ADDIS ABABA UNIVERSITY-COLLEGE OF HEALTH SCIENCES

# INCIDENCE OF ADVERSE EFFECTS AND ASSOCIATED FACTORS AFTER INTRATHECAL ADMINISTRATION OF MORPHINE IN ELECTIVE SURGERIES IN TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA, 2024GC.

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A RESEARCH PAPER SUBMITTED TO THE DEPARTMENT OF ANAESTHESIOLOGY, CRITICAL CARE AND PAIN MEDICINE, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR A SPECIALITY CERTIFICATE IN ANAESTHESIOLOGY, CRITICAL CARE AND PAIN MEDICINE.

# INCIDENCE OF ADVERSE EFFECTS AND ASSOCIATED FACTORS AFTER INTRATHECAL ADMINISTRATION OF MORPHINE IN ELECTIVE SURGERIES IN TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA, 2024GC.

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MAY,2024

ADDIS ABABA, ETHIOPIA

DECLARATION OF THE PRINCIPAL INVESTIGATOR

I, Dr. Firaol Niftalem declare that this research is my original paperwork on the incidence of adverse effects and associated factors after intrathecal administration of morphine in elective surgeries in Tikur Anbessa specialized as partial fulfillment required for specialty certificate in anesthesiology, critical care and pain medicine.

**Name of the student: _____**

Date. _____ Signature _____

APPROVAL OF THE FIRST ADVISOR

Name of the first advisor: _____

Date. _____ Signature _____

**APPROVAL OF THE SECOND ADVISOR**

Name of the second advisor: _____

Date. _____ Signature _____

## SUMMARY

### BACKGROUND

One of the most efficient analgesic techniques in various surgical operations is the intraspinal injection of opioids (1,2). Intrathecal morphine can enhance and prolong intraoperative and postoperative analgesia when used alone or in conjunction with a local anesthetic. However, a wide range of clinically significant adverse effects have been documented. This covers symptoms including nausea, vomiting, pruritus, urine retention, or respiratory depression(1,3).

### OBJECTIVES

Determining the incidence of adverse effects and associated factors after intrathecal administration of morphine in elective surgeries.

### METHODS

A cross-sectional analytic study was conducted on patients who underwent elective surgery with spinal anesthesia combined with morphine at Tikur Anbessa Specialized Hospital. The data was collected within 24 hours after the administration of intrathecal morphine. The study used the binary and logistic regression models to assess the association between morphine-related adverse effects and potential independent factors.

### RESULT

Among 273 study participants who received spinal anesthesia combined with intrathecal morphine, 78(28.6%) and 42(15%) had nausea and vomiting respectively. And 63(23.1%) of the participants reported having pruritus, 11(4%) reported urinary retention and respiratory depression was reported as shortness of breath 10(3.7%) and cyanosis/respiratory rate less than 10 (2.7%) in the study.

### CONCLUSION AND RECCOMENDATION

A study was conducted to determine the adverse effects of intrathecal morphine and associated factors in elective patients. The findings revealed that a considerable proportion of participants experienced nausea, vomiting, pruritus, urinary retention, and respiratory depression. Vigilant monitoring and tailored interventions are needed to mitigate the risk of adverse effects. Further research is warranted to optimize patient outcomes.

# ACKNOWLEDGMENT

I am writing to express my deepest gratitude and appreciation to Dr. Yonathan Abebe (primary advisor) and Dr. Amria Shamil (secondary advisor) for their guidance and support in developing my research paper. Your suggestions will be invaluable and help to shape my research paper into more coherent research, refine my ideas and have a more critical approach toward my research objectives.

**List of Tables and Figures**

## List of abbreviation

| | |
|---|---|
| ACCPM | Anesthesiology, critical care and pain medicine |
| ASA | American Society of Anesthesiology |
| BMI | Body mass index |
| C/S | Cesarean section |
| I.V | Intravenous |
| IT | Intrathecal |
| Mcg | Microgram |
| PONV | Post-operative nausea and vomiting |
| POUR | postoperative urinary retention |
| RRT | Rapid response team |
| SA | Spinal anesthesia |
| SPSS | Statistical package for the social science |
| TASH | Tikur Anbessa Specialized hospital |

Contents

# CHAPTER ONE

# INTRODUCTION

## 1.1 Backgrounds

At the beginning of the twentieth century, surgical procedures were performed under regional anesthetic, which consisted of spinal, caudal, and epidural blocks. Large-scale research conducted in the 1950s revealed that difficulties were uncommon when blocks were carried out expertly and with attention to sterile technique, paired with the better safety profile of injectable drugs. Blocks had previously been regarded as risky because of reports of permanent neurologic harm(4).

Spinal anesthetic has a long history of being safe. It is sometimes the preferred anesthetic and sometimes the safest choice. In addition to being used to provide surgical anesthesia, local anesthetics are frequently coupled with intrathecal (IT) opioids to enhance intraoperative analgesia and offer postoperative analgesia after the local anesthetic wears off. To treat chronic pain, spinal opioids are also sometimes administered as single injections, but implantable infusion pumps are more frequently employed(4,5).

Due to its longer duration of action than fentanyl and sufentanil, morphine is the neuraxial opioid that is utilized the most frequently(5,6).

Morphine intraspinal injection is one of the best analgesic techniques used in various surgical operations. However, several bothersome side effects, such as nausea, vomiting, and itching, are frequently experienced after receiving intrathecal morphine injections(1,2). Even though post-operative nausea and vomiting (PONV) are reported less often with regional than general anesthesia (7,8), they are still a problem, especially in outpatient procedures where regional anesthesia is more frequently used. PONV can delay discharge or result in unplanned hospital admission(9).

It has not yet been figured out what dosage will offer the best postoperative analgesia with the fewest side effects. Even though dose-response associations have been described following the injection of epidural morphine(10,11) there is inconsistent information about the relationship between intrathecal morphine and analgesic efficacy(6,12,13).

### Postoperative nausea and vomiting (PONV)

Nausea is an unpleasant sensation referring to a desire to vomit not associated with expulsive muscular movement whereas Vomiting is the forceful expulsion of even a small amount of upper gastrointestinal contents through the mouth (14). Due to its negative effects, including delayed recovery, unplanned hospital admission, delayed return to work for ambulatory

patients, pulmonary aspiration, wound dehiscence, and dehydration, PONV is still a serious problem in modern anesthetic practice(15).

Post-operative nausea and vomiting (PONV) are defined as nausea and/or vomiting occurring within 24 hours after surgery. PONV physiology is intricate and poorly understood. The vomiting center in the medulla oblongata is where nausea and vomiting are primarily controlled. It consists of the nucleus of the tractus solitarius (NTS) and the reticular formation(16,17).

**Pruritus**

The medical term for itching, known as pruritus, is described as an uncomfortable feeling brought on by the stimulation of sensory nerve endings in the outermost layers of skin, which typically prompts scratching. Each person experiences itching differently(18).

Scratching often occurs only in parts of the face innervated by the trigeminal nerve, with the eyes, nose, cheeks, and trunk being the typical starting points for itching (19,20). According to patient satisfaction surveys, this persistent itch is one of the most distressing, non-life-threatening consequences that patients report, and because it may be so debilitating, it should receive the same level of therapeutic attention as pain(21).

**Urinary retention**

Following anesthesia and surgery, postoperative urinary retention (POUR) is typical. It takes a variety of afferent and efferent neural networks, reflexes, and central and peripheral neurotransmitters to control micturition. Numerous insults that may disrupt this mechanism and encourage the emergence of urine retention occur during the perioperative period. Intrathecal opioids have been shown by urodynamic tests to relax the smooth muscles in the bladder with little to no effect on the internal and external urethral sphincters(22).

