A Retrospective Study Of Toxic Coma Among Patients Admitted To Poison Control Center In Ain Shams University Hospitals During 2015

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Contents

Introduction

Poisoning is a leading cause of morbidity and mortality **(Marraffa et al., 2012).** Chemicals involved in acute poisoning ended in 240,000 deaths worldwide in the year 2004 **(Prüss-Ustün et al., 2011).**

Coma, from the Greek word "koma" meaning deep sleep, is a state of extreme unresponsiveness, in which an individual exhibits no voluntary movement or behavior. Furthermore, in a deep coma, even painful stimuli are unable to affect any response, and normal reflexes may be lost **(Arun et al., 2005).**

Comatose cases are at high risk for morbidity and mortality; a menu of important serum and urine toxicological tests is prepared for clinical laboratories that provide clinical toxicological services **(Wu et al, 2003).**

Many drugs can cause coma; sedative drugs such as benzodiazepines and barbiturates, opioids, and ethanol can cause impairment of consciousness, and psychotropic drugs such as tricyclic antidepressants, lithium, and selective serotonin reuptake inhibitors; anticholinergic drugs,

amphetamines, and illicit drugs all can cause delirium and coma **(Posner et al., 2007).**

Other Common non-structural causes of coma include anoxic-ischemic encephalopathy, seizures, metabolic alterations, endocrinopathies, systemic infections and central nervous system infections **(Yrftwe et al., 2012).**

Aim of the Work

The aim of the current study is;

- First to study toxic coma as regards (frequency, causes, clinical presentation and lines of management) among patients who were admitted to Intensive Care Unit (ICU) of Poison Control Center in Ain Shams University Hospitals (PCC-ASUHs) from January 2015 to December 2015.
- Second to correlate such data collected from files with the outcome.

Physiology of Consciousness

Consciousness (Latin conscientia "moral conscience"), is the awareness of all that occur in the mind of a person. In modern science, it is defined as a continuous state of full awareness of the self and one's relationship to the external and internal environment, describing the degree of wakefulness in which an organism recognizes stimuli (**Jellinger, 2009).**

Consciousness can also be defined as consciously perform elementary and intellectual tasks, to reason, plan, judge and retrieve information as well as the awareness of these functions belonging to the self, that is, being self-aware (**Szirmail and Kamondi, 2006).**

A normal level of consciousness (wakefulness) depends upon activation of the cerebral hemispheres by neurons, Reticular Activating System (RAS), located in the brainstem. Both of these components and the connections between them must be preserved for normal consciousness to be maintained **(Young, 2009).**

Consciousness depends on two fundamental components: arousal and content. The latter consists of those higher

cognitive functions that allow awareness of self and the environment, and expression related to sensation, emotion, memory, and thought. Arousal requires a functioning reticular formation, a physiological structure that extends from the caudal medulla to the rostral midbrain. Fibers from the reticular formation ascend to the thalamus and project to various non-specific thalamic nuclei. From these nuclei, there is a diffuse distribution of connections to all parts of the cerebral cortex. The reticular system and its interconnections are known as the ascending reticular activating system (ARAS; Fig. 1) (**Shilpa and Nicholas, 2014).**

