Systemic Manifestations of Traumatic Brain Injury

Essay Submitted in Partial Fulfillment of the Master's Degree

in Intensive Care Medicine

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2017

Acknowledgment

Thanks first and last to **ALLAH** *as we owe Him for His great care, support and guidance in every step in our life.*

I would like to express my deep gratefulness to
Prof. Dr. Prof. Dr. Hesham Mohammed El-Azzazi*,*

Professor of anesthesia, intensive care and pain management Faculty of Medicine - Ain Shams University, for his concern, his guidance and continuous encouragement. I consider myself very fortunate to work under his supervision.

I am grateful to Dr. Ahmad Kamal Mohamed Ali,

lecturer of anesthesia and intensive care Faculty of Medicine - Ain Shams University, for his generous and continuous help and valuable suggestions as well as his desire to achieve perfection. His great help was very impressive and his meticulous reading and enormous assistance should be appreciated.

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LIST OF ABBREVIATIONS

A10	Clot amplitude at 10 minutes after the beginning of clot formation
ACTH	Adrenocorticotropic hormone
ADH	Antidiuretic hormone
ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
ASPEN	American Society for Parenteral and Enteral Nutrition
ANS	Autonomic nervous system
APTT	Activated partial thromboplastin time
BBB	Blood brain barrier
BD	Brain damage
BG	Blood glucose
BTF	Brain trauma foundation
CARS	Compensatory anti-inflammatory response syndrome
CBF	Cerebral blood flow
CK	Creatinine kinase
COPD	Chronic obstructive pulmonary disease
CO	Cardiac output
CPIS	Clinical pulmonary infection score
CPP	Cerebral perfusion pressure
CSF	Cerebrospinal fluid
CSW	Cerebral salt wasting
CT	Clotting time
CVP	Central venous pressure
DAMPs	Damage associated molecular patterns
DI	Diabetes insipidus
EXTEM	Extrinsically activated thromboelastography test
EVD	Extra ventricular device

FSH	Follicular stimulating hormone
FibTEM	Fibrin based thromboelastometric test
GCS	Glasgow-coma scale
GH	Growth hormone
GFAP	Glial fibrillary acidic protein
GOS	Glasgow-outcome scale
HBOT	Hyperbaric oxygen therapy
HO	Heterotopic ossification
HR	Heart rate
HRT	Hormonal replacement therapy
HTS	Hypertonic Saline
HPA	Hypothalamus pituitary-adrenal
IL	Interleukin
ICP	Increased intracranial pressure
INR	International normalized ratio
LMWH	Low molecular weight heparin
LV	Left ventricle
MCF	Maximum clot firmness
MDR	Multi-drug resistant
MIH	Mild induced hypothermia
NPE	Neurogenic pulmonary edema
NSE	Neuron specific enolase
NSM	Neurogenic stunned myocardium
ODS	Osmotic demylination syndrome
PAID	Paroxysmal autonomic instability and dystonia
PTH	Phenytoin
PTHP	Post-traumatic hypopituitarism
PT	Prothrombin time
PRIS	Propofol infusion syndrome
ROS	Reactive oxygen species
SAH	Subarachnoid hemorrhage
$ScvO_2$	Central venous saturation
SIADH	Syndrome of Inappropriate Antidiuretic Hormone

SIRS	Systemic inflammatory response syndrome
SCCM	Society of critical care medicine
TBI	Traumatic brain injury
TEE	Trans-esophageal echo
TF	Tissue factor
TTE	Trans-Thoracic echo
TSH	Thyroid stimulating hormone
VAE	Ventilator associated events
VAP	Ventilator associated pneumonia
VILI	Ventilator induced lung injury
VPA	Valporate

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Abstract:

Traumatic brain injury (TBI) affects functioning of various organ systems in the absence of concomitant non-neurologic organ injury or systemic infection. The systemic manifestations of TBI can be mild or severe and can present in the acute phase or during the recovery phase. Non-neurologic organ dysfunction can manifest following mild TBI or severe TBI. The pathophysiology of systemic manifestations following TBI is multifactorial and involves an effect on the autonomic nervous system, involvement of the hypothalamic-pituitary axis, release of inflammatory mediators, and treatment modalities used for TBI. Endocrine dysfunction, electrolyte imbalance, and respiratory manifestations are common following TBI. The influence of TBI on systemic immune response, coagulation cascade, cardiovascular system, gastrointestinal system, and other systems is becoming more evident through animal studies and clinical trials. Systemic manifestations can independently act as risk factors for mortality and morbidity following TBI.

