COMBINED SPINAL EPIDURAL ANALGESIA IN LABOR: COMPARISON OF INTRATHECAL 2MG PLAIN BUPIVACAINE VERSUS HEAVY BUPIVACAINE WITH FENTANYL

BY

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ABBREVIATIONS

BR	Bromage Score
CSF	Cerebrospinal fluid
FDA	Federal Drug Association
PAG	Periaqueductal Gray
ME	Met-enkephalin
LE	Leucine Enkephalin
DADLE	D-ala D-lee Enkephalin
GABA	Gaba Amino Butyric Acid
VAS	Visual Analogue Scale
NSAIDs	Non Steroidal Anti Inflammatory Drugs
CGR	Calcitonin-Gene-Related
VRS(vrs)	Verbal Rating Scale

ABSTRAK

Analgesia menggunakan teknik spinal opioid adalah salah satu perkembangan dalam pengubatan sakit akut dan kronik. Tindak balas reseptor opioid dengan opioid yang telah disuntik dengan cara epidural atau intratekal di dalam saraf tunjang telah menyebabkan seseorang itu hilang rasa sakit. Kesan daripada tindakbalas, terhasilnya analgesia tanpa kehilangan fungsi motor atau kehilangan rasa sentuhan.

Kombinasi penggunaan opioid dengan ubat bius setempat contohnya bupivacaine, menggunakan cara epidural atau intratekal menghasilkan analgesia yang berpanjangan. Tindakan sinergistik di antara opioid dengan ubat bius setempat mempunyai implikasi penting, tetapi kesan ini sukar untuk diselidiki di dalam manusia.

Oleh kerana terdapat sedikit sahaja penyelidikan mengenai kesan analgesia bius setempat "plain" bupivacaine, penyelidikan secara rawak telah dijalankan terhadap 90 orang pesakit yang menjalani proses kelahiran secara normal Penyelidikan ini telah dijalankan di Hospital Universiti Sains Malaysia, Kelantan. Tujuan penyelidikan ini khusus untuk mengetahui sekiranya dos bupivacaine yang rendah boleh memberi kesan analgesia yang secukupnya dan tiada kesan sampingan. Hasil kajian membuktikan bahawa 2 mg " heavy" bupivacaine bersama 25 mcg fentanyl menghasilkan kesan analgesia mencukupi pada aras T10 dan tiada insiden "high block". Ia juga membuktikan incidence yang rendah dari segi kesan sampingan.

ABSTRACT

Spinal opioid analgesia utilizing analgesics has been one of the major developments during the past decade in the management of acute and chronic pain. The relief of pain is due to the interaction of the opioid injected epidurally or intrathecally with a specific opioid receptor in the spinal cord. The result is zones of segmental analgesia without the loss of motor function or loss of other sensory modalities such as touch sensation.

The use of opiates in the conjunction with the spinal or epidural local anaesthetic such as bupivacaine afford prolonged post operative pain relief (Aboulish et al, 1988, Akerman et al, 1988). A possible synergistic analgesic effect between the local anaesthetic and opioids may have important clinical implications, however, this effect is difficult to evaluate in man (Akerman et al, 1988).

As there are only few studies on analgesic duration of plain bupivacaine, a double blind randomized prospective study was conducted on 90 patients who had undergone parturient in labour in Hospital Universiti Sains Malaysia , Kelantan. The aim of our study was to ascertain whether a smaller dose of intrathecal bupivacaine can preserve the quality of analgesia while generating fewer adverse effects.

Ninety patients with no complicating obstetric and medical problem, whose age ranges from 18 and 42 years were selected randomly into two groups. Group 1 patients received 2 mg plain intrathecal bupivacaine with 25mcg fentanyl and group 2 received 2 mg intrathecal heavy bupivacaine with 25 mcg fentanyl .The pain was assessed on the variables at time 0 (time at the start of IT injection) and at 5, 15,30 min. The result revealed that the use of 2 mg heavy bupivacaine with 25 mcg fentanyl produce adequate level of analgesia at T10 and no incidence of high sensory block. It was statistically significant comparing both groups with a p value of 0.003. In terms of side effect, our study has shown less incidence of side effect including nausea and/or vomiting as well as incidence of pruritus is significantly reduced in the study population (nausea and/or vomiting p value at 0.049 and pruritus p value = 0.026.