The inability to start the micturition process or empty the bladder is known as urinary retention. Urinary retention lacks distinct defining characteristics, such as a particular volume of urine or amount of time postoperatively without micturition; however, according to the consensus view in the current literature, urinary retention would be defined as the inability to initiate micturition with a bladder volume greater than 500 ml (23).

Although prolonged detrusor dysfunction and longer hospital stays have been observed, the long-term effects of POUR are not often immediately apparent in the perioperative period(23).

**Respiratory depression**

Respiratory depression is rare after IT morphine but it is a serious risk; patients may die or suffer permanent brain damage as a consequence. ASA defines respiratory depression following the administration of opioids as a respiratory rate below 10bpm, arterial oxygen saturation below 90%, hypercapnia above 50mmHg, and clinical signs such as dizziness, sedation, periodic apnea or cyanosis.

Respiratory depression following neuraxial morphine administration is biphasic: it can happen early (30–90 min) after hydrophilic morphine administration via epidural injection due to systemic vascular absorption, or it can happen late (6–18 h) following epidural or intrathecal morphine due to rostral spread in cerebrospinal fluid and slow penetration into the brainstem. Lipophilic opioids, such as fentanyl and sufentanil, however, do not result in delayed respiratory depression(24).

## 1.2 Statement of the problem

Around the world, spinal anesthesia is a widely used anesthetic method. With a stated endpoint, it generates a quick, dense, and predictable block that is reasonably simple to achieve and has a very high success rate(25).

Intrathecal morphine has the benefit of enhancing and extending intraoperative and postoperative analgesia when administered either alone or in conjunction with local anesthetics. However, numerous side effects that are clinically significant have been observed. This includes symptoms such as nausea, vomiting, itching, urine retention, or respiratory depression (1,3).

However, despite the prevalence of intrathecal morphine use and the potential for adverse effects, there is still a lack of studies on the adverse effects of morphine in Ethiopia. This study aims to investigate the adverse effects of intrathecal morphine and identify the factors that contribute to these effects. By doing so, the study will provide insights into the risk factors for adverse effects of intrathecal morphine and inform interventions to mitigate their impact on patient outcomes. Ultimately, the findings of this study may help healthcare providers to better manage pain in patients while minimizing the risk of adverse effects associated with intrathecal morphine.

## 1.3 Rationale of Study

Intrathecal morphine is a potent pain reliever that is administered directly into the cerebrospinal fluid. However, the use of intrathecal morphine is associated with a range of adverse effects, including respiratory depression, nausea, vomiting, pruritus and urinary retention. These adverse effects can be severe and, in some cases, life-threatening.
Therefore, it is important to study the adverse effects of intrathecal morphine to better understand the risks associated with their use and to develop strategies for minimizing these risks. This information can help healthcare providers make informed decisions about the use of intrathecal morphine for pain management and can inform the development of guidelines and protocols for their safe and effective use.
In addition, studying the adverse effects of intrathecal morphine can help identify patients who may be at increased risk for experiencing these effects. This information can be used to guide patient selection and to develop individualized treatment plans that minimize the risk of adverse effects. Intrathecal anesthesia combined with morphine is widely used at TASH, but no studies are addressing the incidence of adverse effects.

Studying the incidence of adverse effects of morphine in TASH is important for healthcare professionals, patients, policymakers, and drug regulatory agencies. It can help to inform prescribing decisions, reduce the harm caused by opioids, and improve the safety and efficacy of these drugs.

The findings of this study can also be used to provide data for further research in the area.

# CHAPTER TWO

# LITERATURE REVIEW

Opioid intraspinal injection is one of the most effective analgesic techniques used in various surgical operations. When compared to general anesthesia, these approaches exhibit higher efficacy and superior safety profiles. It has been demonstrated that patients' intraoperative anesthesia and postoperative pain relief are improved when morphine is added to the local anesthetic(1,26). Intrathecal morphine, however, carries a higher risk of side effects, including PONV, pruritus, urinary retention and respiratory depression (3).

## 2.1 postoperative nausea and vomiting (PONV)

Despite studies on the risk following regional anesthesia with intrathecal morphine are few, they show that intrathecal morphine is highly emetogenic and adds to the PONV risk linked to other forms of anesthesia. The overall risk of PONV after general anesthesia is reported to be around 30% even with prophylactic medications(27).

### *Incidence*

Numerous investigations have shown that intrathecal morphine raises the likelihood of postoperative nausea and vomiting. Depending on the type and dosage of the morphine administered, as well as patient characteristics like age, sex, and a history of motion sickness, the prevalence of nausea and vomiting with intrathecal morphine ranges from 20–60%(27–29).

A prospective observational cohort study of 108 patients in a county hospital in Sweden regarding PONV in patients undergoing hip/knee replacement under spinal anesthesia with intrathecal morphine revealed: that 46% of patients experienced PONV during the 3-day study period, of which 36% of patients did so on the first day following the procedure. likewise, a higher incidence of PONV was linked to feminine gender and/or a history of motion sickness(29).

A study of 1,364 anesthesia records between October 2010 and April 2011 at Siriraj Hospital examined the frequency of nausea, vomiting, and pruritus following spinal anesthesia with intrathecal morphine. showed that the rates of vomiting and nausea were 21.5 and 14.8, respectively(28).

Higher morphine dose, feminine sex, younger age, non-smokers, prior history of nausea and vomiting, and length of operation are risk factors for nausea and vomiting with intrathecal morphine(29).

## 2.2 Pruritus

The symptom is a well-known, albeit uncommon, adverse effect of opiates when given systemically, and when this occurs, the itching is widespread. The itching in the case of epidural and spinal administration may be generalized, but frequently a segmental distribution is discernible, concentrated on the level of injection, or the itching is restricted to a specific location, such as the nose and face. Therefore, it is likely that there is an impact on the spinal cord itself in the latter scenario(1).

### *Incidence*

Studies on the adverse outcomes of morphine after neuraxial anesthesia in pregnant women reported the incidence of pruritus to be 60–100% after intrathecal morphine. Pregnant women appear to be more vulnerable to pruritus after neuraxial morphine administration than other populations(1,20,30,31). In contrarily, the incidence of pruritus following intrathecal morphine varied from 30% to 60% after orthopedic surgery(32–34). This increased incidence in pregnant women may be due to an interaction of estrogen with opioid receptors (31,35,36).

There are contradicting studies on the dose-incidence and dose-severity relation of pruritus and morphine.

In a study comparing the incidence of pruritus after intrathecally administering 0.1 mg and 0.2 mg of morphine, there was no statistically significant difference between the two groups in terms of the quality of the analgesia or the frequency and intensity of itching (37).

Another study examining the incidence, severity, and relationship of pruritus after intrathecal morphine for c/s to serum serotonin levels in subgroups of patients receiving 100 mcg (M100) and 200 mcg (M200) revealed that the postoperative serum serotonin level significantly increased in both groups, by 283% versus 556% (P 0.05) for M100 and M200, respectively. In both the M100 and the M200 groups, the prevalence of pruritus was 55% and 75%, respectively (P=0.32). At six and eight hours but not at other periods, group M200 had substantially more postoperative pruritus than group M100 (P 0.05). Postoperative analgesia, as well as analgesic consumption, was comparable between groups (38).

In a meta-analysis of 28 trials, data regarding the prevalence of pruritus was culled from 25 of them, which included 700 patients getting morphine and 434 receiving a placebo. Pruritus was reported by 12% of patients on the placebo and 37% of patients receiving morphine. increased intrathecal dosage of morphine caused an increase in pruritus(3).

### *Severity*

Depending on the type, route, and dose of opioid taken, pruritus sets in soon after analgesia. With the minimal effective dose and the addition of local anesthetics, pruritus brought on by lipid-soluble opioids like fentanyl and sufentanil lasts for a shorter period and appears to be less severe and common. Intrathecal morphine-induced pruritus lasts longer and is more challenging to manage(39).