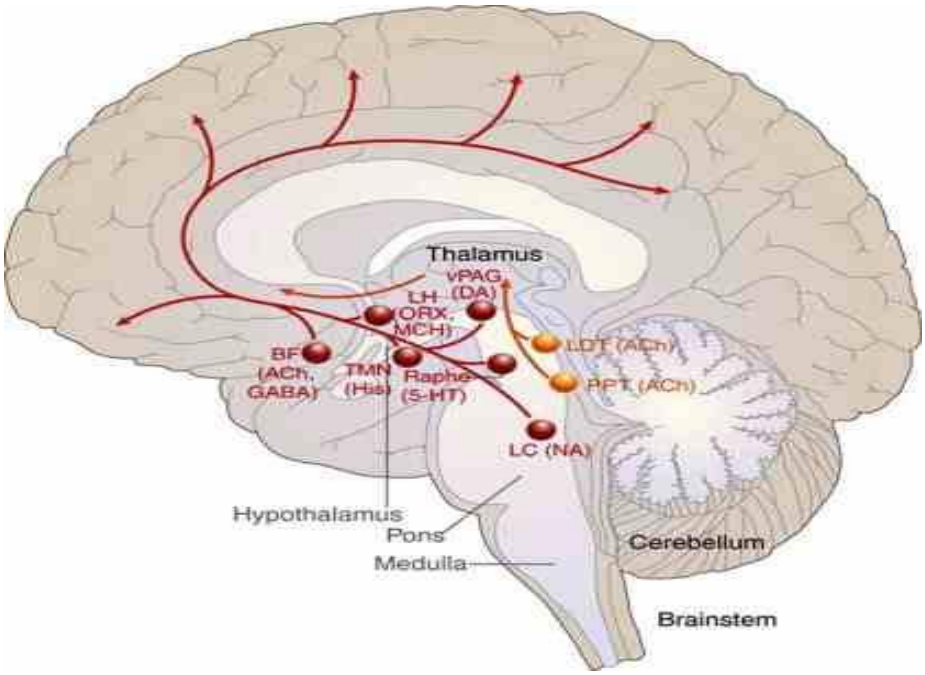

Figure (1): key components of the ascending arousal system ***(Saper et al., 2005).***

The cerebral cortex receives impulses from the ARAS and modulates the incoming information via corticofugal projections to the reticular formation. Content, and therefore awareness of self and environment and thus conscious behavior, is dependent on the integrity of both cerebral hemispheres and their subcortical connections. Any lesion which interferes with full cognitive function diminishes the content of consciousness and renders the patient less than fully conscious **(Posner et al., 2007).**

Arousal, also called wakefulness, refers to the level of alertness (clinically determined by eye-opening). In healthy individuals, varying degrees of arousal correspond to a range of conscious states that extend from deep dreamless sleep, through drowsiness to alert wakefulness (**Portas et al., 2004).**

There are four main anatomical structures involved in the generation of arousal:

- The brainstem
- Thalamus
- Basal forebrain
- Hypothalamus.

Within the brainstem, the ascending activating system composed of excitatory glutamatergic neurons within the upper pontine and lower midbrain tectum relays a variety of stimuli along two pathways, the first to the thalamus and the second to the basal forebrain. Other structures and neurotransmitter from the brainstem, the pedunculopontine tegmental and laterodorsal nuclei (acetylcholine), locus ceruleus (noradrenaline), midline raphe nuclei (serotonin), and

substantia nigra pars compacta (dopamine) modify arousal through both cortical and subcortical (thalamus, basal forebrain, and striatum) connections (**Michelson and Ashwal, 2012).**

The content of consciousness refers to awareness (clinically determined by command following or non-reflex motor behavior such as eye tracking or localized responses to pain). It has been demonstrated that the contents of consciousness can vary independently to the level of consciousness **(Portas et al., 2004).**

Consciousness in this sense can be evaluated objectively using behavioral criteria such as those specified in the Glasgow Coma Scale (GCS) (**Yu and Blumenfeld, 2009).**

In a healthy individual, levels of arousal will vary during wakefulness depending on the individual's activity. Variations in arousal during the day correlate with levels of activity in the structures of the midbrain and thalamus that regulate conscious states (**Andrea et al., 2011).**

In physiological states, there is an intimate positive correlation between arousal and awareness. Sleep is the best

way to describe the relationship between these two components: the less awake we become as we move towards deep sleep, the less aware we become of our surroundings and ourselves. Based on this, subjects in the pathological and pharmacological coma (i.e., anesthesia) are not conscious because they cannot be awakened, even after noxious stimulation **(Carol Di et al., 2014).**

Similarly, under sedation (a drug-dose dependent impairment of consciousness) and in the hypnotic state (a suggestion-dependent alteration of conscious experience), subjects report an altered state of awareness as they move towards lower levels of arousal. Hence, arousal seems to be essential for awareness to emerge, i.e., one needs to be awake in order to be aware. However, being awake is not sufficient in order to be aware **(Boly et al., 2013).**

