Introduction

Traffic accidents kill more than a million people every year worldwide and injure or permanently disable millions more. The Middle East region ranks second highest in terms of road fatalities, according to the WHO, with Egypt alone suffering more than 7,000 deaths annually. **(Jon, 2010)**

Analgesia for trauma patients is one of the greatest challenges in anesthesia. Critically ill patients whose history, status, and injuries are not well known must be treated. The pain management of a trauma patient, with their specific physical and emotional experience, imposes additional demands to anesthesiologists and critical care specialists. Many factors in the management of the trauma victim (hemodynamic fluctuations, respiratory depression, and level of consciousness) contribute to the difficulties faced in the pain control of these patients. In addition, the consequences of inadequate pain management after an injury are more than just psychological. Anesthesiologists have particular skills in the provision of pain relief and this is of vital importance in the early and consequent management of the injured patient. Analgesia should be regarded as part of the resuscitation process because it not only brings pain relief, but also improves hemodynamic stability resulting in improved organ and tissue perfusion. **(Laura & Marina, 2009)**

Acute pain is known to potentiate the physiologic stress response to trauma. The tissue damage and the dynamic of the central nervous system can engage mechanisms and create chronic pain problems that outlast the period of healing. **(Amit et al., 2011)**

Regional analgesia is beneficial for patients with a wide variety of trauma, including hip fracture, shoulder

dislocation and multiple fractured ribs. Therefore, there are a lot of procedures performed to provide regional analgesia for the trauma patients such as, femoral nerve block, Fascia iliaca compartment block, Interscalene brachial plexus block, The supracondylar radial nerve block, Intercostal nerve block, Thoracic epidural analgesia, Intrapleural block and Thoracic paravertebral block. (**Frederik et al., 2012**).

Trained anesthesiologists can expeditiously administer regional analgesia. The quick onset and lack of sophisticated equipment for delivery allow use in distant and austere environments (so long as appropriate monitoring and resuscitation equipment are available). Additionally, regional analgesics allow the patient to remain awake and alert, facilitating ongoing evaluation of mental status. **(Wildsmith, 2003)**

Ultrasound imaging techniques in regional analgesia are becoming a subject of major interest. The quality of blocks and analgesia is relevant to the perioperative outcome of patients and the development of perfect blocks has always been a focus in regional anesthesia research. Ultrasound offers portable real time imaging of neural structures, without radiation risk to either staff or patient. Improvements in technology have both improved image quality and reduced cost, making portable ultrasound affordable. The development of new high frequency transducers has increased image resolution, allowing improved visualization of superficial structures such as nerves, tendons and muscles. **(Plunkett et al., 2006).**

The role of regional analgesia in the trauma patient is both complex and controversial. The decision-making is complex, because trauma patients may present with a spectrum of injuries and in various degrees of shock. Accordingly, simple rules cannot be applied to all patients. Use of regional analgesia in the trauma patient is

controversial, because initial historical reports of spinal anesthesia use in acute trauma predictably resulted in catastrophe, and several common trauma-related conditions constitute either absolute or relative contraindications to regional anesthesia (e.g., full stomach, hemodynamic compromise, unstable/unclear cervical, thoracic or lumbar spine, compartment syndrome of lower extremities, etc.). (**Stephen et al., 2012**)

Aim of The Work

This essay is directed towards highlighting the role of the regional analgesia in the emergency room. The role of ultrasound, the procedures used and their significance in pain management in the trauma patients.

Chapter 1:

Pathophysiology of Pain

Acute and chronic mechanisms of pain:

Pain is defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage." Caregivers involved in pain management suggest that pain and the intensity of discomfort are whatever the patient states and should be managed accordingly. In addition to reducing discomfort and suffering, inadequate treatment of acute pain can increase morbidity, delay recovery, and increase medical costs of post-surgical patients, as well as lead to the development of chronic pain. **(Amit et al., 2011)**

Classification of Pain:

Acute pain, which usually follows trauma to tissue, is limited in duration and is associated with temporal reductions in intensity. In contrast, chronic pain is of longer duration, often 3–6 months longer than expected. Chronic pain often has an unclear etiology and its prognosis is more unpredictable when compared to acute pain. Although acute pain and chronic pain have distinguishing characteristics, there is often overlap, making the diagnosis and management of pain challenging. Physiologic pain can be divided into neuropathic pain and nociceptive pain. *Neuropathic pain* results from irritation or damage to nerves. It is usually characterized as burning, electrical, and/or shooting in nature. However, a common characteristic of neuropathic pain is the paradoxical coexistence of sensory deficits in the setting of increased painful sensation. **(Amit et al., 2011)**