Epinephrine co-administration may have an impact on the side effects of spinal and epidural morphine, such as pruritus. As a vasoconstrictor, epinephrine increases the concentration of morphine in the cerebrospinal fluid, decreasing their vascular absorption from the spinal and epidural regions and perhaps worsening adverse effects(1,20)

In one prospective study over 2 years from October 2012 to October 2014 in KK Women's and Children's Hospital, Singapore showed 56.5% had moderate or severe pruritus (score 4–10), while 43.5% had no or mild pruritus (score 0–3) (40).

### 2.3 Urinary retention

Multiple studies reviewed have shown that intrathecal opioid use increases the incidence of urinary retention.

In a study involving 30 patients undergoing orthopedic surgery, the patients were split into two groups: the control group (16 patients underwent spinal anesthesia with hyperbaric 0.5% bupivacaine) and the experimental group (14 patients underwent spinal anesthesia with hyperbaric 0.5% bupivacaine combined with of 0.2 mg morphine). The length of anesthesia, the elapsed time between micturition and urgency, and the requirement to insert a urinary catheter were all examined. And displayed There was no discernible difference in the length of anesthesia between the groups, but it was found that patients receiving spinal anesthesia with a 0.5% hyperbaric solution of bupivacaine and intrathecal morphine had a higher incidence of urinary catheterization, a longer time to catheterization, and a longer time to micturition. (41).

In a meta-analysis assessing the incidence of urinary retention in patients receiving intrathecal morphine anesthesia, two studies using morphine and intrathecal anesthesia were used; neither study used randomization, and the reported incidence of urinary retention was 36% and 25%, respectively. However, research involving intrathecal fentanyl or sufentanil has shown a low prevalence of urine retention, with rates ranging from 0% to 25%(42)

Intrathecal morphine decreases the urge to urinate, lessens detrusor contractions, increases the volume of urine retained, changes urethral sphincter activity, and impairs the coordination between detrusor contraction and internal urethral sphincter relaxation in humans. One hour after the administration of morphine, suppression of bladder function was seen in healthy participants, and it remained for 24 hours(43).

In one study, the mean times of restoration of lower urinary tract function in patients after administration of intrathecal morphine at doses of 0.1 and 0.3 mg were 14 and 20 hours, respectively(44). A consistent finding from a different study was that it took an average of 17.2 hours from the administration of morphine until micturition. (41).

## 2.4 Respiratory depression

Both early (30 to 90 min) and late (6 to 18 h) respiratory depression can follow neuraxial morphine treatment. While the incidence of respiratory depression in patients who have undergone cesarean section ranges from 0% to 0.9%, it is reported that in non-obstetric studies, the incidence of respiratory depression following neuraxial morphine ranges from 0.01% to 7%. This variation in reported incidence is caused by the absence of a standardized definition of respiratory depression. Respiratory depression is rare after intrathecal dosages of 0.1 or 0.25 mg of morphine; instead, patients who get greater doses are more frequently reported to have it(24).

Higher doses of given opioids, as well as patient comorbidities such as obesity, obstructive sleep apnea (OSA), and cardiovascular disease, are thought to increase the risk of respiratory depression (45).

The prevalence of respiratory depression following neuraxial morphine administration in the post-cesarean delivery population was examined in a study involving 4963 participants. The spinal dose of morphine ranged from 100 to 450 g intrathecally and from 3 to 5 mg epidurally. The study's findings revealed that no respiratory RRT episodes occurred during the investigation. There were no desaturation incidents noted, and no patients received naloxone or further oxygen therapy(46).

The incidence of respiratory depression was found to be 3% in a study to assess the safety and effectiveness of intrathecal morphine analgesia for acute postoperative pain over seven years with 5969 surgical patients at Indiana University Hospital; it is not life-threatening and is responsive to naloxone(47).

In conclusion, Intrathecal opioids can improve intraoperative anesthesia quality and prolong postoperative analgesia. Conversely, they can cause undesirable effects, including nausea, vomiting, pruritus, urinary retention and respiratory depression. Some Opioid effects depend on the dose administered and opioid physicochemical properties, particularly lipid solubility. Lipophilic opioids have a more rapid onset and shorter duration of action than hydrophilic opioids, whereas hydrophilic opioids may provide longer analgesia duration but have greater risks of late respiratory depression. Overall, while intrathecal morphine can be effective in managing pain, it should be used with caution and only under the supervision of a healthcare provider to minimize the risk of adverse effects.

# CHAPTER THREE

## OBJECTIVES

### General objective

Determining the incidence of adverse effects and associated factors after intrathecal morphine administration on elective surgeries.

### Specific objectives

- To determine the incidence of PONV and its associated factors
- To determine the incidence of postoperative pruritus and its associated factors
- To determine the incidence of postoperative urinary retention and its associated factors
- To determine the incidence of postoperative respiratory depression and its associated factors.

# CHAPTER FOUR

## METHODS AND MATERIALS

### 4.1. Study area

The study had been conducted at Tikur Anbessa Specialized Hospital which is found in Addis Ababa. It is one of the biggest hospitals in the country and serves people coming from four corners of the country.

### 4.2. Study period

From August 1, 2023, to April 30, 2024, GC.

### 4.3. Study Design

Prospective Cross-sectional Analytic Study

### 4.4. Population

#### *4.4.1. Source population*

All patients who have received spinal anesthesia combined with morphine for elective surgeries in obstetric, orthopedic and endo urology tables.

#### *4.4.2. Study Population*

All selected patients who received spinal anesthesia combined with morphine for elective surgeries obstetric, orthopedic and endo urology tables.

### 4.5. Inclusion and Exclusion Criteria

#### *4.5.1 Inclusion criteria*

All patients who received spinal anesthesia combined with morphine for elective surgery were included.

#### *4.5.2 Exclusion criteria*

Patients with known medical illnesses including liver, kidney, allergy, skin or diabetes.

Patients who have allergies to opioids or any of the components used during the intrathecal administration

Recent systemic administration of opioids (less than 24 hours.)

Patient refusal of the study

### 4.6. Sample size determination

There are four dependent variables in this study (PONV, POUR, Pruritus and Respiratory depression) which were analyzed independently. For this reason, the P value for each dependent variable is taken from previous studies which had adequate sample sizes.

The sample size is calculated by the following formula:

$$N = \frac{z^2 p(1-\rho)}{D^2}$$

The sample size for PONV:

A study from a county hospital in Sweden with a prospective observational cohort study regarding PONV in patients undergoing hip/knee replacement under spinal anesthesia combined with intrathecal morphine showed that 36% of patients developed PONV within 24 hrs. [45].

N= Sample size

P= Population proportion (from the previous study=0.36)

Z = Z value corresponding to a 95% level of significance = 1.96

D= Margin of error (5%)

$$N = \frac{1.96^2 0.36(1-0.36)}{0.05^2}$$

N~ 354

If the population to be studied in a year is less than 10,000 (finite population) then the next formula, which uses the required sample size obtained from the above formula was applied.

$$n' = \frac{n}{1+\frac{n}{N}}$$

n'- Sample size for finite population

n- The sample size required if the population would have been more than 10,000.

N- The estimated population size (estimated number of elective spinal surgeries done in the first six months of the year 2023 GC in TASH was 962).

$$n' = \frac{354}{1+\frac{354}{962}}$$

n'= 260

The sample size required for PONV is 260.

So similar procedures were taken for POUR, Respiratory depression and Pruritus.

The sample size for Pruritus:

A study from KK Women's and Children's Hospital in Singapore from October 2012 to October 2014 showed that 56.5% of patients developed pruritus after intrathecal morphine [32].

