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Randomized Controlled Clinical Study to Compare the Effect of Intravenous Magnesium Sulphate Versus Diclofenac Sodium As Post Operative Analgesic After Abdominal Hysterectomy Under General Anaesthesia

Thesis

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AMPA: .....Amino 3 hydroxy 5 methyl 4 isoxazolepropionic acid
BMI: .....Body mass index
COX .....Cyclo oxygenase enzyme
HR: .....Heart rate
IV: .....Intra venous
MAP: .....Mean arterial pressure
MG: .....Magnesuim
NMDA .....Nmethyl D aspartate
NMDARS: ..... Nmethyl D aspartate receptors
NRS: .....Numerical rating system
NSAIDS .....Non steroidal anti inflammatory drugs
PCA.....Patient controlled anaesthesia
PONV.....Post operative nausea and vomiting
SVR: .....Systemic vascular resistance
TAH: .....Total abdominal hysterectomy
VAS: .....Visual analogue score

INTRODUCTION

Hysterectomy is the most common major gynaecological operation and second most common gynecological surgery done after caesarean section all over the world ***(Duhan et al., 2010).***

Abdominal hysterectomy is associated with postoperative pain. Traditional methods for postoperative pain management include opioids administered systemically using patient-controlled intravenous analgesia (PCA), or neuroaxially via epidural or spinal injections. However, pain relief, specifically on movement, is not always adequately controlled when using PCA, despite moderate to large doses of morphine. This is associated with side-effects such as postoperative nausea and vomiting (PONV), tiredness, pruritus, headache, and constipation ***(Perniola et al., 2009).***

The major goal in postoperative pain management is to minimize the dose of medications and decrease side effects, while still providing adequate analgesia. Postoperative pain relief leads to earlier mobilization, shortened hospital staying, reduced hospital costs, and increased patient satisfaction ***(Recart et al., 2005).***

Narcotics are the most common analgesics which are used after the surgeries. But physicians are always looking for replaceable methods with fewer side effects and cost, one of the

intravenous adjuvant that has been shown potential in analgesia is magnesium sulfate ***(Albrecht et al., 2013).***

The mechanism of the analgesic effect of Magnesium is not clear but interference with calcium channels and N-methyl-D-aspartate (NMDA) receptor seem to play an important role ***(Haryalchi et al., 2013).***

As there is no studies in our region to compare the effect of both magnesium sulphate and diclofenac as analgesic in post hysterectomy patients we will do this one.

Aim of the Work

To compare the effect of intravenous magnesium sulfate versus intravenous diclofenac on postoperative analgesia in patients undergoing total abdominal hysterctomy.

Chapter 1

PAIN

Pathophysiology of pain

Pain is a term used to define the range of transient sensations we experience in response to stimuli that are of sufficient intensity to threaten to damage tissue or produce small localized areas of injury, but which neither provoke an extensive inflammatory response nor damage the nervous system ***(Nowak et al., 1982).***

There is no single pathophysiological mechanism responsible for the production of pain. Physiological pain results from the activation of high threshold receptors in the periphery (nociceptors) which feed in complex ways to a series of ascending pathways that carry information from the spinal cord to the brain ***(Raja et al., 1988).***

Pain pathway

A pain signal can be generated by intense enough stimulation of *any* sensory receptor, has been soundly disproved. Some sensory fibers do not differentiate between noxious and non-noxious stimuli, while others, nociceptors, respond only to noxious, high intensity stimuli ***(Price et al., 1977).***

At the peripheral end of the nociceptor, noxious stimuli generate currents that, above a given threshold, send signals along the nerve fiber to the spinal cord. The "specificity" (whether it responds to thermal, chemical or mechanical features of its environment) of a nociceptor is determined by which ion channels it expresses at its peripheral end. Dozens of different types of nociceptor ion channels have so far been identified, and their exact functions are still being determined ***(Debono et al., 2013).***

The pain signal travels from the periphery to the spinal cord along an A-delta or C fiber. Because the A-delta fiber is thicker than the C fiber, and is thinly sheathed in an electrically insulating material (myelin), it carries its signal faster (5–30 m/s) than the unmyelinated C fiber (0.5–2 m/s). Pain evoked by the A-delta fibers is described as sharp and is felt first. This is followed by a duller pain, often described as burning, carried by the C fibers. These "first order" neurons enter the spinal cord via Lissauer's tract ***(Raja et al., 1988).***

These A-delta and C fibers connect with "second order" nerve fibers in the central gelatinous substance of the spinal cord (laminae II and III of the dorsal horns). The second order fibers then cross the cord via the anterior white commissure and ascend in the spinothalamic tract. Before reaching the brain, the spinothalamic tract splits into the lateral, neospinothalamic tract and the medial, paleospinothalamic tract.