Nociceptive pain can be further divided into somatic and visceral pain, and is defined as noxious perception resulting from actual tissue damage following surgical, traumatic, or disease-related injuries. This pain is detected by specialized transducers called nociceptors, which are the peripheral endings of A-delta (Aδ) and C fibers. Nociceptive pain involves peripheral inflammation and the release of inflammatory mediators, which play a major role in its initiation and development. **(Woolf, 2004)**

Somatic nociceptive pain is well-localized sharp, crushing, or tearing pain that usually follows a dermatomal pattern and often occurs after mechanical trauma. In contrast, visceral nociceptive pain is poorly localized dull, cramping, or colicky pain generally associated with peritoneal irritation, dilation of smooth muscle, or tubular passages. Visceral pain radiating in a somatic dermatomal pattern is described as referred pain. **(Amit et al., 2011)**

Appreciating the clinical features of the different types of pain not only helps to properly classify pain and its etiology, but also guide the often complex multimodal medical management that accompanies pain management. The health care provider must be detailed in attaining the qualitative factors and history associated with a patient's pain.

The Pain Pathway—The Initial Insult:

The pain pathway begins with the "**activation"** of peripheral nociceptors. Nociceptors are located anywhere in the body and convey noxious sensation, either externally (i.e., skin, mucosa) or internally (i.e., joints, intestines). Nociceptors can be triggered by any painful stimuli, most of which can be categorized as either mechanical, chemical, or thermal in nature. Nociceptors are classified by the specific stimulus they respond to (eg. "Thermal

nociceptor") and have a sensory specificity. Therefore, they will only be activated and an action potential occurs when a certain threshold has been reached. **(Helms & Barone, 2008)**

"Transduction" refers to the process in which noxious stimuli, chemical, thermal, or mechanical, are translated into electrical activity at the level of the nociceptors. The cell bodies of these nociceptors are found in the dorsal root ganglia (DRG) of the spinal cord. In addition, following the initial insult, or tissue injury, several cellular mediators activate the terminal endings of the nociceptors such as potassium, hydrogen ions, prostaglandins, and bradykinin. Prostaglandin (PGE), which is synthesized by cyclooxygenase-2 (COX-2), is responsible for nociceptor sensitization and plays an important role in peripheral inflammation. **(Woolf, 2004)**

Action potential through sensitized nociceptors also leads to the release of several peptides in and around the site of injury. These include substance P (sP), cholecytokinin (CCK), and calcitonin gene-related peptide (CGRP). Substance P is responsible for the further release of bradykinin and also fuels the release of histamine from mast cells and serotonin (5-HT) from platelets, which further increases vascular permeability and nociceptor irritability. **(Reddi & Curran, 2014)**

Conduction:

Pain stimuli are conducted from peripheral nociceptors to the dorsal horn via both unmyelinated and myelinated fibers. Nociceptive nerve fibers are classified according to their degree of myelination, diameter, and conduction velocity. Nociceptors have two different types of axons that transmit pain impulses to the dorsal root ganglion. The first are the Aδ-fiber axons. These axons are

myelinated and allow action potentials to travel at a very fast rate of approximately 20 m/s toward the central nervous system (CNS). The other type is the more slowly conducting non-myelinated C-fiber axons. These only conduct at speeds of about 2 m/s. Thus, in the classic example of touching a hot stove, the Aδ fibers transmit the "first pain, " a rapid onset well-localized, sharp pain of short duration while the C fibers are responsible for the "second pain" or delayed pain. Second pain is associated with a delayed latency and is described as a diffuse burning, stabbing sensation that is often prolonged and may become progressively worse. **(Woolf, 2004)**

Transmission:

After the synapse in the dorsal root, the second-order neurons send their signals contralaterally and upward through the spinothalamic tract. The signals of the spinothalamic tract travel up the spinal cord through the medulla and synapse on neurons in the thalamus. Nerves from the thalamus then relay the signal to various areas of the somatosensory cortex, where pain perception takes place. Glutamate, the excitatory amino acid implicated in transmission from primary afferent nociceptors to dorsal horn neurons, has a number of receptors it activates. The various combinations of these receptors exist on neurons in various laminae of the dorsal horn. **(Amit et al., 2011)**

Modulation:

Modulation can be described as manipulating a noxious stimulus so it is perceived as a pain-suppressive transmission. This occurs at higher levels of the brainstem and midbrain. It is accomplished by an electrical or pharmacological stimulation of certain regions of the midbrain producing relief of pain. **(Charlotte, 2009)**

Not all analgesics are exogenous. Since opioid receptors in the brain are unlikely to exist for the purpose of responding to the administration of opium and its derivatives, then it must be *endogenous* compounds for which these receptors had evolved. Endogenous analgesics, including enkephalin (ENK), norepinephrine (NE), and gamma-aminobutyric acid (GABA) activate opioid, alpha-adrenergic, and other receptors that either inhibit release of glutamate from primary nociceptors or diminish post-synaptic responses of second-order neurons. **(Amit et al., 2011)**

Ascending and Descending Pathways:

Several ascending tracts are responsible for transmitting nociceptive impulses from the dorsal horn to supraspinal targets. Of these, the spinothalamic tract is considered the primary perception pathway. The descending pathways originate in the somatosensory cortex, which relays to the thalamus and the hypothalamus. Thalamic neurons descend to the midbrain. There, these neurons synapse on ascending pathways in the medulla and spinal cord and inhibit ascending nerve signals, producing an analgesic effect which comes from the stimulation of endogenous endorphins, dynorphins, and enkephalins. **(Charlotte, 2009)**

Transition from Acute to Persistent Pain:

"Neural plasticity"; the capacity of neurons to change their function, chemical profile, or structure, is the basis for learning and memory and is also responsible for alterations in noxious perception. More so, neural plasticity underlies peripheral and central sensitization.The sensitization theory of pain perception suggests that brief high-intensity noxious stimulation in the absence of tissue injury activates the nociceptive endings of unmyelinated or

thinly myelinated (high-threshold) fibers, resulting in physiologic pain perception of short duration. Following tissue injuries and release of noxious mediators, peripheral nociceptors become sensitized and fire repeatedly. Peripheral sensitization occurs in the presence of inflammatory mediators, which in turn increases the sensitivity of high-threshold nociceptors as well as the peripheral terminals of other sensory neurons. This increase in nociceptor sensitivity, lowering of the pain threshold, and exaggerated response to painful and non-painful stimuli is termed *primary hyperalgesia*. **(Feizerfan & Sheh, 2014)**

The ongoing barrage of noxious impulses sensitizes second-order transmission neurons in the dorsal horn via a process termed *windup*. "***Windup***" is a term used to describe the process of increased central sensitization of the body's pain pathways in response to sustained input from nociceptive afferents. Central sensitization results in *secondary hyperalgesia* and the spread of the hyperalgesic area to nearby uninjured tissues. Inhibitory interneurons and descending inhibitory fibers modulate and suppress spinal sensitization, whereas analgesic under medication and poorly controlled pain favors sensitization. In certain settings, central sensitization may then lead to neurochemical/ neuroanatomical changes (plasticity), prolonged neuronal discharge and sensitivity (windup), and the development of chronic pain. This creates several problems, including sprouting of Wide Dynamic Range (WDR) neurons and induction of glutamate-dependent *N*-methyl-D-aspartate (NMDA) receptors. Glutamate is the primary agonist of the NMDA receptor and therefore, the primary excitatory agonist for noxious transmission. The NMDA receptor appears to be responsible for not only amplifying pain, but also causing *opioid tolerance*. There is evidence that NMDA antagonists, such as ketamine, have a

role in preventing opioid-induced hyperalgesia. **(Kelly et al., 2001)**

Activation of spinal and supraspinal NMDA receptors are major requisites for the development of *central sensitization*. It is the sensitization of CNS neurons that underlies the transition from acute to persistent pain. Excitatory neurotransmitters are believed to cause spinal cord hypersensitivity to nociceptive inputs from the periphery. Excitotoxicity defines the pathological alterations observed in nerve cells stimulated by overactivation of NMDA.The extent of autonomic responses to pain (tachypnea, tachycardia, hypertension, diaphoresis, etc.) can be depressed in the cortex through descending pathways. Of interest, the influences of the descending pathways may also be responsible for psychogenic pain (pain perception that has no obvious physical cause) . **(Amit et al., 2011)**

"***Opioid-induced hyperalgesia***" is a process that is associated with the long-term use of opioids for pain management. Opioid-induced hyperalgesia is a clinical picture which is characterized by increasing pain in patients who are receiving increasing doses of opioids. With time; individuals using opioids can develop an increasing sensitivity to noxious stimuli, sometimes even staging a painful response to non-noxious stimuli. Therefore, patients given opioids for acute pain may have a paradoxical increase in pain. **(Jensen & Finnerup, 2014)**

