# Comparison between Nalbuphine and Ketamine as an Adjuvant to Heavy Bupivacaine on Post Dural Puncture Headache

## Thesis

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## By


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***Mina Zakria***

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# List of Abbreviations

| Abb. | Full term |
|---|---|
| ADRs | Adverse drug reactions |
| ASA | American Society of Anesthesiologists |
| BMI | Body mass index |
| CNS | Central nervous system |
| CSE | Combined spinal-epidural |
| CSF | Cerebrospinal fluid |
| DBP | Diastolic blood pressure |
| DHS | Dynamic hip screw |
| DOR | δ-opioid receptor |
| EBP | Epidural blood patch |
| FDA | Food and Drug Administration |
| HR | Heart rate |
| ICP | Intracranial pressure |
| IICP | Increased intracranial pressure |
| IOP | Intraocular pressure |
| IV | Intravenous |
| KOR | Kappa-opioid receptor |
| LA | Local anesthetic |
| LAST | Local anesthetic systemic toxicity |
| LP | Lumbar puncture |
| MAOIs | Monoamine oxidase inhibitors |
| MOR | mμ opioid receptor |
| MRI | Magnetic resonance imaging |
| NA | Neuraxial anesthesia |
| NSAIDs | Nonsteroidal antiinflammatory drugs |
| PDPH | Postdural puncture headache |
| RR | Relative risk |
| SBP | Systolic blood pressure |
| SHE | Spinal-epidural hematoma |

# List of Abbreviations Cont...

| Abb. | Full term |
|---|---|
| SNRI | Serotonin and norepinephrine reuptake inhibitors |
| SPGB | Sphenopalatine ganglion block |
| $SpO_2$ | Oxygen saturation |
| TNS | Transient neurologic symptoms |
| TURP | Transurethral resection of the prostate |
| UDP | Unintentional dural puncture |

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# INTRODUCTION

Post dural puncture headache (PDPH) is one of the most common complications of spinal anesthesia and it is defined as any headache after lumber puncture that worsens within 15 minutes of sitting position and it is relieved within 15 minutes of lying down. About 90% of post dural puncture headache occurs within 3 days of the procedure and about 66% start in the first 48 hours ***(Balestrieri, 2003).*** Incidence of post dural puncture headache is directly related to the needle diameter that pierces the dura mater, so smaller diameter needle will be used to decrease risk of post dural puncture headache ***(Lambart et al., 1997).***

There are **many theories** regarding the pathophysiology of PDPH ***(Grant et al., 1991; Morewood, 1993; Balestrieri, 2003; Evans, 1998; Luo and Huizen, 2019).*** However, the actual mechanism is not yet settled.

Nalbuphine is semi synthetic opioid with mixed (μ) antagonist and (κ) agonist properties. It binds to kappa opioid receptors in brain and spinal cord. It prolongs the duration of analgesia without affecting the autonomic nervous system ***(Mostafa et al., 2011).*** Ketamine (NMDA-receptor antagonist) exhibits analgesic properties. It provides long duration of analgesia with cardiovascular stability ***(Kawasaki et al., 2001).*** Both nalbuphine and ketamine have been used as adjuvants in spinal anesthesia, to prolong the analgesic duration or to minimize side effects ***(Singh et al., 2017).*** However, their effects on PDPH were not studied.

# AIM OF THE WORK

So, the aim of this research was to study the incidence and severity of post dural puncture headache when nalbuphine or ketamine is added as an adjuvant to hyperbaric bupivacaine in spinal anesthesia (primary outcome). Secondary outcomes were the effects of adding nalbuphine or ketamine as an adjuvant to hyperbaric bupivacaine on motor and sensory functions, duration of analgesia, hemodynamics and side effects.

# REVIEW OF LITERATURE

# I. SPINAL ANESTHESIA

## A. Anatomy:

Neuraxial anesthesia (NA) is performed by placing a needle between vertebrae and injecting local anesthetic (LA) into the epidural space (epidural anesthesia) or the subarachnoid space (spinal anesthesia) ***(Broadbent et al., 2010)***. Spinal anesthesia is most commonly used for anesthesia and/or analgesia in a variety of lower extremity, lower abdominal, pelvic, and perineal procedures ***(Saifuddin et al., 2011)***.