CHAPTER 1 : INTRODUCTION

1.1 : Combined spinal epidural

The use of intrathecal and epidural opiods in obstetric has become popular in recent years. The epidural administration of opiods has gained popularity in various settings as a sole analgesic agent or an adjunct to low dose local anaesthetic regimens (Datta et al, 1992). The use of low dose of local anesthetic solutions in a continuous epidural infusion with an initial dose of intrathecal opiods, has allow for exellent analgesia with a low incidence of side effect such as hypotension and motor blockade (Camann et al, 1994). The term used to describe this procedure is the combined spinal-epidural technique, (CSE).

The main advantage of this technique is the speed of onset and completeness of analgesia . The combined spinal-epidural technique gives rapid, reliable analgesia without motor block, and allows patient to get out of bed safely and walk about (Collis et al, 1994) Intrathecal opiods has to be effective in relief of pain in the first stage of labour with the major advantage. The technique offers the possibility of combining rapid onset of subarachnoid analgesia with the flexibility of continuous epidural analgesia. The rapidity of onset and reliability of the CSEA technique improves the quality of analgesia and the overall maternal satisfaction. The appearance of CSF in the hub of the spinal needle may indirectly confirm (reconfirm) the correct epidural needle placement, which is of increased importance in patients with difficult anatomic landmarks and/or increased skin–epidural space distance.

Although some have expressed concern about unknown functional status of the epidural catheter following subarachnoid drug injection, it has been well established that the epidural failure rate for the CSE technique does not exceed that of conventional epidural analgesia for labor. Bupivacaine , the most widely investigated and extremely used spinal anaesthesia, was first to receive FDA approved for epidural and intrathecal use. The quantity of intrathecal fentanyl required to provide a given level of analgesia is typically much smaller than the amount that must be given intravenously.

Intrathecal administration of opioids has the advantages of simplicity, reliability, low dose requirements, and absence of the need to place a catheter into the epidural space. Simplicity and reliability are assured by the technically easy identification of the subarachnoid space assuming proper placement of the opioids (Robert et al, 1989).

1.2 : Definition

Analgesia: Diminished sensation of pain, particularly the relief of pain without loss of consciousness.

Epidural analgesia: Analgesia produced by introduction of the opioid into the subarachnoid space of the vertebral canal

Anesthesia: Loss of feeling or sensation produced by the number of the agents capable of bringing about partial or complete loss of sensation. It is induced primarily to permit the performance of surgery or other painful procedures.

Conduction anesthesia: The lack of sensitivity produced by a local anesthetic injection into the nerve sheath of tissues.

Epidural anesthesia: Anesthesia produced by given injection of the agent between the ligamentum flavum and the dura into the epidural space, also called the extradural or peridural space.

Hypotension: Hypotension is a decrease in systolic blood pressure by more than 20% from patient's baseline.

Local anesthetic: A chemical agent which produces blockade of nerve conduction resulting in transient loss of sensory and or motor function in a specific region of the body.

Motor blockade: The interruption of conduction of motor neurons which impairs or produces inability to consciously move an extremity.

Opioids: Chemical substance which are either endogenous or exogenous to the body that bind specifically to any of the several opioid receptors and produce some agonist opiate effects. Opioid can be administered to produce analgesia without loss of touch, propioception, or conciousness.

Regional anesthesia: Injection of local anesthetics into a particular area of the body to produced temporary loss of sensory and or motor capabilities.

Sensory blockade: The interruption of neuronal conduction of sensory neurons which produces loss of sensation to superficial and deep touch, temperature and pain.

Spinal anesthesia: Anesthesia produced by given injection of the agent between the subarachnoid space between the subarachnoid mater and the pia meter, usually produces differential block of motor, sensory autonomic neurons.

Sympathectomy: The blockade of sympathetic neuronal conduction arising from thoracolumbar spinal segment resulting in systemic vasodilatation.

CHAPTER 2 : OBJECTIVES AND HYPOTHESIS

2.1 : Objectives

The main objective of this study is to compare 2mg plain bupivacaine with 25mcg fentanyl and 2mg heavy bupivacaine with 25mcg fentanyl in combined spinal epidural in labour.

- To compare the maximum block spread.
- To compare the duration of analgesia during intrathecal.
- To compare intensity of motor block between two group
- To compare haemodynamic parameter : blood pressure, heart rate, respiratory rate.
- To compare in term of the severity of the side effects between plain and heavy bupivacaine with fentanyl.

2.2 : Null Hypothesis

- There is no difference in term of analgesic effects between 2mg plain bupivacaine and 2mg heavy bupivacaine with 25mcg fentanyl in labour.
- There is no difference in term of side effects between 2mg plain bupivacaine and 2mg heavy bupivacaine with 25 mcg fentanyl in labour.

