Update on adjuvants in regional anesthesia

Essay

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المواد المساعده فى التخدير الناحى

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بكالوريوس الطب والجراحه

توطئه للحصول علي درجه الماجيستير في علم التخدير

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استاذ التخدير والعنايه المركزه وعلاج الألم

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Ahmed Mohamed Abd El Monem

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List of Abbreviations

5-HT	:	5-hydroxytryptamine
ACLS	:	Advanced Cardiac Life Support
ASRA	:	American society for regional Anesthesia
ABC	:	ATP-binding Cassette
ASA	:	American society of anesthesia
AUC	:	Area under the curve
BBB	:	Blood brain barrier
CABG		Coronary artery bypass grafting
CNS	:	Central nervous system
CSE	:	Combined spinal epidural
CVS	:	Cardiovascular system
ERPs	:	Event-related potentials
ESRA	:	European Society of Regional Anesthesia
GA	:	General anesthesia
ICU	:	Intensive Care Unit
IPLA	:	Intraperitoneal local anesthetic
IT	:	Intrathecal
ITO		Inrathecal opioids
K	:	Kappa receptor
LA	:	Local anesthesia
LAST	:	Local Anesthetic Systemic Toxicity

M	:	Morphine
MAC	:	Minimal alveolar concentration
MAG	:	Magnesium
MAIOs	:	Monoamine oxidase inhibitors
MAP	:	Mean arterial pressure
M6G	:	Morphine-6-glucuronide
$MgSO_4$	:	Magnesium sulphate
MPTP	:	N-methyl-4-phenyl-1,2,3,6 tetrahydropyridine
M-re	:	Muscarinic receptor
NMDA	:	N-methyl-D-aspartate
NNH	:	Number needed to harm
NNT	:	Number needed to treat
NSAID	:	Non steroidal-anti-inflammatory drugs
PABA	:	Para-aminobenzoic acid
PACU	:	Post Anesthesia Care Unit
PCA	:	Patient controlled analgesia
PCEA	:	Patient-controlled epidural analgesia
P-gp	:	P-glycoprotein
PNB	:	Peripheral nerve blocks
PNS	:	Peripheral nervous system
S	:	Sufentanil
SSRIs	:	Selective serotonin reuptake inhibitors
ST-91	:	2,6-diethylphenylamine 2-imidazoline
SAB	:	Spontaneous abortion
VAPS	:	Visual analogue pain scale
VAS	:	Visual analogue scale

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Introduction

Although the medical world cannot cure every disease, the control of pain to ensure patient comfort should be a goal. One step toward improving pain management is through increased knowledge of pain physiology. Within the nervous system, there are several pathways that transmit information about pain from the periphery to the brain. There is also a network of pathways that carry modulatory signals from the brain and brainstem that alter the incoming flow of pain information ***(Renn and Dorsey, 2005).***

Acute pain is typically associated with neuroendocrinal stress response that is proportional to pain intensity. It has been hypothesized that a reduction in surgical stress response (endocrinal, metabolic and inflammatory) will lead to a reduced incidence of postoperative organ dysfunction and there by to an improved outcome ***(Richardson and Mustard 2009).***

Local anesthetic agents have a wide variety of applications. They are used as the backbone ingredients for local and regional anesthetic techniques and for analgesia in the operative and postoperative period. They are also used in the management of chronic pain where local anesthetic

injections may have a prolonged effect. Modern local anesthetics are safer than their predecessors, but risks persist. The cornerstone of safe practice is a thorough understanding of the pharmacology and toxicity of the agents used, in particular, dose and concentration required, speed of onset and duration of action. Clinicians administering local anesthetic agents must be capable of recognizing impending toxicity, and have access to the equipment, current knowledge and skills to manage these events ***(McLure and Rubin, 2005).***