Using the same formula and procedure as above: n'=272

The sample size for POUR:

A study at the University Hospital of Larissa, Greece showed that 36% of patients undergoing Laparoscopic transabdominal preperitoneal repair of inguinal hernia under spinal anesthesia combined with morphine developed POUR [50].

Using the same formula and procedure as above: n'=260

The sample size for respiratory depression:

In study to determine the safety and efficacy of intrathecal morphine with 5969 surgical patients at Indiana University Hospital showed the incidence of respiratory depression is 3% in patients who received intrathecal morphine [57].

Using the same formula and procedure as above: n'=43

Since the largest sample size from the above is 272, it was taken to achieve the desired sample size for this study.

### 4.7. Sampling Procedure

Study participants were selected from the daily surgical list of patients scheduled for surgery under spinal anesthesia combined with intrathecal morphine using a systematic randomization technique using skip intervals.

### 4.8. Data collection procedure

The data were collected by the principal investigator and ACCPM residents assigned to elective operation theatre through a structured questionnaire. The data was checked for completeness every day after collecting questionnaire papers.

The structured questionnaire includes:

Part I: Socio-demographic variables and preoperative assessment.

Part II: Assessments for PONV, Pruritus, POUR and Respiratory Depression

### 4.9. Data Analysis Procedure

After the data collection and completeness were confirmed, it was entered into the SPSS version 27. Data cleaning was performed to check for outliers, missed values and any inconsistencies before the data were analyzed using the software.

### 4.10. Data quality assurance

A pilot survey (pre-test on 5% of individuals before the actual data collection time) was carried out before the formal use of the questionnaire to ensure that the statement of each question was clear and understandable, and that data was cleaned daily. The questionnaire was checked for completeness to ensure the quality of the data.

### 4.11. Study variables

*4.11.1. Dependent variables*

- Post-operative nausea and vomiting (PONV)
- Pruritus
- Urinary retention (POUR)
- Respiratory depression

*4.11.2. Independent variables*

- Age
- Sex
- Body mass index (BMI)
- ASA class
- Previous post-spinal adverse effects
- History of motion sickness
- History of smoking
- Dose of the morphine

### 4.12. Operational definition

Post-operative nausea and vomiting (PONV)

- Nausea is an unpleasant sensation referring to a desire to vomit not associated with expulsive muscular movement(14).
- Vomiting is the forceful expulsion of even a small amount of upper gastrointestinal contents through the mouth(14).

Pruritus:

- Defined as uncomfortable itching that occurred within 24 hrs. after intrathecal opioids may or not require intervention from health care providers (18,20).

Urinary retention

- Urinary retention is the inability to initiate micturition or empty the bladder (23).

Respiratory depression

- Respiratory depression following the administration of opioids is a respiratory rate below 10bpm, arterial oxygen saturation below 90%, hypercapnia above 50mmHg, or clinical signs such as dizziness, sedation, periodic apnea or cyanosis (ASA definition).

### 4.13. Ethical issue

• Ethical clearance and support letter was obtained from Anesthesiology, critical care and pain medicine department, and Chief Clinical and Academic Director Offices.

Verbal informed consent was taken from respondents after an explanation was given on the objective, procedure, potential risks and benefits of participating in the study, and the right to withdraw from the study at any time throughout their interview.

• Study participants were assured of their information confidentiality and their information will not be shared with anyone other than the study team. The data collection was held with strict privacy and participants were reassured of confidentiality whenever necessary.

### 4.14. Result dissemination plan

The study results will be presented to the Department of Anesthesiology, Critical Care and Pain Medicine, School of Medicine and College of Health Sciences at Addis Ababa University. Every effort will be made to publish in relevant scientific journals.

# CHAPTER FIVE

## RESULTS

A total of 273 adult patients who took spinal anesthesia combined with intrathecal morphine scheduled for elective surgery took part in the study. The study evaluated intrathecal morphine-related complications occurring within 24 hours after spinal anesthesia and the associated factors. Patients who declined to participate were not included in the study. Three operating tables, Obstetrics, Endo-urology, and Orthopedics, were selected as strata. Patients were selected from each stratum using systematic sampling with skip intervals.

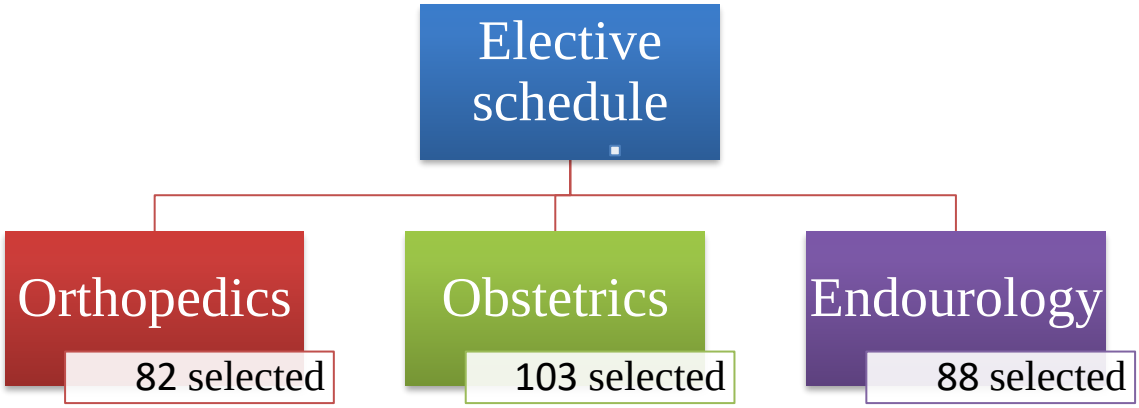


Figure 1: Three selected strata from which systemic random sampling is applied

**5.1 - Socio-demographic Characteristics of Study Participants:**

The study included participants aged 18 to 87, with an average age of 38.66. Female participants made up 56.4% of the study, while male participants made up 43.6%. In terms of education, 26% had no formal education, 41.8% completed elementary or high school, 31.1% completed a diploma or bachelor's degree, and 1.1% completed a master's degree or higher. In regards to marital status, 65.6% of participants were married, 26.4% were unmarried, and 8.1% were widowed.

### 5.2 - Physical Characteristics of Participants

Of the participants, 36.3% were classified as ASA I and 63.7% were classified as ASA II. 6.6% reported a history of smoking and 5.1% reported a history of motion sickness.

**5.2 Incidence of Postoperative Nausea and vomiting**

Among 273 study participants, 78(28.6 %) of them reported having nausea within 24 hrs. after intrathecal administration of morphine. Whereas 42(15.4) of the study participants reported to have vomiting. Among those who reported having nausea or vomiting, 37% of them requested medical management.

***5.2.1. Factors associated with the incidence of Nausea***

Binary logistic regression was performed to assess the association of each independent variable (Age, Sex, BMI, ASA Classification, History of motion sickness, previous post-spinal adverse effects, operating table, Morphine dose) with the dependent variable and the factors that showed a p-value of 0.25 and less(Age, BMI, sex, ASA Class, History of motion sickness, previous history of nausea, previous history of vomiting, previous history of pruritus, operating table and morphine dose ) were added to the multivariate regression model to detect the statistically significance variables.

The outcome of logistic regression static stated that the selected model was a good logistic regression model fit since the Hosmer-Lemeshow goodness of fit p-value was 0.214, it is greater than 0.05, then fails to reject the null hypothesis and it is stated the logistic regression models a good fit for the data set.

