Postoperative Analgesia using Levobupivacaine Wound Infiltration with Intravenous Tramadol versus Dexamethasone Following Obstetric Spinal Anesthesia

Thesis

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List of Abbreviations

Abb.	Full term
AAG	*α-acid glycoprotein*
AAGBI	*Association of Anesthetists of Great Britain and Ireland*
ABC	*Airway, Breathing, Circulation*
C.S	*Cesarean section*
CNS	*Central nervous system*
COPD	*Chronic obstructive pulmonary disease*
COX	*Cyclooxygenase*
K+	*Potassium ion*
logP	*Log partition coefficient*
MPQ	*McGill Pain Questionnaire*
Na+	*Sodium ion*
NSAIDS	*Nonsteroidal anti-inflammatory drugs*
PABA	*Para-aminobenzoic acid*
PI	*Paralytic ileus*
PONV	*Post-operative nausea and vomiting*
RAS	*Reticular activating system*
VAS	*Visual analog scale*
VASC	*Voltage activated Na+ channel*

INTRODUCTION

Most women undergoing cesarean section (C.S) experience inadequate postoperative pain relief ***(Edomwonyi and Ekwere, 2006).***

Acute postoperative pain may result in chronic incapacitating pain after surgery. Effective postoperative pain management facilitates early ambulation, infant care (including breastfeeding and maternal-infant bonding) as well as prevention postoperative morbidity ***(Kainu et al., 2010).***

Multimodal analgesia combining both local infiltration of local anesthetic around the surgical wound with systemic intra venous analgesics and anti-inflammatory has shown promising results for adequate postoperative pain management ***(American Society of Anesthesiologists, 2012).***

Levobupivacaine wound infiltration at various concentrations has been used to significantly decrease postoperative pain with less cardiovascular and neurological toxicity than racemic bupivacaine ***(Andrew et al., 2002)***.

Intravenous dexamethasone has an anti-inflammatory effect by acting on the glucocorticoid receptor resulting in the decreased release of inflammatory mediators decreasing the inflammatory response to surgical incision which is one of the factors causing pain; it is used at doses ranging from 1.25 to 20

mg; 8 mg is a common dose used for this purpose ***(Werner et al., 2002; Kaan et al., 2006; Becker, 2013).***

Intravenous Tramadol is a popular analgesic routinely used for postoperative pain management after cesarean section at the dose of 100 mg ***(Farshchi and Ghiasi, 2010; Merrikhihaghi et al., 2015).***

Aim of the Work

This study aim to compare the analgesic effect of combining Levobupivacaine wound infiltration with either intravenous dexamethasone or intravenous tramadol for caesarian section performed under spinal anesthesia; providing coast effective multimodal safe post-operative analgesic plan with the best patient satisfaction.

Chapter 1
PAIN PHYSIOLOGY

The word pain is derived from the Latin "poena", meaning punishment ***(Morgan et al., 2006)***. 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." This definition recognizes the interplay between the objective, physiological sensory aspects of pain and its subjective, emotional, and psychological components. The response to pain can be highly variable among persons as well as in the same person at different times ***(International Association for the Study of Pain, 2015).***

Pain can be classified according to pathophysiology (i.e., nociceptive or neuropathic pain). Nociceptive pain is caused by activation or sensitization of peripheral nociceptors. Neuropathic pain is the result of injury or acquired abnormalities of peripheral or central neural structures ***(Świeboda et al., 2013).***

Perception of pain involves receptors that detect pain and pathways that relay the information to the central nervous system for processing. Pain receptors are found throughout body tissues such as the viscera, joints, and dermis. These free nerve endings or nociceptors are normally at rest (non–signal transferring) and are classified as A delta fibers (thinly

myelinated, fast conduction) and C fibers (unmyelinated, slow conduction) ***(Świeboda et al., 2013).***

Beginning with the peripheral insult (e.g., a surgical incision), the local response from injured tissue cells includes the release of biochemicals such as bradykinin, histamine, serotonin, and hydrogen ions. Release of these substances into the extracellular fluid that surrounds the A delta and C fibers stimulates them and directly excites the nociceptors. Other biochemicals such as substance P and prostaglandins increase nociceptor sensitization. The prostaglandins produced in injured tissue have a major role in the inflammatory and pain response ***(Świeboda et al., 2013).***

