Benefits and Risks of Intrathecal Midazolam in Lower Limb Orthopedic Surgeries

Thesis
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بسم الله الرحمن الرحيم

وَأَنْزَلَ اللهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللهِ عَلَيْكَ عَظِيمًا

صدق الله العظيم

سورة النساء آية (113)

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LIST OF ABBREVIATIONS

ACC	*Anterior cingulated cortex*
ACTH	*Adrenocoticotrophic hormone*
ADH	*Antidiuretic hormone*
ASA	*American Society of Anesthesiologists*
BIS	*Bispectral index*
CBC	*Complete blood count*
C_m	*Minimum concentration*
CNS	*Central nervous system*
CSF	*Cerebrospinal fluid*
CT	*Computed tomography*
DRG	*Dorsal root ganglia*
ECG	*Electrocardiogram*
GABA	*Gamma aminobutyric acid*
INR	*International normalization ratio*
MAC	*Minimum alveolar concentration*
MAP	*Mean arterial pressure*
MRI	*Magnetic resonance imaging*
NS	*Nociceptive specific*
OAA/S	*Observer's assessment of alertness/ sedation*
PCS	*Patient controlled sedation*
PDPH	*Post dural puncture headache*
PFC	*Prefrontal cortex*
PT	*Prothrombin time*
PTT	*Partial thromboplastin time*
RR	*Respiratory rate*
VAS	*Visual analogue scale*
WDR	*Wide dynamic range*

INTRODUCTION

One of the primary aims of anesthesia is to alleviate the patient's pain and agony, by permitting the performance of surgical procedures without any discomfort. Relief of postoperative pain has gained real importance in recent years considering the central, peripheral and immunological stress response to tissue injury. Any expertise acquired in this field should be extended into the postoperative period, which is the period of severe, intolerable pain requiring attention. So there is need of extended analgesia without any side effects to achieve this goal.

Intrathecal administration of midazolam has been reported to exert a spinally mediated anti-nociceptive action ***(Ho and Ismail, 2008).***

Several investigations have shown that intrathecal administration of midazolam is not associated with neurotoxicity, respiratory depression or sedation ***(Rudra et al., 2004).***

This study was conducted to evaluate the isolated effect and possible side effects (if any) of intrathecal midazolam alone without intrathecal local anesthetic.

Sixty patients were enrolled in this study and were equally randomized into two groups. Midazolam group (group M) received intrathecal injection of midazolam diluted with 3 ml normal saline. The control group (group C) received intrathecal 3 ml normal saline only. Then general anesthesia was conducted using a standard technique.

Intraoperatively, all patients were monitored for heart rate, mean blood pressure, arterial oxygen saturation and end-tidal carbon dioxide. Intra-operative fentanyl consumption and MAC of isoflurane were assessed.

Postoperative analgesia was assessed using the visual analogue scale. The time of first analgesic dose and the total consumption of the analgesic drug used as well as any adverse effects were monitored.

AIM OF THE WORK

This study was conducted to evaluate the isolated effects and possible side effects (if any) of intrathecal midazolam alone without intrathecal local anesthetic.

ANATOMY OF PAIN

Pain pathway:

Specificity theory states that there is a specific pain system that transfers information about potential or actual tissue damage to the place of perception: the brain. Nociceptive energy is transduced into electro-physiological signals that are transmitted to perceptive apparatus. However, the pain pathway is not 'hard wired", but undergoes profound functional changes and modulation under certain conditions, such as tissue damage and inflammation (e.g. postoperative pain). This plasticity is mediated by many mechanicsms, including peripheral primary and central secondary sensitization. The substrate for these changes is a plethora of chemical mediators peripherally and spinally, comparable in complexity to neuro-transmitters in the brain ***(Smith, 2007)***.

I. Primary afferent neurons:

There are three classes of primary afferent fibers in the skin that may be activated by a given cutaneous stimulus. The fibers that are largest and have the fastest conduction velocity (>40m/s) are the large-diameter myelinated A-beta (Aß) fibers.

These fibers, when activated, do not normally result in a sensation of pain, but rather of light touch, pressure, or hair movement. The axons of the nociceptive neurons are generally unmyelinated (C fibers) or thinly myelinated A-delta(Aδ) fibers ***(Dubner, 1994)***.

Unmyelinated C polymodal fibers which are activated by many potentially tissue-damaging modalities, are associated with prolonged 'burning' pain, and are slowly conducting (0.5-2.0 m/s). Some may have a differential sensitivity to heat or mechanical stimuli ***(Smith, 2007)***.

The Aδ are thinly myelinated fibers that are thought to mediate a briefer 'sharp' pain. These larger fibers are more rapidly conducting (5-20 m/s). Aδ fibers are also delineated into two types, depending on their differential responsiveness to intense heat ***(Smith, 2007)***.

A final group of fibers do not appear to exhibit sensitivity to noxious stimuli. These 'silent' fibers develop novel sensitivity usually after tissue injury or inflammation. Silent fibers have been well characterized in the visceral domain, although there is some evidence to support the existence of somatic counterparts ***(Smith, 2007)***.

II. Spinal cord to brain:

Secondary afferents decussate and pass up the spinal cord to the midbrain via the spinothalamic, spinoreticular and spinomesencephalic tracts to the thalamus and to sensory cortex, but also have many other links, such as to reticular formation, limbic and hippocampal areas (figure1). The different pathways may have functional correlates involving memory, cognition and emotion, which contribute to the neural network of overall pain perception. Moreover, neurons that project from these areas of the brain provide descending modulation of spinal cord processing ***(Brooks and Tracey, 2005)***.

The first synapse in somatosensory signaling occurs either at the spinal dorsal horn or in the dorsal column nuclei at the spinal cord-brain stem junction. Evidence has accumulated to indicate that both nociceptive and non nociceptive fibers provide input to both of these initial targets. However, under normal circumstances, the dorsal column nuclei can be considered to selectively process inputs from the large myelinated fiber classes related to light touch, whereas the spinal dorsal horn primarily processes inputs of the nociceptive primary afferent fibers ***(Dubner, 1994).***