Additionally, the pseudo-R-square, the regression result showed that the square of the correlation between the model predicted values and the actual values the outcome of this correlation was 45.8% (Nagelkerke R2)

| Variables | Categories | COR (95%CI) | P value | AOR (95%CI) | P value |
|---|---|---|---|---|---|
| Sex | Male | 1 | | 1 | |
| | Female | 1.78(2.558,9.001) | 0.001 | 2.260(0.818,6.239) | 0.116 |
| ASA Class | ASA I | 1 | | 1 | |
| | ASA II | 4.431(2.252,8.717) | 0.001 | 3.494(1.056,11.555) | 0.040* |
| Operating theater | Obstetrics | 1 | | 1 | |
| | Orthopedics | 0.218(0.109,0.436) | 0.001 | 1.310(0.313,5.482) | 0.712 |
| | Endourology | 0.201(0.101,0.400) | 0.001 | 0.962(0.234,3.536) | 0.911 |
| History of motion sickness | No | 1 | | 1 | |
| | Yes | 17.545(3.827,80.448) | 0.001 | 10.831(1.879,62.415) | 0.008* |
| Previous history of nausea | No | 1 | | 1 | |
| | Yes | 15.083(7.470,30.456) | 0.001 | 6.832(2.734,17.071) | 0.001* |
| Previous history of vomiting | No | 1 | | 1 | |
| | Yes | 28.444(8.251,98.059) | 0.001 | 4.527(1.028,19.941) | 0.046* |
| Previous history of vomiting | No | 1 | | 1 | |
| | Yes | 4.883(1.845,12.925) | 0.001 | 1.540(0.369,6.427) | 0.554 |
| Morphine Dose | 100to200mcg | 1 | | 1 | |
| | 200to300mcg | 0.651(0.388,1.094) | 0.105 | 1.574(0.802,3.087) | 0.187 |
| Age | | 0.983(0.965,1.002) | 0.076 | 0.982(0.960,1.004) | 0.115 |
| BMI | | 1.147(1.049,1.254) | 0.003 | 1.019(0.915,1.133) | 0.737 |

1=indicate for reference range *significant p value(P<0.05)

Table 1: Bivariate and multivariate analysis to identify factors associated with nausea (Selected variables only)

From these variables, ASA classification, History of motion sickness, and previous post-spinal nausea and vomiting showed a significant relationship with postoperative nausea. This study has shown that ASA II patients were 3.494 times more likely to develop nausea compared with ASA I patients [AOR=3.494,95%CI (1.056,11.555)], patients with a history of motion sickness are 10.831times more likely to develop nausea compared to those who don't have it [AOR=10.831%CI (1.879,62.415)]. Patients with previous post-spinal nausea are 6.832 times more likely to develop nausea compared to those who don't have it [AOR=6.832%CI (2.734,17.071)]. Also, patients with previous post-spinal vomiting are 4.527 times more likely to develop nausea compared to those who don't have it [AOR=4.527 %CI (1.028,19.941)]

### *5.2.1 Factors associated with the incidence of vomiting*

Binary logistic regression was performed to assess the association of each independent variable with the dependent variable and the factors that showed a p-value of 0.25 and less were added to the multivariate regression model to detect the statistical significance variable. From binary logistic regression, those factors that showed a p-value of less than 0.25(Age, Sex, BMI, ASA Classification, operating theater, History of motion sickness, previous post-spinal nausea, vomiting and pruritus) were entered into multivariate logistic regression.

The outcome of logistic regression static stated that the selected model was a good logistic regression model fit, since the Hosmer-Lemeshow goodness of fit, the p-value was 0.273, it is greater than 0.05, then fails to reject the null hypothesis and it is stated the logistic regression models a good fit for the data set.

Additionally, the pseudo-R-square, the regression result showed that the square of the correlation between the model predicted values and the actual values the outcome of this correlation was 47.8% (Nagelkerke R2)

From the multivariate analysis patients with a previous history of post-spinal nausea and vomiting showed a significant($p<0.05$) association with the occurrence of vomiting. Patients with a previous history of nausea are 3.998 times more likely to develop post-intrathecal morphine-related vomiting compared to those who have no previous post-spinal history of nausea [AOR=3.998%CI (1.353,11.810)]. Also, patients with a previous history post spinal vomiting are 10.860 times more likely to develop post-spinal intrathecal morphine-related vomiting compared to those who had no history of post-spinal vomiting [AOR=10.860 %CI (3.135,37.6078)].

| Variables | Categories | COR (95%CI) | P value | AOR (95%CI) | P value |
|---|---|---|---|---|---|
| Sex | Male | 1 | | 1 | |
| | Female | 4.706(2.008,11.027) | 0.001 | 1.346(0.303,6.135) | 0.686 |
| ASA Class | ASA I | 1 | | 1 | |
| | ASA II | 5.077(1.952,13.395) | 0.001 | 5.558(0.893,34.594) | 0.066 |
| Operating theater | Obstetrics | | | | |
| | Orthopedics | 0.263(0.113,0.612) | 0.002 | 2.237(0.310,17.481) | 0.412 |
| | Endo-urology | 0.116(0.039,0.344) | 0.001 | 0.630(0.095,4.4164) | 0.632 |
| History of motion sickness | No | 1 | | 1 | |
| | Yes | 6.4(2.116,19.352) | 0.001 | 2.315(0.456,11.761) | 0.311 |
| History of previous nausea | No | 1 | | 1 | |
| | Yes | 14.500(6.826,30.803) | 0.001 | 3.998(1.353,11.810) | 0.012* |
| History of the previous vomiting | No | 1 | | 1 | |
| | Yes | 37.500(13.637,103.116) | 0.001 | 10.860(3.136,37.608) | 0.001* |
| History of previous pruritus | No | 1 | | 1 | |
| | Yes | 7.708(2.911,20.412) | 0.001 | 2.271(0.565,9.1132) | 0.248 |
| Age | | 0.976(0.952,1.001) | 0.059 | 0.973(0.928,1.021) | 0.272 |
| BMI | | 1.103(0.994,1.225) | 0.066 | 0.895(0.760, 1.054) | 0.184 |

1=indicate for reference range *significant p value(P<0.05)

Table 2: Bivariate and multivariate analysis to identify factors associated with vomiting (Selected variables only)

**5.3 Incidence of pruritus**

Among study participants, 63(23.1%) of them reported having the sensation of itching or pruritus. Of these respondents who reported having pruritus 48(76.2%) of them reported having whole-body pruritus whereas the remaining 15(23.8 %) of them reported having pruritus localized to specific body parts. Of respondents who reported having pruritus whether whole body or localized 11.8% of them requested medical intervention

**Factors associated with the incidence of pruritus**

Binary logistic regression was performed to assess the association of each independent variable with the dependent variable and the factors that showed a p-value of 0.25 and less were added to the multivariate regression model to detect the statistical significance variable. From binary logistic regression, those factors that showed a p-value of less than 0.25(History of motion sickness, previous post-spinal nausea, vomiting and pruritus) were entered into multivariate logistic regression.

The outcome of logistic regression static stated that the selected model was a good logistic regression model fit, since the Hosmer-Lemeshow goodness of fit, the p-value was 0.797, it is greater than 0.005, then fails to reject the null hypothesis and it is stated the logistic regression models a good fit for the data set.