Spinal anesthesia is performed no higher than the mid to low lumbar vertebral level to avoid puncturing the spinal cord with the spinal needle. In most patients, the spinal cord terminates as the conus medullaris at the lower border of the first lumbar vertebral body (L1), though it may end lower. Therefore, the spinal needle is inserted at the L3 to L4 or L4 to L5 interspace ***(Saifuddin et al., 2011)***. The intercristal line (ie, the line between iliac crests) is used as a rough guide for spinal needle placement. In many patients, this line crosses the body of L4, though it may cross the spine from L1 to L2 to L4 to L5, and tends to be higher in obese and female patients ***(Margarido et al., 2011)***.

The epidural space is the space between the dural sac and the inside of the bony spinal canal. The tough ligamentum flavum forms the posterior border of the epidural space at each interlaminar space. The interspinous ligament stretches between the spinous processes of successive vertebrae, and the supraspinous ligament anchors the tips of the spinous processes in a continuous column (figure 1) ***(Saifuddin et al., 2011)***.

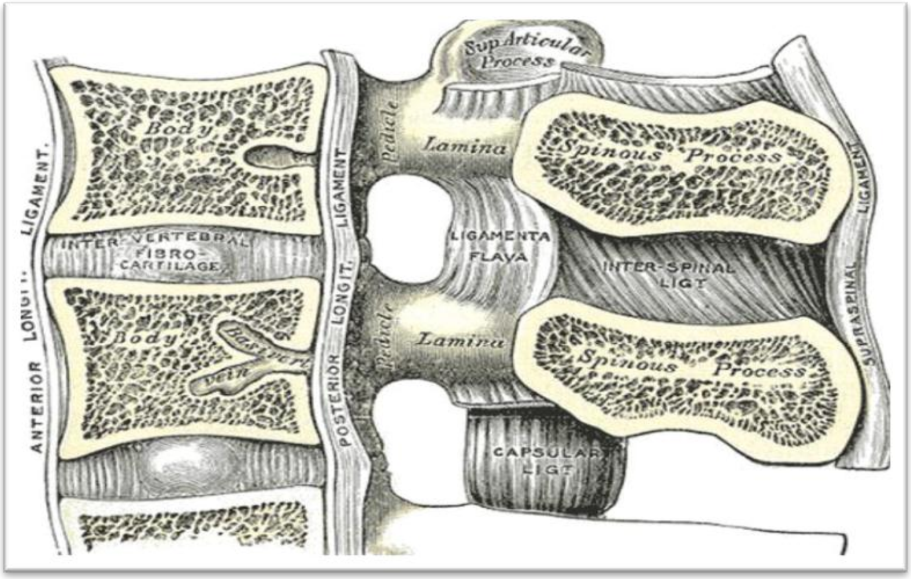


**Figure (1):** Spinal ligaments ***(Saifuddin et al., 2011)***.

Within the bony vertebral canal, the spinal cord is surrounded by three membranes: the pia mater, the arachnoid mater, and the dura mater (innermost to outmost). The dura and arachnoid maters loosely adhere to each other in the spinal canal and comprise the "dural sac" in which the spinal cord is suspended. The subarachnoid space within the dural sac is located between the pia and arachnoid maters and contains cerebrospinal fluid (CSF), spinal nerves, and blood vessels. A loose trabecular network exists between the pia and dura-arachnoid (figure 2) ***(Margarido et al., 2011)***.