Second order, spinal cord fibers dedicated to carrying A-delta fiber pain signals, and others that carry both A-delta and C fiber pain signals to the thalamus have been identified. Other spinal cord fibers, known as wide dynamic range neurons, respond to A-delta and C fibers, but also to the large A-beta fibers that carry touch, pressure and vibration signals ***(Debono et al., 2013).***

Pain-related activity in the thalamus spreads to the insular cortex (thought to embody, among other things, the feeling that distinguishes pain from other homeostatic emotions such as itch and nausea) and anterior cingulate cortex (thought to embody, among other things, the affective/motivational element, the unpleasantness of pain). Pain that is distinctly located also activates primary and secondary somatosensory cortex ***(Nowak et al., 1982).***

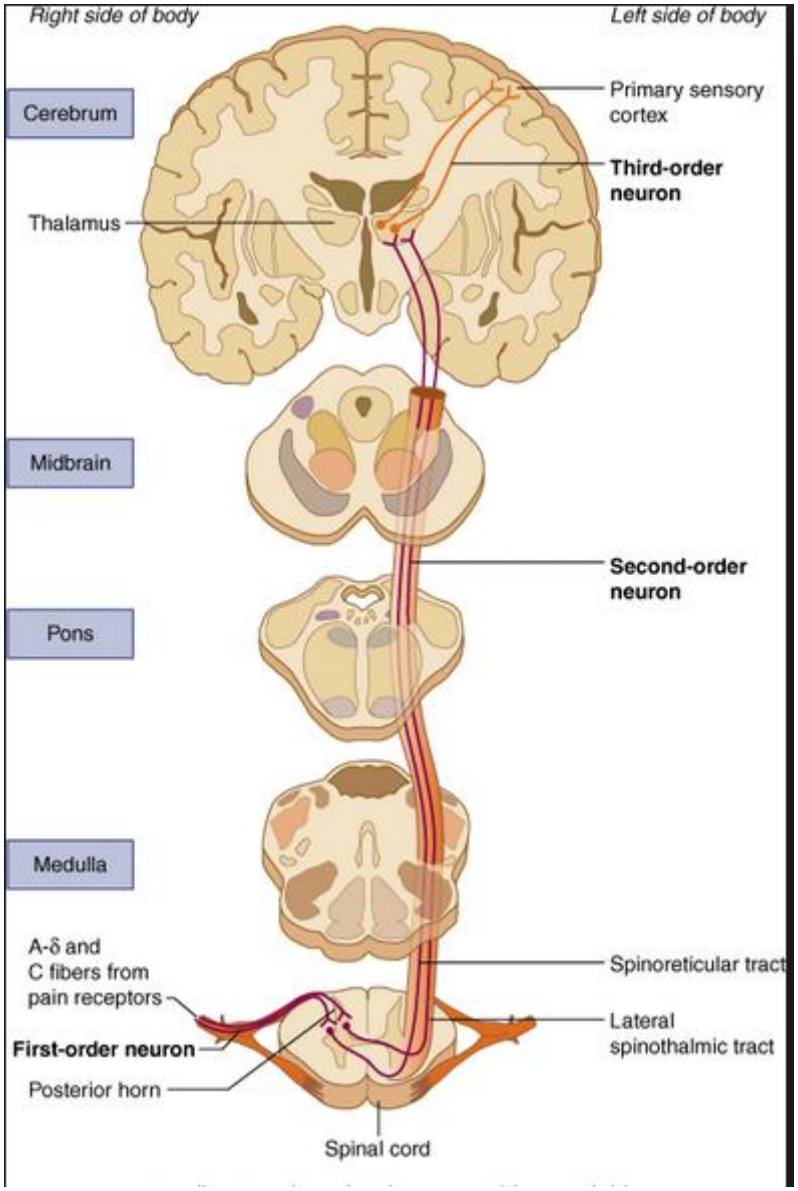

Figure (1): Pain pathway ***(Debono et al., 2013).***

Pain assessment

Pain measures fall into 2 categories:

- Single-dimensional scales - These scales assess a single dimension of pain and, through patient self-reporting, measure only pain intensity; these scales are useful in acute pain when the etiology is clear; see the image below.
- Multidimensional scales - These measure the intensity, nature, and location of pain, as well as, in some cases, the impact that pain is having on a patient's activity or mood; multidimensional scales are useful in complex or persistent acute or chronic pain ***(Carlesso et al., 2018).***

Pain management

Mild pain

Paracetamol (acetaminophen), or a nonsteroidal anti-inflammatory drug (NSAID) such as ibuprofen.

Mild to moderate pain

Paracetamol, an NSAID and/or paracetamol in a combination product with a weak opioid such as tramadol, may provide greater relief than their separate use. Also a combination of opioid with acetaminophen can be frequently used ***(Arendt-Nielsen et al., 2010).***

Moderate to severe pain

When treating moderate to severe pain, the type of the pain, acute or chronic, needs to be considered. The type of pain can result in different medications being prescribed. Certain medications may work better for acute pain, others for chronic pain, and some may work equally well on both. Acute pain medication is for rapid onset of pain such as from an inflicted trauma or to treat post-operative pain. Chronic pain medication is for alleviating long-lasting, ongoing pain ***(Macpherson, 2010).***

Morphine is the gold standard to which all narcotics are compared. Semi-synthetic derivatives of morphine such as hydromorphone (Dilaudid), oxymorphone (Numorphan, Opana), nicomorphine (Vilan), hydromorphinol and others vary in such ways as duration of action, side effect profile and milligramme potency. Fentanyl has the benefit of less histamine release and thus fewer side effects. It can also be administered via transdermal patch which is convenient for chronic pain management. In addition to the intrathecal patch and injectable Sublimaze, the FDA has approved various immediate release fentanyl products for breakthrough cancer pain ***(Sofat et al., 2011)***

Diamorphine, methadone and buprenorphine are used less frequently. Pethidine, known in North America as meperidine, is not recommended for pain management due to its low potency, short duration of action, and toxicity associated with repeated use.