Additionally, the pseudo-R-square, the regression result showed that the square of the correlation between the model predicted values and the actual values the outcome of this correlation was 16.9% (Nagelkerke R2)

From the multivariate analysis, only patients with a previous history of post-spinal pruritus showed significant association with post-operative pruritus, which is 13.281 times than those who don’t have a history of previous post-spinal pruritus [AOR=13.281 %CI (3.961,44.531)].

| Variables | Categories | COR (95%CI) | P value | AOR (95%CI) | P value |
|---|---|---|---|---|---|
| **History of motion sickness** | **No** | **1** | | **1** | |
| | **Yes** | **2.658(0.886,7.973)** | **0.081** | **1.596(0.440,5.787)** | **0.476** |
| **Previous post-spinal nausea** | **No** | **1** | | **1** | |
| | **Yes** | **2.248(1.185,4.265)** | **0.013** | **0.876(0.342,2.247)** | **0.783** |
| **Previous post-spinal vomiting** | **No** | **1** | | **1** | |
| | **Yes** | **3.640(1.609,8.234)** | **0.002** | **2.208(0.684,7.125)** | **0.185** |
| **Previous post-spinal pruritus** | **No** | **1** | | **1** | |
| | **Yes** | **16.094(5.112,50.665)** | **0.001** | **13.281(3.961,44.531)** | **0.001*** |

1=indicate for reference range *significant p value(P<0.05)

Table 3: Bivariate and multivariate analysis to identify factors associated with Pruritus (Selected variables only)

**5.4 Postoperative Urinary Retention**

Among study participants who were not catheterized or those whose catheter was removed shortly after surgery 11 (4%) of them reported having difficulty initiating or completing urination within 24 hours postoperatively. Of these 11 patients reported to have difficulty in initiation or completion of urination, 9 of them (81.8%) requested medical intervention, and 8(72.7%) of them were catheterized or Re-catheterized.

**Factors associated with the incidence of urinary retention**

Binary logistic regression was performed to assess the association of each independent variable with the dependent variable and the factors that showed a p-value of 0.25 and less were added to the multivariate regression model to detect the statistically significant variable. From binary logistic regression, those factors that showed a p-value of less than 0.25 (Age, Sex, History of smoking) were entered into multivariate logistic regression. From this variable sex and history of smoking showed a significant relationship with urinary retention.

The outcome of logistic regression static stated that the selected model was a good logistic regression model fit, since the Hosmer-Lemeshow goodness of fit, the p-value was 0.555, it is greater than 0.005, then fails to reject the null hypothesis and it is stated the logistic regression models a good fit for the data set.

Additionally, the pseudo-R-square, the regression result showed that the square of the correlation between the model predicted values and the actual values the outcome of this correlation was 25.1% (Nagelkerke R2)

The multivariate analysis showed that patients with a history of smoking are 5.299 times more likely to develop urinary retention compared to nonsmokers [AOR=5.299,95%CI (1.230,22.821)]

| Variables | Categories | COR (95%CI) | P value | AOR (95%CI) | P value |
|---|---|---|---|---|---|
| **Sex** | **Female** | **1** | | **1** | |
| | **Male** | **14.037(1.771,111.267)** | **0.012** | **5.709(0.596,54.708)** | **0.131** |
| **History of smoking** | **No** | **1** | | **1** | |
| | **Yes** | **15.962(4.301,59.232)** | **0.001** | **5.299(1.230,22.821)** | **0.025*** |
| **Morphine Dose** | **100 mcg to 200mcg** | **1** | | **1** | |
| | **200mcg to 300** | **4.169(0.884,19.667)** | **0.071** | **1.792(0.309,10.399)** | **0.516** |
| **Age** | | **1.043(1.009,1.079)** | **0.014** | **1.023(0.982,1.065)** | **0.276** |

1=indicate for reference range *significant p-value(P<0.05)

Table 4: Bivariate and multivariate analysis to identify factors associated with urinary retention (Selected variables only)

**5.5. Respiratory Depression**

Among 273 study participants, 10(3.7%) study participants reported having shortness of breath or dizziness within 24 hrs. after completion of surgery. 8 (2.9%) patients had saturation levels less than 90 percent or respiratory rate less than 10. There were no reported apneic or cyanotic episodes in this patient.

**Factors associated with the incidence of shortness of breath**

Binary logistic regression was performed to assess the association of each independent variable with the dependent variable and the factors that showed a p-value of 0.25 and less were added to the multivariate regression model to detect the statistically significant variable. From binary logistic regression, those factors that showed a p-value of less than 0.25 (Age, BMI, History of smoking) were entered into multivariate logistic regression.

As the age of study participants increases the incidence of shortness of breath also increases [AOR=1.058,95%CI (1.019,1.099)]

| Variables | Categories | COR (95%CI) | P value | AOR (95%CI) | P value |
|---|---|---|---|---|---|
| **Age** | | **1.065(1.027,1.105)** | **0.001** | **1.058(1.019,1.099)** | **0.003*** |
| **BMI** | | **0.880(0.724,1.068)** | **0.196** | **0.827(0.650,1.051)** | **0.120** |
| **History of smoking** | **No** | **1** | | **1** | |
| | **Yes** | **7.086(1.663,30.190)** | **0.008** | **3.547(0.722,17.431)** | **0.119** |

1=indicate for reference range *significant p value(P<0.05)

Table 5: Bivariate and multivariate analysis to identify factors associated with shortness of breath (Selected variables only)

**Factors associated with the incidence of saturation less than 90%/Respiratory rate less than 10**

Binary logistic regression was performed to assess the association of each independent variable with the dependent variable and the factors that showed a p-value of 0.25 and less were added to the multivariate regression model to detect the statistically significant variable. From binary logistic regression, those factors that showed a p-value of less than 0.25 (Age, BMI, History of smoking) were entered into multivariate logistic regression.

| Variables | Categories | COR (95%CI) | P value | AOR (95%CI) | P value |
|---|---|---|---|---|---|
| **Age** | | **1.091(1.041,1.141)** | **0.001** | **1.083(1.032,1.136)** | **0.001*** |
| **History of smoking** | **No** | **1** | | **1** | |
| | **Yes** | **10(2.180,45.870)** | **0.003** | **4.098(0.788,21.307)** | **0.094** |

1=indicate for reference range *significant p value(P<0.05)

Table 6: Bivariate and multivariate analysis to identify factors associated with saturation less than 90%/ Respiratory rate less than 10(Selected variables only)

As the age of study participants increases the incidence of saturation less than 90/respiratory rate less than 10 also increases [AOR=1.083,95%CI (1.032,1.136)]. In this study, there was no reported incidence of respiratory arrest requiring advanced airway management and ventilation.

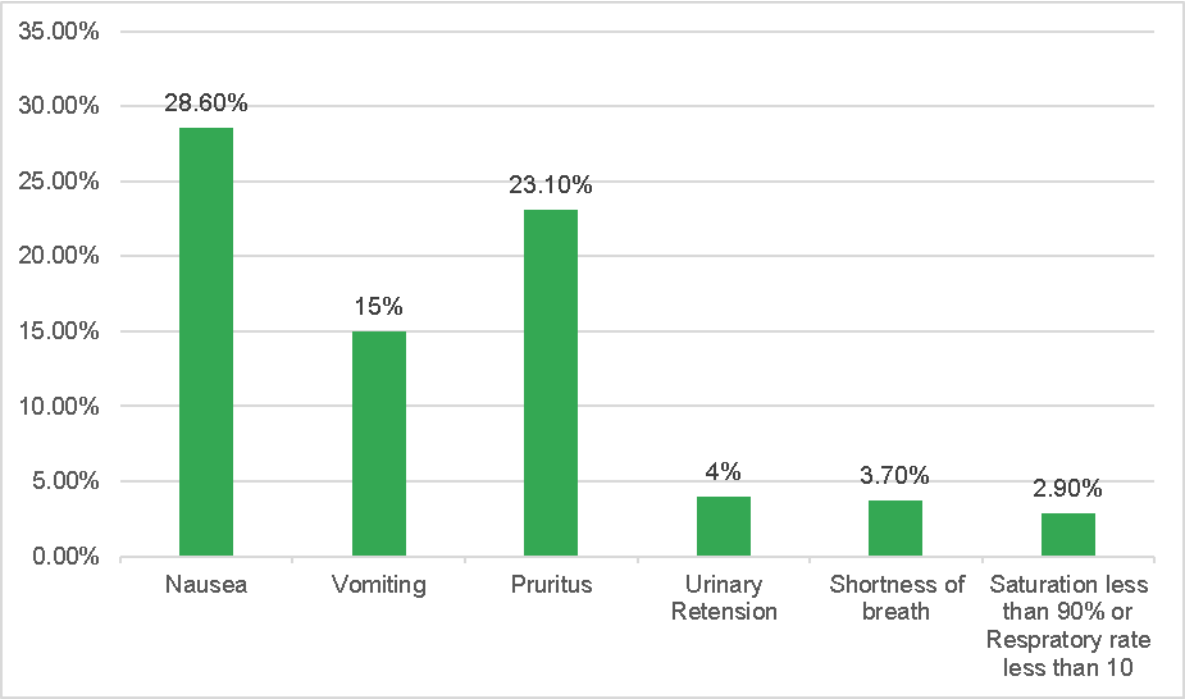


Figure 2: Incidence of adverse effects within 24 hours after intrathecal morphine