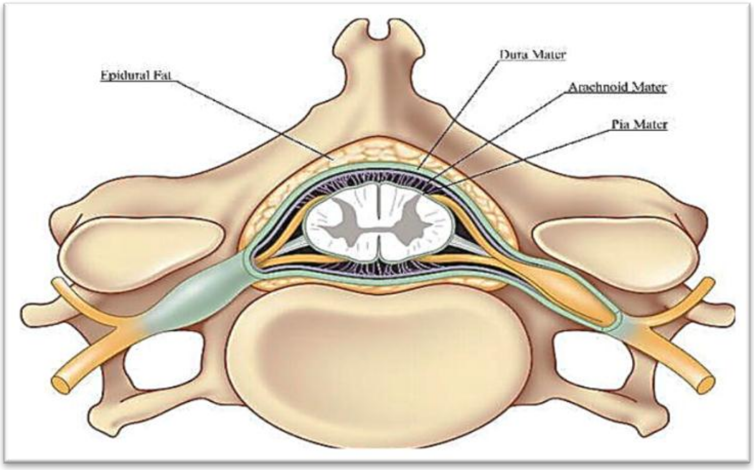


**Figure (2):** Meninges ***(Margarido et al., 2011)***.

The central nervous system (CNS) is surrounded by CSF which is formed continuously by the choroid plexuses and serves to protect the brain and spinal cord by providing a cushion. It also serves as a conduit for delivery of anesthetic agents to the spinal cord. It circulates in the spinal canal, with both bulk flow and oscillatory movements. This flow may explain some of the movement of anesthetic agents toward the brain after injection into the lumbar subarachnoid space. The density of CSF at body temperature averages 1.0003 ± 0.0003 g/mL; density relative to injected local anesthetic (LA) solution affects distribution of spinal block ***(Davis and King, 2012)***.

Autonomic nerves are blocked by spinal anesthesia, in addition to sensory and motor nerves. The extent of sympathetic block depends on the height of spinal block. Preganglionic sympathetic nerve fibers arise from the intermediolateral tract of spinal cord from T1 to L2. The axons exit the spinal cord with the ventral nerve root of the spinal nerves and synapse with cell bodies in the ganglion of sympathetic trunk. Sympathetic cardioaccelerator fibers arise from T1 to T4 ***(Richardson et al., 2015)***.

## B. Indications

Neuraxial anesthesia (NA) is most commonly used for lower abdominal and lower extremity surgery. The "sensory level" required for a specific surgery is determined by the dermatome level of the skin incision and by the level required for surgical manipulation; these two requirements may be different. As an example, a low abdominal incision for cesarean delivery is made at T11 to T12 dermatome, but a T4 spinal level is required to prevent pain with peritoneal manipulation ***(Ituk et al., 2019)***.

## C. Physiologic effects

The physiologic effects of neuraxial anesthesia (NA) are the result of blockade of sympathetic, motor and sensory nerves, the compensatory reflexes, and unopposed parasympathetic tone. The magnitude of various physiologic effects depends on the extent and speed of onset of the block, and patient factors ***(Hebl et al., 2016)***.

### 1. Cardiovascular

Hypotension and bradycardia are the most common and important physiologic effects of neuraxial anesthesia, ***(Hartmann et al., 2012)***. **Hypotension** occurs in about 47% of cases of spinal anesthesia, due to decreased systemic vascular resistance, peripheral blood pooling with decreased venous return to the heart, or both. These effects are due to sympathetic block and block of adrenal medullary secretion. With spinal block below T4, vasoconstriction above the level of the block may compensate and mitigate the decrease in blood pressure ***(Carpenter et al., 2012)***.

Clinically significant **bradycardia** occurs in 10 – 15% of cases of spinal anesthesia. Mechanisms for bradycardia are direct and indirect. Direct effect is due to blockade of sympathetic cardio-accelerator fibers. Indirect mechanisms include decreased output of the myocardial pacemaker cells due to decreasove these wordse in venous return, stimulation of low-pressure baroreceptors in right atrium and vena cava, and stimulation of mechanoreceptors in left ventricle (paradoxical Bezold-Jarisch reflex) ***(Pollard, 2011)***.

### 2. Pulmonary

Bronchial tone at rest is controlled in part by the balance between parasympathetic and sympathetic tone. Sympathetic block associated with high spinal anesthesia may allow parasympathetic predominance, and lead to bronchospasm.