So, understanding pain pathways and pain processing is the key to the optimal management of both acute and chronic pain. Our understanding of pain perception is evolving as we now recognize that humoral factors as well as neural transmission are responsible for the activation and sensitization of regions involved in pain perception, suffering, and avoidance behavior. **(Kang & Bruera, 2013)**

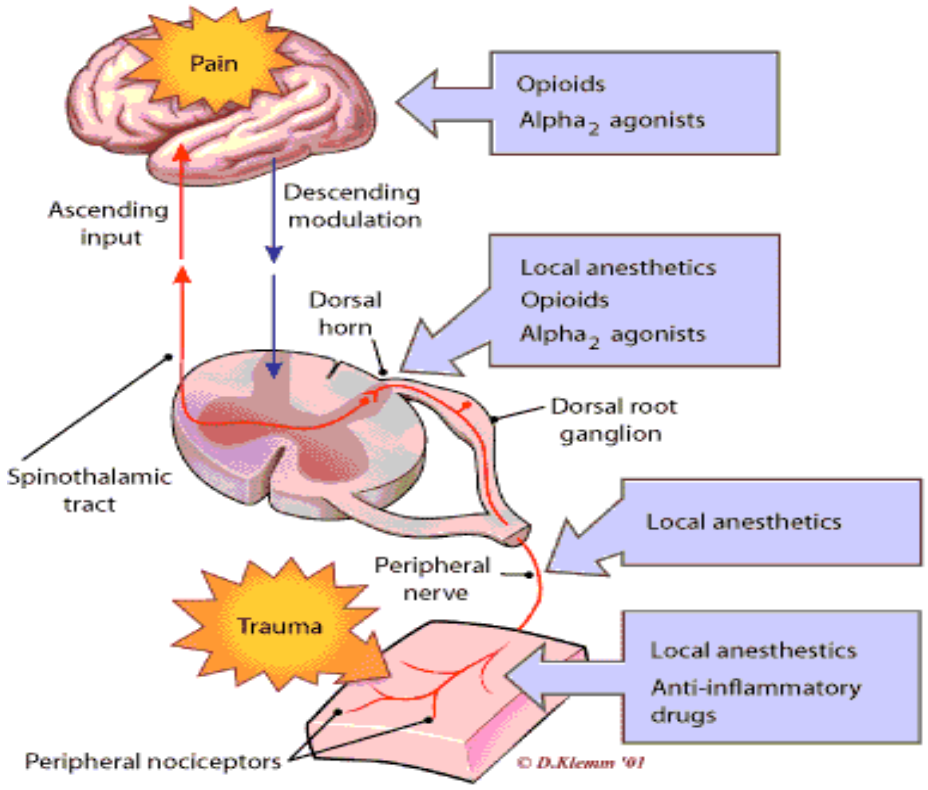

Fig. 1: The pain pathway and interventions that can modulate activity at each point. **(Kehlet & Dahl, 1993)**

Stress response for trauma :

The stress response is the name given to the hormonal and metabolic changes which follow injury or trauma. This is part of the systemic reaction to injury which encompasses a wide range of endocrinological, immunological and haematological effects. The responses to trauma have been of interest to scientists for many years. In 1932, Cuthbertson described in detail the metabolic responses of four patients with lower limb injuries. He documented and quantified the time course of the changes. The terms ‘ebb’ and ‘flow’ were introduced to describe an initial decrease and subsequent increase in metabolic activity. **(Little & Girolami, 1999)**

After the early work on the stress response to accidental injury, attention turned to surgical trauma, and responses to most types of surgery were reported. Following on from this, the ability of anesthetic agents and neural blockade to modify the endocrine and metabolic responses has been studied enthusiastically.

1) The endocrine response to trauma:

The stress response to trauma is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system. The changes in pituitary secretion have secondary effects on hormone secretion from target organs. **(Desborough, 2000)**

The hypothalamic–pituitary–adrenal axis:

The endocrine response is activated by afferent neuronal impulses from the site of injury. These travel along sensory nerve roots through the dorsal root of the spinal cord, up the spinal cord to the medulla to activate the hypothalamus.

