Management of Postoperative Cognitive Dysfunction

Essay

Submitted for partial fulfillment of Master Degree
in Anesthesiology

By

Sarah Ahmed Salem Ahmed Elbadawy
M.B.B.Ch, Faculty of Medicine, Ain Shams University

Supervised by

Prof. Dr. / Galal Abou El-Seoud Saleh
Professor of Anesthesia and Intensive Care
Faculty of Medicine, Ain Shams University

Dr. / Dalia Abd Elhamid Nasr
Assistant Professor of Anesthesia and Intensive Care
Faculty of Medicine, Ain Shams University

Dr. / Mohamed Sayed Shourbagy
Lecturer of Anesthesia and Intensive Care
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2014

Acknowledgement

First, I wish to express my deep thanks, sincere gratitude to ***ALLAH****, Who always helps me, cares for me and grunted me the ability to accomplish this thesis.*

I would like to express my deepest gratitude, thanks and gratefulness to ***Prof. Dr./ Galal Abou El-Seoud Saleh,*** *Professor of Anesthesiology and Intensive Care Medicine, Faculty of Medicine – Ain Shams University, for his enthusiastic support, continuous encouragement, valuable scientific advices and great help throughout the accomplishment of this work.*

My sincere thanks to ***Ass. Prof. Dr./ Dalia Abd El-hamid Nasr,*** *Assistant Prof. of Anesthesiology and Intensive Care Medicine, Faculty of Medicine – Ain Shams University, for her kind and meticulous supervision, support and help all through the work.*

Many thanks and sincere gratitude to ***Dr./ Mohamed Sayed Shourbagy,*** *Lecturer of Anesthesiology and Intensive Care Medicine, Faculty of Medicine – Ain Shams University, for his kind supervision, encouragement and meticulous revision of this work.*

Words can never express my sincere thanks to my family for their generous support and continuous encouragement.

I would like to express my everlasting gratitude to all my dear friends, colleagues and all who offered me any kind of help, encouragement wishing them all the best.

Sara Ahmed Salem Ahmed

List of Contents

Subject *Page No.*

List of Abbreviations ..... **i**

List of Tables ..... **iii**

List of Figures ..... **iv**

Introduction **1**

Aim of the Essay **3**

Chapter (1): Brain Anatomy and Basic Brain Physiology **4**

Chapter (2): Pathomechanism of Postoperative Cognitive Dysfunction **19**

Chapter (3): Diagnosis and Assessment of Postoperative Cognitive Dysfunction **37**

Chapter (4): Prevention and treatment **66**

Summary **80**

References **82**

Arabic Summary ..... **—**

List of Abbreviations

AD	: Alzheimer's disease
ALS	: Amyotophic lateral sclerosis
AMPA	: A-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor
APOEE4	: Apolipoprotein E epsilon 4
ATP	: Adenosine triphosphate
BBB	: Blood Brain Barrier
Ca^{2+}	: Calcium
CaM Kinase II	: Ca^{++} - Calmodulin dependent protein kinase II
CBF	: Cerebral blood flow
CMR	: Cerebral metabolic rate
$CMRO_2$	: Cerebral metabolic rate of oxygen
CPB	: Cardiopulmonary bypass
CVR	: Cerebral vascular resistance
DSM-IV-TR	: Diagnostic and Statistical Manual for Mental Disorders, Fourth edition, Text Revision
EA/ED	: Emergence agitation / emergence delirium
EEG	: Electroencephalograph
GABA	: Gamma amino butyric acid
H^+	: Hydrogen
ICP	: Intracranial pressure
IGF-1	: Insulin growth factor-1
ISPOCD-II	: International Study of POCD-II
ISPOCD-I	: International Study of POCD-I
K^+	: Potassium
LTP	: Long term potentiation
MAP	: Mean arterial pressure

List of Abbreviations *(Cont...)*

MCR	: Muscarinic cholinergic receptors
Mg^{2+}	: Magnesium
MMSE	: Mini Mental State Examination
MRI	: Magnetic resonance imaging
N_2O	: Nitrous oxide
NCR	: Nicotinic cholinergic receptors
NMDA	: N-methyl-D-aspartate receptor
NO	: Nitric oxide
Non-REM	: Non rapid eye movement
$PaCo_2$	: Partial pressure of carbon dioxide
PACU	: Postanesthesia Care Unit
PaO_2	: Partial pressure of oxygen
PKC	: Phosphokinase C
PLA2	: Phospholipase A2
POCD	: Postoperative cognitive dysfunction
POD	: Postoperative delirium
RASS	: Richmond agitation-sedation scale
REM	: Rapid eye movement
VIPergic	: Vasoactive intestinal peptide
5-HT_3	: 5-hydroxy tryptamine, type 3