Despite the low level of arousal, rapid eye movement sleep is associated with the dreaming state and a raised content of consciousness, the exception to the otherwise positive correlation between level and content of consciousness in normal physiological states (**Laureys, 2005).**

The principal causes of coma are therefore: (1) widespread damage in both hemispheres from ischemia, trauma, or other less common brain diseases; (2) suppression of cerebral function by extrinsic drugs, toxins, or hypoxia or by internal metabolic derangements such as hypoglycemia, azotemia, hepatic failure, or hypocalcaemia; and (3) brainstem lesions that cause proximate damage to the RAS **(Zeman, 2001).**

Pathophysiology of coma

Insults to the cerebral cortex or brainstem can each independently cause depressed consciousness or coma. Typically, both cerebral hemispheres need to be affected to induce coma, and this also depends on the size and speed of progression of the insult. Localized, unilateral lesions in the cerebral cortex usually do not induce depressed consciousness or coma even if other cognitive functions are impaired **(Wakamoto et al., 2009).**

In contrast, a completely intact brainstem is necessary for arousal. Small focal lesions in the brainstem can affect the ARAS. If the ARAS is impaired, the cerebral cortex cannot be aroused and depressed consciousness or coma occurs **(Benjamin and Jeremy, 2014).**

Thus, in order to cause coma, a process must either affect the brainstem primarily or both cerebral hemispheres concomitantly. Processes that affect both cerebral hemispheres and cause coma are typically diffuse metabolic or toxic processes, such as drug intoxication or severe electrolyte/metabolite abnormalities, meningoencephalitis,

hydrocephalus, multifocal cerebral insults (e.g. multiple large concomitant cerebral emboli) or cardiac and respiratory arrest **(Frances, 2018)**

Coma due to brainstem compression from an ischemic stroke typically occurs during the time of peak edema, around 3- 5 days after the ictus. Processes that primarily affect the brainstem are most commonly structural, such as infarction or hemorrhage **(David et al., 2015).**

The neurons of the brain are dependent on cerebral blood flow (CBF), oxygen, and glucose. CBF is approximately 75 mL per 100 g/min in gray matter and 30 mL per 100 g/min in white matter (mean=55mLper 100 g/min). Oxygen consumption is 3.5 mL per 100g/min, and glucose consumption is 5 mg per 100 g/min. Brain stores of glucose provide energy for approximately 2 min after blood flow is interrupted, and consciousness is lost within 8 to 10 min **(Gjedde et al., 2002).**

There are numerous encephalopathies due to organ failure (hepatic, renal, pulmonary, cardiovascular, or adrenal), electrolyte disturbance (hyponatremia, hypernatremia, hypocalcemia, hypercalcemia, hypomagnesaemia,

hypermagnesaemia, or hypophosphatemia), hypoglycemia, hyperglycemia, disturbances in thyroid function, or inborn errors of metabolism (e.g., porphyria and mitochondrial disorders). Most of these cause reversible, functional dysfunction of the ARAS and cause more diffuse disturbance without localizing signs, e.g. Hemiplegia or pupillary unreactivity **(Young, 2009).**

Coma of metabolic origin is produced by interruption of energy substrate delivery (hypoxia, ischemia, and hypoglycemia) or by alteration of the neurophysiologic responses of neuronal membranes (drug, alcohol intoxication, toxic endogenous metabolites, anesthesia, or epilepsy). These same metabolic abnormalities can cause widespread neuronal dysfunction in the cortex that reduces all aspects of mentation and results in an acute confusional state **(Bateman, 2001).**

The pathophysiology of toxic and metabolic coma is specific to the underlying cause and in many instances incompletely understood. In a simplified view, these conditions have been linked to an interruption in the delivery or utilization of oxygen or substrate (hypoxia, ischemia, hypoglycemia and carbon monoxide), alterations in neuronal excitability and signaling