CHAPTER 3 : LITERATURE REVIEW

3.1 : Pain

A patient's psychological state contributes significantly to complaints of pain and suffering was well recognized and form part of the basis for the IASP's definition of pain as, "An unpleasant sensory and emotional experience associated with actual and potential tissue damage or described in terms as such damage". Pain can instead be divided into two distinct and qualitatively different categories. These were what I have chosen to call physiological pain and pathological pain. The distinction between the two depends on the argument that physiological pain was a "normal" sensation, unlike the pathological pain was the consequence of an abnormal state (Woolf et al, 1987).

3.1.1 : Physiological pain

Physiological pain was the term used to define the range of transient sensations experienced in response to stimuli that are of sufficient intensity to damage tissue or produce small localized area of injury, but which neither provoke an extensive inflammatory response nor damage the nervous system. Sherington et al, 1906, at the turn of century devised the term "noxious" to describe precisely such stimuli.

Physiological pain can be elicited by mechanical, thermal or chemical stimuli and clearly defined thresholds can be established experimentally in trained subjects, at which the sensation stops being one of pressure, hot or cold and becomes painful (LaMotte et al, 1983). The intensity of the stimuli that reach the pain threshold was almost identical to that which activates the flexion withdrawal reflex (Willer et al, 1980).

The reason for calling the sensation elicited by transient non-tissue damaging noxious stimuli "physiological pain" was two folds. First, in term of the sensory apparatus involved and the nature of the stimulus-response relationship there were similarities with other physiological sensation. Second, from a teleological perspective, physiological pain has a protective role : because of the unpleasant nature of the sensations involved, we learned to avoid certain stimuli and because of the simultaneous activation of the flexion withdrawal reflex there was an automatic removal of the body from the sources of the stimulus (Woolf et al, 1989).

Physiological pain was something we all experienced frequently in our daily lives by touching hot or cold objects or by exposure to intense external mechanical stimuli that may scratch or prick our skin. Indeed, such pain occurred frequently in the clinical context with intervention such as injection (Woolf et al, 1989).

3.1.2 : Pathological pain

Pathological pain was that sensation that arises as a consequence of either inflammatory response that accompanies substantial tissue injury, or damage to nervous system. Pathological pain was divided into inflammatory and neuropathic pain (Woolf et al, 1987). In spite of their differences, there were important common features in which both types of pain differ from physiological pain. There were :

- The pain may occur in the absence of any apparent stimulus.
- The response to suprathreshold stimuli may be exaggerated in either amplitude or duration.
- The threshold for eliciting the pain decreases to a level what would normally be an innocuous stimuli begins to elicit pain.

- The sensation of pain may spread from the site of an injury or a lesion to uninjured or unaffected tissue.
- Pathological interactions between the sympathetic and somatosensory systems may occur.

The presence of all or most of these features (spontaneous pain, hyperpathia / hyperalgesia, allodynia, referred pain, sympathetic dystrophy, sympathetically maintained pain) was what makes clinical pain pathological. Pathological pain involved the disruption of the normal selectivity or specialization of the somatosensory systems. Instead, there was aberrant convergence and the mismatch of stimulus for pathological pain. It may occur in response to the lightest of touches (e.g in causalgia) or in response to mildly noxious stimuli. The sensation was excessive and more prolonged than would be expected for the nature of the stimulus, and it may even occur in the absence of any apparent stimulation, as after brachial plexus avulsion injury (Woolf et al, 1989).

3.2 : The Pathophysiology 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. In contrast, inflammatory and neuropathic pain appears to be the consequences of adaptive and maladaptive disturbances, which occur within the somatosensory system and can be triggered by a wide variety of different situations. Inflammatory pain retains teleological resemblance to physiological pain in that a protective role for the phenomenon can readily be appreciated: tenderness will help to avoid further damage to an injured area while healing takes place. However, neuropathic pain appears to offer no such

benefit to the patient and instead was the pathological product of a disturbed nervous system (Woolf et al, 1989).

The plasticity of the nervous system can be either adaptive or maladaptive. Adaptive plasticity underlies the ability of the nervous system to compensate for damage or to produce changes in function appropriate to changes in the environment. Maladaptive plasticity comprises those changes in the nervous system that led to a disruption of function and, therefore, it may be considered to be a disease state. To a large extent physiological pain was a sensation that reflects certain specific types of peripheral stimuli, while pathological pain was a sensation that was a consequences of change within the nervous system. This result in alteration in the way, in which inflammatory from the periphery, some of which may be quite normal, was handled (Woolf, 1989).