List of Tables

Table No.	Title	Page No.
Table (1):	Neurotransmitters.	8
Table (2):	Normal Cerebral Physiologic Values.	10
Table (3):	Best Estimates of the Influence of Pure Catecholamine Receptor Agonists and Specific Pressor Substances on Cerebral Blood Flow and Cerebral Metabolic Rate	16
Table (4):	Clinical features of delirium	20
Table (5):	Delirium subtypes	43
Table (6):	DSM-IV-TR diagnostic criteria for delirium	46
Table (7):	Mini Mental State Examination (MMSE)	48
Table (8):	Ramsay Sedation Score	49
Table (9):	The Richmond Agitation-Sedation Scale (RASS)	49
Table (10):	Confusion Assessment Method (CAM)	50
Table (11):	Distinguishing delirium from dementia	53
Table (12):	Distinguishing characteristics of delirium, psychotic disorders and depression	54
Table (13):	Medications with anticholinergic effects	58
Table (14):	Preventive measures for delirium	66
Table (15):	Environmental factors in treating delirium	72
Table (16):	Pharmacologic treatment of delirium	76

List of Figures

Figure No.	Title	Page No.
Figure (1):	Anatomy of central nervous system	6
Figure (2):	The effect of neurotransmitters at synaptic level	8
Figure (3):	Changes in cerebral blood flow (CBF) caused by independent alterations in $PaCo_2$, PaO_2 and mean arterial pressure (MAP)	12
Figure (4):	Time frame of delirium and POCD.	41

Introduction

Cognition is defined as the mental processes of perception, memory and information processing. Cognitive dysfunction is thus impairment of these processes **(Ramaiah and Lam, 2009).**

Perioperative cognitive changes are often overlooked until a patient presents with an agitated delirium several days after surgery. These acute changes in cognitive function, while sometimes dramatic, often are known as "emergence delirium" or "ICU psychosis" and are simply permitted to run their course. Delirium, however, is not a benign disease. Rather, it is associated with a significant increase in postoperative morbidity, disability and death. Recently attention has focused on a broader set of disorders of postoperative cognitive dysfunction (POCD) which may represent a spectrum of organ system dysfunction of varying severity, duration and reversibility. Different age groups can be affected but it is more common in aged persons **(Witlox et al., 2010).**

Cardiac surgery using Cardiopulmonary bypass and major orthopedic surgeries have been the poster child for postoperative cognitive morbidity over the past 10-15 years. However, it has become increasingly clear that disruption or decline in cognitive function is also fairly widespread among elderly non-cardiac surgical patients. Both general and regional anesthesia may contribute to POCD, probably because of the variable depth of accompanying sedation **(Fong et al., 2006).**

Postoperative cognitive dysfunction can present days to weeks after surgery and may remain a permanent disorder. The exact pathophysiological mechanism of POCD is still unknown. POCD is multifactorial in origin but it remains unclear whether its occurrence is a result of surgery or general anesthesia **(Hu et al., 2010).**

Hypoxia, hypothermia, major electrolytes disturbances, lengthy operations, postoperative sleep disturbances, pain, environmental factors, neurodegeneration due to surgery-induced inflammatory reaction in hippocampus and others may contribute to POCD development.

Potential prophylactic intervention may include minimal invasive surgery, multi-modal non-opioid pain management and pharmacological manipulation of the inflammatory response especially against neuroinflammatory response and sleep architecture **(Hovens et al., 2012).**

Aim of the Essay

The purpose of this essay is to discuss postoperative cognitive dysfunction and postoperative delirium as regard etiology, risk factors, incidence, diagnosis, assessment, prevention and management.

Chapter (1):
Brain Anatomy

The nervous system is divided into two components: The central nervous system which is composed of the brain and the spinal cord and the peripheral nervous system, which is composed of ganglia and peripheral nerves that lie outside the brain and spinal cord.

A. The central nervous system: (Figure 1)

The central nervous system consists of six main regions:

I. The cerebral hemispheres:

They consist of the cerebral cortex, the white matter under the cortex and three deeply located nuclei:

1. **The basal ganglia:** The basal ganglia have an important role in regulation of movement and also contribute to cognitive functions.

2. **The Hippocampus and amygdala:** The hippocampus and amygdala are called limbic system. The hippocampus is involved in memory storage **(Levin, 2000).**

II. The Diencephalon:

It consists of the thalamus and hypothalamus and it lies between the cerebral hemispheres and the midbrain. The thalamus distributes almost all sensory and motor information going to the cerebral cortex. In addition, it is thought to regulate

levels of awareness and some emotional aspects of sensory experiences. The hypothalamus lies ventral to the thalamus and regulates autonomic activity and the hormonal secretion by the pituitary gland **(Blumenfeld, 2002).**

III. The midbrain:

This is the smallest brain stem component which lies rostral to the pons. The midbrain contains essential relay nuclei of the auditory and visual system.