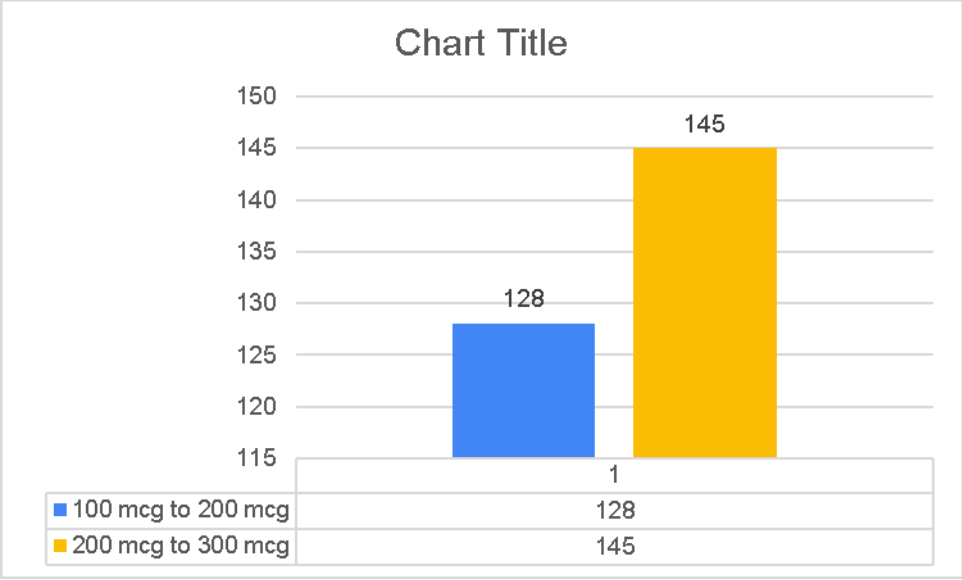


Figure 3: An administered dose of morphine intrathecally

# CHAPTER 6

## Discussion

**Post-operative Nausea and Vomiting (PONV)**

Several studies have found that using intrathecal morphine can increase the risk of postoperative nausea and vomiting (PONV), with rates varying from 20% to 60%.

The results of this study align closely with those of previous research, with 28.6% of participants experiencing nausea and 15.4% experiencing vomiting after receiving intrathecal morphine. In research conducted at a county hospital in Sweden in 2013(29), patients undergoing hip/knee replacement surgery reported that the incidence of vomiting after intrathecal morphine was 36%, while a similar study conducted at Siriraj Hospital in Thailand (28), showed that the incidence of nausea and vomiting was 14.8% and 21.5% respectively.

Studies conducted in the area in Ethiopia are limited and showed a higher incidence of PONV. A study conducted by *basazinew chekol et al* at South Gonder Hospitals in Ethiopia in 2020(48) showed the incidence of PONV was around 40%.

This study showed being classified as ASA II, having a history of motion sickness, previous post intrathecal morphine adverse effects I.e. nausea and vomiting are significantly associated with the incidence of nausea and vomiting, which has been shown with other studies done by Chinachoti et al and Moraitis et al (28,29) in Thailand and Sweden respectively.

However, unlike some other related studies, this study did not find any association between PONV and the dosage of morphine or the smoking status of the participants. This could be due to the uniform use of morphine dosage in the study area in which all patients received intrathecal morphine in the range of 100 to 300mcg, with no morphine dose provided less than 100 mcg or above 300mcg which failed to demonstrate statistical significance.

**Pruritus**

Numerous studies have concluded that pruritus, a severe itching sensation, is a prevalent side effect of administering intrathecal morphine. A systemic review conducted by *Szarvas S et al* (20) has indicated that the incidence of pruritus after intrathecal morphine administration ranges from 30 to 60 percent. However, our research has reported a lower incidence rate of pruritus, which is 23.1 percent. There are no other studies done in Ethiopia to compare the incidence with. Our study has shown that patients who had previous post-spinal pruritus have a higher risk of developing post-intrathecal morphine-related pruritus.

Multiple studies including studies done by *Ballantyne JC et al, Yeh HM et al* and *Kumar K et* al have shown that pregnant women appear to be more vulnerable to pruritus after neuraxial morphine administration than other populations that are related to hormonal changes related to pregnancy. However, our study doesn't show a significant association between incidence of pruritus and pregnancy,

There are contradictory studies regarding the association of pruritus and intrathecally administered morphine doses. A study conducted by *Aly m et al*, to compare the effect of

morphine dose (0.1mg vs 0.2mg) on the incidence of pruritus (38), showed that those patients who received 0.2mg of morphine intrathecally had a higher incidence of pruritus with increased severity compared to those who received 0.1mg of intrathecal morphine. On the contrary, a study done by *Wong et al* (49), found no statistically significant difference in the incidence of pruritus between doses of 100 or 200 μg intrathecal morphine for cesarean delivery. Similar to the study done by *Wong et al,* our study doesn't reveal a significant association between the dose administered and with incidence of pruritus.

**Urinary Retention**

The use of intrathecal morphine can increase the risk of urinary retention, according to the literature. A systemic meta-analytic review conducted by *Stephen Choi et al*, incorporating studies done from 1980 to 2011, has reported the incidence of urinary retention after intrathecal administration of morphine to be between 25% and 36% (42). However, in this study, the investigator found that most patients were kept catheterized postoperatively, making it difficult to assess the incidence of urinary retention. Among patients who were not catheterized or had their catheter removed before 24 hours postoperatively, the incidence of urinary retention was only 4% from the study participants. The study showed significant associations between urinary retention and smoking history.

The much lower incidence of urinary retention in this study can be explained by the trend of keeping patients catheterized postoperatively and partly by participants undergoing surgical procedures at the endourology table, requiring postoperative catheterizations for surgical indications.

**Respiratory Depression**

While respiratory depression following intrathecal morphine administration is rare, it can occur, with incidence rates ranging from 0% to 7% as reported by a systemic review done by *Brendan Carvalho* (24). Factors such as opioid dosage and patient comorbidities contribute to the risk.

A study conducted by *Gwirtz KH et al* (47), at Indiana University Hospital to assess the incidence of respiratory depression after intrathecal anesthesia with morphine with 5969 surgical patients over seven years found the incidence to be 3% with not life-threatening respiratory depression.

Similarly, our research found shortness of breath or dizziness of 3.7%, and saturation of less than 90/ respiratory rate less than 10 of 2.9%. The investigator believes the real incidence of respiratory depression could be higher or lower than this since we used mainly subjective reports of shortness of breath or dizziness, both of which can be due to other patient or surgical-related factors that may not be related to intrathecal-induced morphine. Additionally, most surgical wards lack pulse oximetry to follow patients postoperatively which can affect the validity of this report on respiratory depression. The study has shown elderlies are at increased risk of developing post-spinal intrathecal morphine-related respiratory depression.