There were four categories of change to the nervous system that can result in the pathogenesis of clinical pain:

- Peripheral sensitization of primary afferents.
- Central sensitization of dorsal horn neurons.
- Abnormal properties in central circuits.
- Permanent change in the nervous system.

The first three tend to occur during inflammatory pain, while the last three tend to occur during neuropathic pain (Woolf, 1989).

3.3 : Characteristic of Acute Pain

Acute pain may be defined as the conscious awareness of tissue or emotional injury. Its perception reflects the activation of nociceptor afferent transmission to the spinal cord and relay via dorsal horn to higher centers. Pain perception consists of two major components:

- Sensory component :

  It describes the location and quality of the stimulus, is transmitted via myelinated A delta fibers and relayed to the neothalamus and somatosensory cortex. This component quickly alerts the organism, resulting in prompt withdrawal from the noxious stimuli.

- The affective – motivational component :

  This component is slowly conducted via peripheral unmyelinated C fibers and establishes neuron synaptic contacts within brain stem and midbrain nuclei and the cortical limbic system.

Pathophysiologic changes associated with acute pain commonly include the following :

- Neurohumoral alteration at the site and in region adjacent to the injury.
- Alteration in synaptic function and nociceptive processing occurring within the spinal cord dorsal horn.
- Neuroendocrine response.
- Sympathoadrenal activation (Cousins, 1989).

3.3.1 : Initiation and propagation of nociception

A complex cascade of events was initiated after a peripheral injury. Several endogenous chemicals including bradykinin, histamine, serotonin, products of arachidonis acid cascade, and neuropeptides such as substance P are released. These chemicals activate receptors on the peripheral terminals of sensory afferent, which begins the process of nociceptive transmission. Many of the chemicals that were released after injury were these substances that were involved in the process of inflammation (Ohara et al, 1988).

3.3.2 : Modulation of Nociception

At the spinal level, transmission may be modulated by either inhibiting the release of neurotransmitters from primary afferent fibers or inhibiting the activation of second order dorsal horn neurons. The source of spinal modulation may either be intrinsic or descend from supraspinal sites.

3.3.3 : Opioid Receptors

The dorsal horn of the spinal cord contains receptors for μ, δ and k receptors. These receptors are located presynaptically as well as postsynaptically on second order neurons. The localization of these receptors provides an anatomic basis for the ability of special opioids to modulate nociceptive transmission.

The inhibitor effects of morphine on the evoked release of substance P have been demonstrated in vivo (Yaksh et al, 1987). An examination of receptor-selective agonist has revealed that both μ- and δ-opioid receptor agonist produce inhibition of evoked release substance P (Yaksh et al,

1987). Pohl et al 1989 have demonstrated the ability of μ and δ agonist to inhibit the evoked release of CGR from dorsal spinal cord slices, but such ability has not yet been examined in vivo.

Evidence for a postsynaptic as well as presynaptic action of spinal opioid has been reported. Opioid agonist will inhibit the firing of second order dorsal horn neurons (Sabbe et al, 1990). The intrathecal administration of opioid receptor agonists will inhibit the nociceptive behavior produced by intrathecal administration of substance P.

3.3.4 : Gamma-Aminobutyric Acid Receptors

The intrathecal administration of γ aminobutyric acid (GABA) agonist yields antinociceptive effects. The spinal administration of the GABA B- but not the GABA A- receptors agonist has been shown to modulate nociceptive processing. Although receptors for GABA have been located on primary afferent nerve terminals, unlike opioid and α_2 agonists, GABA has not been shown to inhibit the release of substance P. Thus, the antinociceptive properties of GABA may serve to modulate segmentally the firing of second order dorsal horn neurons. The used of the GABA B-receptor selective agonist baclofen as an analgesic may be associated with its ability to inhibit other spinal reflex pathways (Goodchild et al, 1987).

3.3.5 : Adrenergic Receptors

The adrenergic system has also been shown to play a role in the modulation of nociceptive information (Fisher et al, 1991). The high concentration of binding sited for α-adrenergic ligands were found in the substansia gelatinosa. α_2 binding sites were concentrated in the dorsal horn. The ability of intrathecal norepinephrine to inhibit nociceptive behavior produced by intrathecally administered substance P indicates that postsynaptic modulation contributes to the