COLLEGE OF HEALTH SCIENCE

SCHOOL OF MEDICINE

DEPARTMENT OF ANESTHESIA

A COMPARISON OF THE EFFECT OF INTRAVENOUS DEXAMETHASONE AND PETHIDINE FOR PREVENTION OF POST SPINAL ANESTHESIA SHIVERING IN PATIENTS WHO UNDERWENT TRANSURETHRAL RESECTION OF THE PROSTATE AT DAGMAWI MINILIK SECOND HOSPITAL; 2020: A PROSPECTIVE COHORT STUDY

Investigator: Belete Destaw (B.Sc.)

Advisors: Eyayalem Melese (M.Sc.)

Suleiman Jemal (M.Sc.)

A THESIS SUBMITTED TO THE COLLEGE OF HEALTH SCIENCE, SCHOOL OF MEDICINE, DEPARTMENT OF ANESTHESIA, ADDISABABA UNIVERSITY, FOR THE PARTIAL FULFILLMENT OF THE REQUIRMENT FOR DEGREE OF MASTER IN ANESTHESIA.

JUNE 2020

ADDIS ABABA, ETHIOPIA

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF ANESTHESIA

TITLE: A COMPARISON OF THE EFFECT OF INTRAVENOUS DEXAMETHASONE AND PETHIDINE FOR PREVENTION OF POST SPINAL ANESTHESIA SHIVERING IN PATIENTS WHO UNDERWENT TRANSURETHRAL RESECTION OF THE PROSTATE.

Name of investigator: - Belete Destaw (Final year Msc in Anesthesia Student)

Email: baleanst@gmail.com

Telephone +2510978834744

Name of advisors:

1 .Eyayalem melese (Bsc, MSC in Clinical Anesthesia, Lecturer and Clinical Anesthetist)

2. Suleiman Jemal (BSC, MSC in Clinical Anesthesia, Lecturer and Clinical Anesthetist)

Declaration

I, the undersigned, declare that this thesis is my original work in partial fulfilment of the requirements for the Master of Science degree in Anesthesia. I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced

Name: _____

Signature: _____

Submission to MSc Tutor, Department of Anesthesia, Addis Ababa University.

Date of Submission: _____

This thesis work has been submitted for examination with my/our approval as Advisors and Tutors on the Master of Science degree in Anaesthesia

Name	Signature
1. _____	_____
2. _____	_____
3. _____	_____

Acknowledgment

First of all, I would like to express my appreciation to the department of Anesthesia for its encouragement to conduct this thesis and Addis Ababa University as to be a fund source for this thesis project. My deepest gratitude extends to my advisor Mr. Eyayalem Melese and Suleiman Jemal for their close advice, guidance and constructive comments throughout the conduct of this thesis.

Finally I would like to warmly acknowledge Mr.Abebayehu Zemedikun, Bedru Jemal, and Assistant professor Semagne Mekonnen for their invaluable comments and advice throughout the development of this thesis.

Lastly, but not the least I would like to thank my data collectors and study participants for their invaluable contribution to make this thesis real.

Abstract

Background: Shivering is commonly observed as a complication after Regional Ansthesia; even it is more common for urologic operations and causes several complications that have serious physiologic effects. Pethidine have been thought as a standard for prevention and treatment of shivering but it is not without side effects. Studies showed that dexamethasone also has promising effect with fewer side effects even though there is controversies about its comparable effect with the standard antishivering drug that of pethidine.

Objective: The main objective of this study was to compare the effect of prophylactic dexamethasone and pethidine on prevention of post spinal anesthesia shivering for patients who underwent transurethral resection of the prostate (TURP) .

Methods: An institutional based prospective cohort study was conducted on 64 patients who fulfilled inclusion criteria and underwent transurethral resection of the prostate. Convenient sampling technique was used to recruit study participants and data was collected by pre-tested structured questioner. The data was entered in SPSS version 20 for analysis of variable, independent sample t-test statistics and Mann-Whitney U test were used for quantitative data that was distributed normally and non normally respectively. Chi square test was used to compare difference in categorical data. P -value <0.05 was considered as statistically significance.

Result: The incidence and severity of shivering was comparable between pethidine and dexamethasone group (p value>0.05).There was no statistically significance difference in mean time to first onset of shivering between dexamethasone (65minute) and pethidine (81minute) group (p=0.23).The median consumption of total antishivering medication was comparable between dexamethasone (54.2mg of tramadol) and pethidine (68.8mg of tramadol) group (p=0.21).