IV. The pons and cerebellum:

It contains a large number of neurons that relay information from the cerebral hemispheres to the cerebellum. The cerebellum lies dorsal to the pons and medulla. The cerebellum receives somatosensory input from the spinal cord, motor information from the cerebral cortex and balance information from the vestibular organs of the inner ear. The cerebellum plays a major role in the control of posture, head and eye movements.

V. The medulla:

This structure is the direct rostral extension (this means toward the head and nose) of the spinal cord. It resembles the spinal cord in both organization and function **(Levin, 2000).**

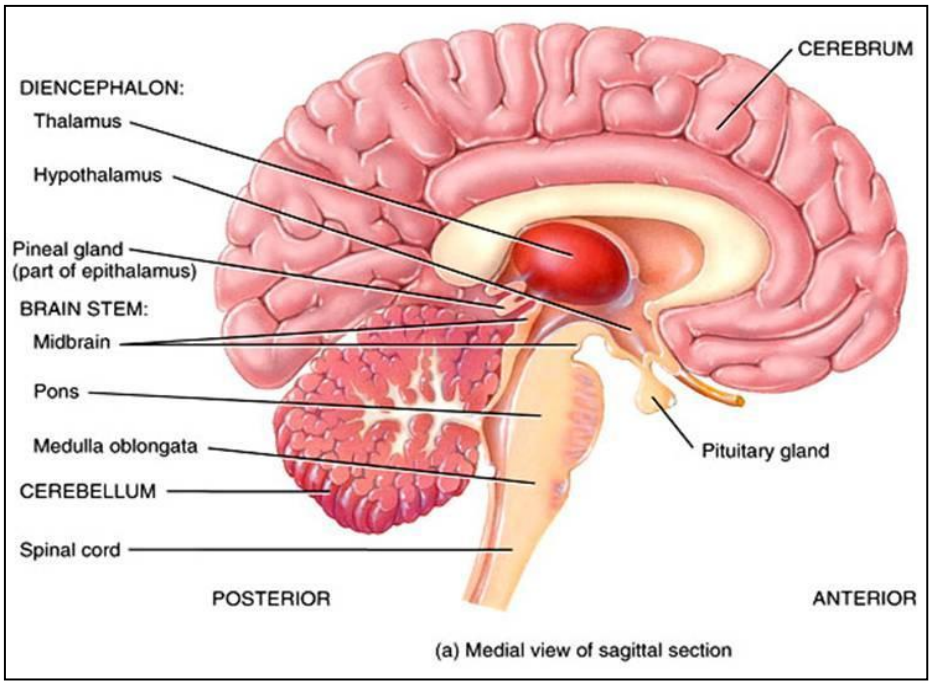

Figure (1): Anatomy of central nervous system **(Levin, 2000).**

VI. The spinal cord:

It extends from the base of the skull as extension of the medulla oblongata through the foramen magnum then through the first cervical vertebra. The spinal cord receives sensory information from the skin, joints, muscles of the trunk and limbs and contains the motor neurons responsible for both voluntary and reflex movements. It also receives sensory information from the internal organs and control many visceral functions **(Blumenfeld, 2002).**

B. The peripheral nervous system:

The peripheral nervous system is divided into two subsystems: Somatic and autonomic **(Blumenfeld, 2002).**

Basic Brain Physiology

A. Central neurotransmitters:

Neurotransmitters are small molecules that are liberated by a presynaptic neuron into the synaptic cleft and cause a change in the postsynaptic membrane potential **(Elinore, 2002).**

They are divided into three principal classes. The **first class** is made up of acetylcholine alone; the **second class** are the monoamines, that are molecules formed by an amino acid losing a hydroxyl or carboxyl group. The **third class** is made up of amino acids **(Table 1).** There is also a specific chain of enzymatic reactions that decompose the transmitter, either for destruction or for recycling **(Elinore, 2002).**

Neurotransmitters can act as inhibitory or excitatory signals to the postsynaptic cell by either hyperpolarizing or depolarizing its membrane, the same molecule can function as an inhibitor or an excitator. Acetylcholine, for instance can act as an excitator when it binds to one type of receptor, and as an inhibitor when bound on another kind, even if both types of receptors are present in the same cell **(Carlson, 2001).**

Acetylcholine is the major neurotransmitter in the peripheral nervous system (the other peripheral neurotransmitter is norepinephrine). Acetylcholine is usually (but not always) an excitatory neurotransmitter in contrast to the monoamine neurotransmitters, which are nearly always inhibitory **(Elinore, 2002).**