# CHAPTER 7

## Strength and limitation

### 7.1 Strengths:

1. **Comprehensive Assessment:** The study provides a comprehensive assessment of the incidence and factors influencing adverse effects following intrathecal morphine administration, including post-operative nausea and vomiting, pruritus, urinary retention, and respiratory depression. This allows for a thorough understanding of the risks associated with this technique.

2. **Large Sample Size:** With a total of 273 participants, the study encompasses a relatively large sample size, enhancing the robustness and generalizability of the findings.

3. **Statistical Analysis:** Rigorous statistical analysis, binary and multivariate logistic regression, was conducted to evaluate the relationships between independent factors and the incidence of adverse effects. This strengthens the validity of the study's conclusions.

4. **Clinical Relevance:** The study's findings have direct clinical relevance, providing insights that can inform healthcare providers in managing and mitigating the risks associated with intrathecal morphine use.

### 7.2 Limitations:

1. **Single-Center Study:** The study was conducted at a single center, which may limit the generalizability of the findings to other healthcare settings or populations with different demographic characteristics and healthcare practices.

2. **Limited Assessment of Severity:** While the study reports the incidence of adverse effects, it does not provide detailed information on the severity or duration of these effects, which could impact clinical management decisions and patient outcomes.

3. **Limited ability to assess urinary retention and respiratory depression:** most patients are catheterized intraoperatively and the catheter is left in situ for hours and sometimes for days. This makes it difficult to assess urinary retention postoperatively. It was also difficult to assess and follow respiratory depression in the ward because of limited pulse oximetry and ward nurses/physicians tend to respond subjectively for signs of respiratory depression like a respiratory rate of less than 10 or cyanosis.

Overall, while the study offers valuable insights into the incidence and factors associated with adverse effects following intrathecal morphine administration, it is essential to interpret the findings within the context of its limitations and consider additional research to further validate and expand upon these findings.

# CHAPTER 8

# CONCLUSION AND RECCOMENDATION

## CONCLUSION

This study aimed to determine the incidence of adverse effects and associated factors following the intrathecal administration of morphine in postoperative patients. The findings offer significant insights into the prevalence and factors influencing various adverse effects, including nausea, vomiting, pruritus, urinary retention, and respiratory depression.

The study indicates that a considerable proportion of participants experienced postoperative nausea (28.6%) and vomiting (15.4%), with a significant number requiring medical management. Regarding pruritus, 23.1% of participants reported its occurrence, with a majority experiencing whole-body pruritus. Postoperative urinary retention was reported by 4% of participants. Respiratory depression was observed in 3.7% of participants, primarily characterized by shortness of breath and decreased oxygen saturation levels.

These findings highlight the importance of vigilant monitoring and tailored interventions to mitigate the risk of adverse effects following intrathecal morphine administration. Further research exploring intervention strategies is warranted to optimize patient outcomes in postoperative care settings.

## RECOMMENDATION

This study has shown that adverse effects of intrathecal morphine are relatively common. These adverse effects except respiratory depression are self-limited without major complications. Though the complications are self-limited, they need vigilance as they affect the post-operative care of patients.

Further studies have to be done to explore the severity of these adverse effects with special attention being given to respiratory depression, as this is the most feared complication of adverse effects of intrathecal morphine.

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# ANNEXES

## Consent

ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF ANESTHESIOLOGY, CRITICAL CARE AND PAIN MEDICINE

INCIDENCE OF ADVERSE EFFECTS AFTER INTRATHECAL ADMINISTRATION OF MORPHINE IN ELECTIVE SURGERIES IN TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA, 2023GC.

General Information

My name is_____; I'm here on behalf of Addis Ababa University. These questionnaires aim to determine the incidence of adverse effects after intrathecal morphine administration for elective surgeries at Tikur Anbessa Specialized Hospital.

This study will help to fill the information gap on the incidence of adverse effects after intrathecal morphine for elective surgeries, which can contribute to the improvement of perioperative anesthesia management and increase patient satisfaction with anesthesia service. You are randomly selected to participate in this study and provide an appropriate response to questions.

Your participation is voluntary. Only anonymous data will be analyzed, and the secrets of the participants will be strictly kept confidential. Participating or not participating in this study will not bring any harm or benefit to you.

We strongly value your honest response to the questions. If you feel or face any problem regarding your participation, you can contact the principal investigators by 0912307235 or firaoln@gmail.com.

Do you agree to participate? 1. If agree go to the next page 2. If you do not agree, get to the next participant

Name of the data collector: _____ Date: _____ Sig. _____ Name of the supervisor: _____ Date: _____ Sig. _____

## Questionnaire

| Part I: Identification (Socio-demographic) | | | |
|---|---|---|---|
| S. NO | | Response | Remark |
| 1 | Card no | | |
| 2 | Age | | |
| 3 | Marital status | | |
| 4 | Level of education | | |
| 5 | Height | | |
| 6 | Weight | | |
| 7 | BMI | | |
| Preoperative assessment | | | |
| 8 | ASA class | | |
| 9 | Gravidity (for mothers) | | |
| 10 | Parity (for mothers) | | |
| 11 | History of smoking | A. Yes<br>B. No | |
| 12 | History of motion sickness | A. Yes<br>B. No | |
| 13 | Previous history of post-spinal adverse effects | A. Nausea<br>B. Vomiting<br>C. Pruritus<br>D. Urinary retention<br>E. Respiratory depression<br>F. Others | |
| Part II: Postoperative nausea and vomiting (PONV) | | | |
| 14 | Do you have nausea that occurred within 24 hours after spinal anesthesia? | 1. YES 2. NO | |
| 15 | Do you have vomiting that occurred within 24 hours after spinal anesthesia? | 1. YES 2. NO | |
| 16 | Have you requested medical intervention communicated health intervention or communicated with health professionals for nausea or vomiting? | 1. YES 2. NO | |
| Pruritus/itch Incidence | | | |
| 17 | Do you have a sensation of pruritus/ itching that occurred within 24 hours after spinal anesthesia? | 1. YES 2. NO | If yes proceed to question 18. |
| 18 | Is the pruritic/itchy sensation localized to one body part or the whole body? | 1. Localized<br>2. Whole body | |

| | | | |
|---|---|---|---|
| 19 | Have you requested medical intervention or communicate with health professionals about the pruritus? | 1. YES 2. NO | |
| Urinary retention | | | |
| 20 | Do you have difficulty initiating or completing micturition in the past 24 hr.? | 1. YES 2. NO | If yes answer question number 21. |
| 21 | Have you requested medical intervention or communicate with health professionals about urinary retention? | 1. YES 2. NO | If yes answer question number 22. |
| 22 | Did you require catheterization? | 1. YES 2. NO | |
| Respiratory depression | | | |
| 23 | Do you have shortness of breath or dizziness over the past 24 hrs.? | 1. YES 2. NO | |
| 24 | Does the patient have a saturation level of less than 90 percent, respiratory rate of less than 10, or apneic episode in the past 24 hrs.? | 1. YES 2. NO | This question is for health professionals only |
| 25 | Does the patient have cyanosis or sedation in the past 24 hrs.? | 1. YES 2. NO | This question is for health professionals only |
| Only for anesthesia providers | | | |
| 26 | Have you added morphine as an additive? | 1. YES 2. NO | If yes, please answer the next questions. |
| 27 | Dose of opioids used? | Morphine<br>a) Less than 100 mcg<br>b) 100 mcg to 200 mcg<br>c) 200 mcg to 300 mcg<br>d) 300 mcg to 400 mcg<br>e) Above 400mcg | |