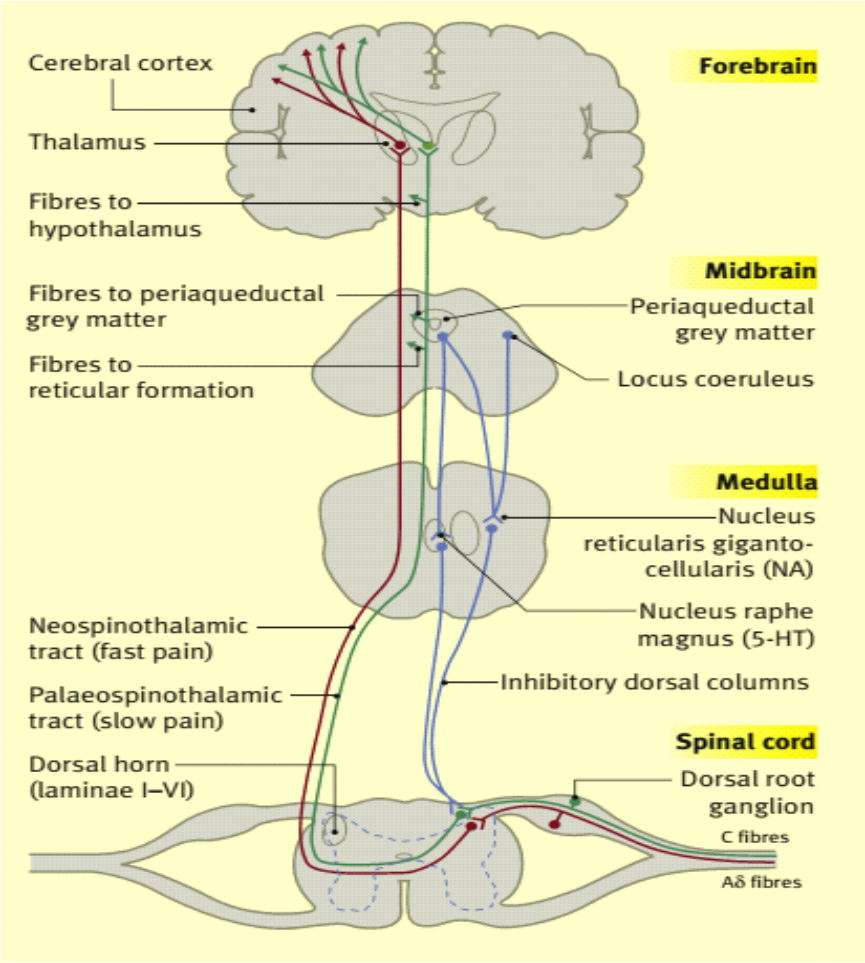

Fig. 2: Spinal and Supraspinal pathways of pain. Ascending nociceptive fast (red) and slow (green) pathways while Descending inhibitory tracts (blue); NA, noradrenaline; 5-HT, 5-hydroxytryptamine. **(Charlotte, 2009)**

Sympathoadrenal response:

Hypothalamic activation of the sympathetic autonomic nervous system results in increased secretion of catecholamines from the adrenal medulla and release of norepinephrine from presynaptic nerve terminals. Norepinephrine is primarily a neurotransmitter, but there is some spillover of norepinephrine released from nerve terminals into the circulation. The increased sympathetic

activity results in the well recognized cardiovascular effects of tachycardia and hypertension. In addition, the function of certain visceral organs, including the liver, pancreas and kidney, is modified directly by efferent sympathetic stimulation and/or circulating catecholamines. **(Desborough, 2000)**

Secretions of pituitary hormones:

Anterior pituitary:

Anterior pituitary hormone secretion is stimulated by hypothalamic releasing factors. The pituitary synthesizes corticotrophin or adrenocorticotrophic hormone (ACTH) as part of a larger precursor molecule, pro-opiomelanocortin. The precursor is metabolized within the pituitary into ACTH, β-endorphin and an N-terminal precursor. Growth hormone and prolactin are also secreted in increased amounts from the pituitary in response to trauma. Concentrations of the other anterior pituitary hormones, thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH) do not change markedly during trauma. **(Lyons & Meeran, 1997)**

Growth hormone:

Growth hormone secretion from the pituitary increases in response to trauma, in relation to the severity of the injury. Its release is stimulated by growth hormone releasing factor from the hypothalamus. In addition to the regulation of growth, growth hormone has many effects on metabolism. It stimulates protein synthesis and inhibits protein breakdown, promotes lipolysis (the breakdown of triglycerides into fatty acids and glycerol) and has an anti-insulin effect. This means that growth hormone inhibits glucose uptake and use by cells, which spares glucose for use by neurones in situations of glucose