Regional anesthesia is obtained by administering local anesthetics near the spinal cord and nerve roots (spinal, epidural), spinal nerves (paravertebral), or close to peripheral nerves. The same techniques are used for regional analgesia, but this is obtained by using more dilute solutions of local anesthetics, and other analgesic drugs are often added. Pain impulses are inhibited, but sensation of touch and muscle functions are intact. Regional analgesia gives superior relief of pain provoked by movement. This facilitates early postoperative mobilization of patients, even after major surgery in weak patients. For these patients optimally performed regional analgesia may reduce postoperative

morbidity and mortality better than general anesthesia and ***Breivik***postoperatively ***(Norum and Breivik, 2010).***

The identification of opioid receptors has opened new horizons in pain management, Yaksh and Rudy, in 1976, were the first investigators to demonstrate direct opioid analgesia at the spinal cord level. Their study involved subarachnoid fentanyl and morphine in rats. However, the first application of neuraxial opioids can be traced to that in 1901, when a Japanese surgeon used 10 mg intrathecal (IT) morphine with the local anesthetic eucaine in two cancer patients***(Matsuki,1983)***

Combination of different drugs that prolong analgesia would therefore be advantageous. Diverse classes of drugs, such as local anesthetics, epinephrine, clonidine, and neostigmine, have been added to intrathecal opioids in attempts to prolong analgesia and reduce the incidence of adverse effects, observed when opioids are used alone ***(Owen et al.,2000)***

Chapter 1

Mechanism of Pain and Analgesia

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."***(Benzon et al., 2011)***

Thus, an understanding of the anatomic substrates and physiologic mechanisms by which noxious and non-noxious stimuli are perceived provides the essential background to apprehend the mechanisms of acute and chronic pain, and the sites of action of pharmacologic therapies for pain. ***(Brennan et al., 2007).***

Nociception is the physiologic process of activation of neural pathways by stimuli that are potentially or currently damaging to tissue. ***(Benzon et al., 2011)***

Pain in contrast to nociception, is a conscious experience. While the stimulus-induced activation of afferent neural pathways plays an important role, other factors such as alterations in somatosensory processing following injury to

tissues and/ or nerves and psychosocial factors may influence the overall perception of pain. ***(Benzon et al., 2011)***

Pain pathway:

The ascending pain pathways transmit nociceptive information from peripheral tissues to the cerebral cortex for interpretation as pain. The ascending pathways are complex structures, involving both the peripheral (PNS) and central nervous systems (CNS). ***(Brennan et al., 2007)***

Nociceptors:

Specialized peripheral sensory neurons known as nociceptors alert us to potentially damaging stimuli at the skin by detecting extremes in temperature and pressure and injury-related chemicals, and transducing these stimuli into long-ranging electrical signals that are relayed to higher brain centers.The term noxious is applied to nociceptive stimuli because nociceptors are activated in response to strong stimuli that fall in the tissue-damaging range, whereas non-nociceptive mechanoreceptors, thermoreceptors, and chemoreceptors respond to milder stimuli that fall in a range below the tissue-damaging level. In addition to exogenous chemicals that stimulate nociceptors, a number of endogenous chemicals have been identified that can activate nociceptors, including

potassium, bradykinin, serotonin, histamine, prostaglandins, and others. ***(Adrienne and Adrem, 2010)***

First order neuron:

When a noxious stimulus is transduced by a nociceptor, a signal is generated that is transmitted as an electrical action potential along small diameter A-delta (myelinated, fast transmission, sharp or pricking first pain) and C (unmyelinated, slow transmission, dull or burning second pain) primary afferent nerve fibers to the gray matter of the spinal cord. ***(Benzon et al., 2011)***.

On crosssection, the spinal gray matter forms a butterfly shape and can be divided into 10 laminae, or layers, which are numbered I through IX, from dorsal to ventral, with X surrounding the central canal. Pain processing occurs predominantly in laminae I, II, and V. The primary afferent fibers enter the spinal cord in the dorsolateral aspect of the gray matter (the dorsal horn) through the dorsal root. Upon entering the dorsal horn, the primary afferents bifurcate in a "T" pattern and travel 2 to 3 spinal segments within Lissauer'stract in both the cephalic and caudal directions. As the primary afferents travel in Lissauer's tract, they send collateral projections to the gray matter along the entire 4 to 6 segment length thus