mL 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 50 g, 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 recirculates 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 et al, 2000)*** .

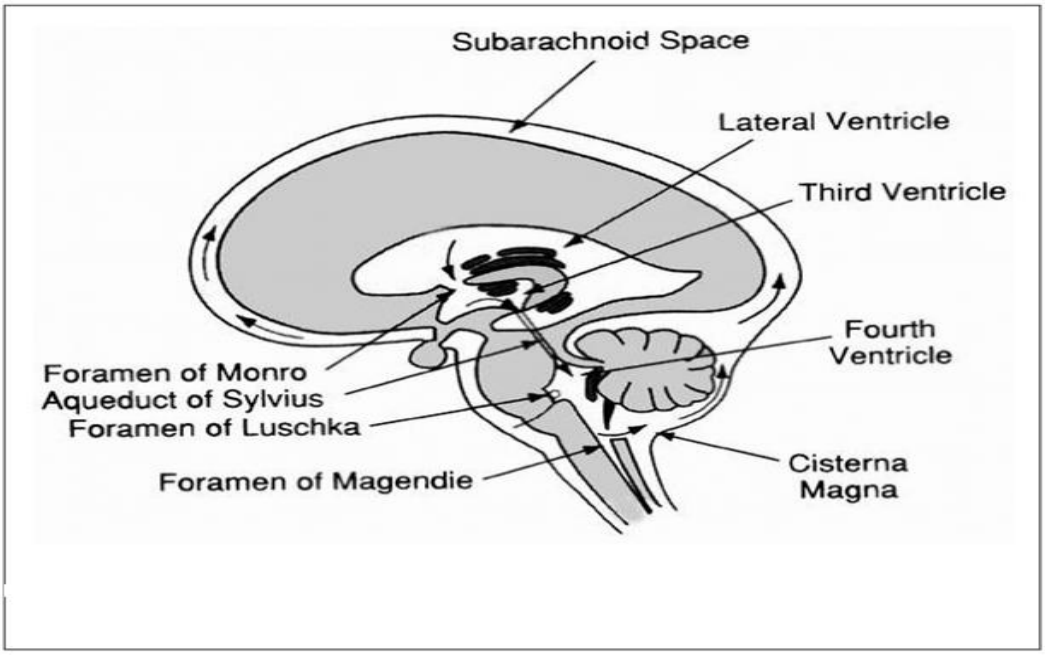

Figure1-1Cerebrospinal *fluid circulation*(***Stoelting et al,2006).***

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