Key words: Endocrine dysfunction; autonomic dysfunction; coagulopathy; immune response; neurogenic pulmonary edema

Introduction

Introduction

The pathophysiology of traumatic brain injury (TBI) involves the initial primary brain injury that occurs at the time of accident and the secondary brain injury that follows which results in increased intracranial pressure (ICP) and decreased cerebral perfusion. Secondary brain injury is due to the several biochemical cascades that occur in brain after TBI. Systemic insults such as hypoxia, hypotension, fever, and anemia can potentiate the process of secondary brain injury. The current evidence-based management of TBI mainly includes intensive monitoring of physiological parameters like ICP and cerebral perfusion pressure (CPP), anticipation of secondary insults, their early recognition and adequate management (medical and/or surgical).However, there is an increasing awareness that apart from the cerebral manifestations there are several systemic manifestations of TBI which can act as independent prognostic factors ***(Zygun et al., 2005).***

The systemic manifestations occur in the absence of any coexisting specific organ injury or systemic infection. The nature and severity of the systemic manifestations of TBI mainly depend on the severity of the brain injury. Mild TBI causes systemic manifestations such as fatigue and

dizziness whereas severe TBI can adversely affect the functioning of multiple organ systems. Following severe TBI, endocrine dysfunction and electrolyte imbalances are common while renal and hepatic manifestations are unusual. These systemic manifestations can occur either in the acute phase following severe TBI or/and during the chronic phase of rehabilitation. The manifestations in any particular organ system can vary from mild organ dysfunction to organ failure. Zygun et al. reported organ dysfunction in 89% of patients, and organ failure in 35% of patients in their observational study of 209 patients with severe TBI ***(Zygun et al., 2005).***

The systemic manifestations can result in both increased mortality (with one organ system involvement mortality is 40%, with two organ systems 47%, while with no organ system dysfunction it is 26%) and adverse outcomes following severe TBI ***(Lim and Smith, 2007).***

Endocrine dysfunction is common and the symptoms of these hormonal abnormalities overlap with the chronic symptoms that persist after TBI, especially fatigue, weakness, memory and attention problems. Current recommendations for screening of TBI patients include acute assessment for cortisol and thyroid deficiency and

treatment is indicated for documented deficiency of these hormones. At 3–6 months, the additional following screening is recommended: morning cortisol level, insulin-like growth factor, thyroid stimulating hormone, free thyroxine, luteininzing hormone, follicle stimulating hormone, estradiol (females), and testosterone(males) ***(Ghigo et al., 2005).***

Zygun et al., (2005) reported pulmonary complications in 80% of patients with severe TBI. In patients with severe brain injury (GCS <8), acute lung injury (ALI) is seen in 20% of patients.

Following TBI there is a surge in catecholamines in the blood. This sympathetic hyperactivity results in tachycardia and systemic hypertension which increases the work load of heart. As catecholamines can also cause constriction of coronary vessels, ischemia of the myocardium especially in the subendocardial regions may result. This myocardial ischemia is responsible for the several ECG changes that are seen after TBI. Prolonged QTc on ECG is more common after traumatic SAH and can result in cardiac arrhythmias ***(Collier et al., 2004)***.

Although coagulation abnormalities after TBI is common and contribute to devastating complications of delayed intracranial hemorrhage, the pathophysiology of coagulation abnormalities after TBI is not well understood and may involve tissue factor release from injured tissue, fibrinolysis, thrombocytopenia, and activated protein C and other cytokines ***(Laroche et al., 2012).***