The arachidonic acid pathway within the injured cell mediates the synthesis of a large class of prostaglandins. An essential enzyme for this conversion is cyclooxygenase (COX), COX-2 prostaglandins are released from inflammatory cells into the nociceptive field and sensitize A delta and C-type receptors to the biochemical produced in the injured tissue ***(Świeboda et al., 2013).***

Once stimulated, nociceptors transmit an electrical signal along the A delta and C fibers to the central nervous system. The fibers enter the spinal cord through the dorsal root ganglia into appropriate spinal cord dorsal horn laminae. A delta fibers synapse in laminae I and V, and C fibers synapse in laminae II and III. Here, they release excitatory neurotransmitters such as

glutamate and substance P onto postsynaptic interneurons that ascend in spinal tracts to the thalamus. Axons traveling up the lateral (neospinothalamic) tract project to the thalamus' posterior region. The pain stimulus is then transmitted to the sensory cortex for spatial aspects of pain processing ***(Świeboda et al., 2013).***

Axons traveling up the medial (paleo spinothalamic) tract project to the thalamus' medial region and transmit to the limbic and reticular activating system (RAS) for emotional and autonomic aspects of pain processing, and the cognitive centers of the cerebral cortex for intensity-response processing. Note that the signal is carried on the A delta and C-type fibers. These signals enter the spinal cord, where a synapse occurs and information is sent to the brain ***(Jacobson & Marcus, 2011).***

Opioid binding at μ receptors, however, hyperpolarizes Gamaa Aminobutyric acid (GABA)-releasing cells, which decreases the GABA release and remove its block on the descending pathway, thereby decreasing the sensation of pain ***(Świeboda et al., 2013)***. At the end of the descending analgesic pathway in the spine, nociceptive signal interruption is accomplished by the release of endogenous opioids (enkephalins and endorphins) that bind to receptor sites. Presynaptically, opioid binding decreases calcium ion conductance to inhibit the release of substance P; postsynaptically, opioid binding increases potassium conductance, hyperpolarizing interneurons ***(Świeboda et al.,***

2013). Several drugs are currently used postoperatively to attenuate pain by interrupting the nociceptive pathway. Unfortunately, no drug has been developed that provides adequate pain control without inducing side effects that range from being unpleasant (constipation) to life-threatening (respiratory depression) ***(Julius and Basbaum, 2001).***

Pain measurement

Reliable measurement of pain severity helps determine therapeutic interventions and evaluate the efficacy of treatments. This is a challenge, however, because pain is a subjective experience that is influenced by psychological, cultural, and other variables. Clear definitions are necessary, because pain may be described in terms of tissue destruction or bodily or emotional reaction. Descriptive scales such as mild, moderate, and severe pain or verbal numerical scales are non-continuous and generally unsatisfactory ***(International Association for the Study of Pain: Pain Definitions, 2015).***

The numerical rating scale, faces rating scale, visual analog scale (VAS), and the McGill Pain Questionnaire (MPQ) are most commonly used. In the numerical scale, 0 corresponds to no pain and 10 designate the worst possible pain *(Figure 1).* ***(International Association for the Study of Pain: Pain Definitions, 2015).***

The most common VAS consists of a 10-cm horizontal or vertical line with the two endpoints labeled "no pain" and "worst pain ever (or similar verbal descriptors). Patients are required to place a mark on the 10-cm line at a point that corresponds to the level of pain intensity they feel. The distance in centimeters from the low end of VAS to the patient's mark is used as a numerical index of the severity of pain ***(Ludger et al., 2017).***

A major advantage of the VAS as a measure of sensory pain intensity is its ratio scale properties. In contrast to many other pain-measurement tools, equality of ratios is implied, making it appropriate to speak meaningfully about percentage differences between VAS measurements obtained at multiple points in time or from independent samples of subjects. Other advantages of the VAS include its ease and brevity of administration and scoring ***(Ludger et al., 2017).***