Conclusion and Recommendation: we conclude that dexamethasone (4mg) is equally effective as pethidine (25mg) that of standard antishivering drug and we recommend the use of dexamethasone (4mg) as an alternative of pethidine as a prophylaxis for prevention of shivering for patients undergoing TURP procedures under spinal ansthesia.

Acronyms and Abbreviations

AAU	Addis Ababa University
ASA	American society of Ansthesiology
BP	Blood pressure
GC	Gregorian calendar
HR	Heart rate
IV	Intravenous
L3	Lumbar Vertebrae 3
L4	Lumbar Vertebrae 4
LA	Local Anaesthesia
ML	Millilitres
Mg/kg	Milligram per Kilogram
Msc	Master of Science
OR	Operation room
PACU	Post Anesthesia Care Unit
Post Op	Postoperative
PS	postoperative shivering
RR	Respiratory Rate
SA	Spinal Anesthesia
SPO2	Blood oxygen saturation
SPSS	Statistical Package for Social Sciences
TURP	Transurethral Resection of Prostate

Table of Contents

Contents

List of tables

List of figures

Chapter one: Introduction

1.1. Background:

Benign prostatic hyperplasia is a non malignant enlargement of prostatic cells in size which results in the development of bladder outlet obstruction and lower urinary tract symptoms which can be manifested by symptoms of Urinary voiding (e.g., straining to void, urinary intermittency, dysuria, hesitancy, etc), symptoms of urinary storage (e.g., urgency, frequency, nocturia, etc) and post-voiding symptoms (e.g., sensation of incomplete bladder emptying, post-void urinary dribbling, etc) (1).

Benign prostatic hyperplasia occurs in elderly men with historical reports of 50% occurrence at the age 50 and increases markedly with increasing age and transurethral resection of the prostate by using electrocautery devices endoscopically to resects prostate tissue under urethra remains as the gold standard for surgical management and is commonly performed by spinal anesthesia (2).

Spinal Anesthesia produces sympathetic block leading to peripheral vasodilatation and slightly decreases the threshold for vasoconstrictions which in addition to the use of cold irrigating fluids predisposes the occurrence of shivering (3).

Shivering is defined as a syndrome of involuntary contractions of skeletal muscles involves fasciculation of muscles of the face, jaw or head or muscle which lasting longer than 15 seconds. It occurs as a physiologic compensatory response after peripheral vasoconstriction to preserve heat during cold exposure and decreasing body temperature and this shivering commonly affect anesthetized patients(4).

Even though the aetiology of shivering is not clearly understood yet it is claimed that it has thermoregulatory causes and non thermoregulatory causes like disinhibited spinal reflexes, decreased sympathetic activity, pain and respiratory alkalosis(4).

Shivering after spinal anesthesia is due to its effects on central and peripheral thermoregulation it enlarges the inter threshold range by rising the sweating threshold and decreasing the vasoconstriction and shivering threshold thus more heat will be lost and more

incidence of shivering will occur after spinal anesthesia than general anesthesia which affects only by impairing central thermoregulation(5,6).

Anesthesia induced thermoregulatory inhibition which leads to reduction in body temperature which activate simple thermoregulatory shivering by decreasing the threshold is conventionally taken as explanation but the occurrence of shivering in normothermic patients and even it is not frequently observed in markedly hypothermic patients, this makes it inconclusive explanation and it indicates that there is another aetiology for the shivering(4).

Activation of the inflammatory response which leads to release of cytokines during tissue damage at the time of surgery which causes vasodilatation and heat loss makes reduction in body temperature is considered as non thermoregulatory cause of post anesthesia shivering(7).Those agents which have anti inflammatory activities ,such as dexamethasone could thus reduce the occurrence of post ansthesia shivering by decreasing the gradient between skin an core body temperature(8).

Shivering has been prevented and treated by both non pharmacological methods and by using different drugs which have antishivering medications.

Non pharmacological methods and equipments are more expensive and even are not available in our set up even though they are commonly used for the prevention of shivering and study suggests that are of limited benefit at best (9).which seeks further research to dig out ways of preventing shivering by using available, cost effective, and affordable drugs in study area.

Many drugs are tested for prevention of postoperative shivering from those Pethidine has promising effects and many authors explained it as a gold standard .which is μ and κ opioid receptor agonist principally acting on the central nervous system and increases shivering threshold (10) but pethidine causes excessive sedation, respiratory depression and post operative nausea and vomiting, which may be stimulated with previously administered opioids or anesthetics(11,12).

1.2. Statement of the problem

It is widely accepted that complications related to surgery and delivery of ansthesia care are inevitable .Post ansthesia shivering is one of the potential complications of ansthesia which may increase patients morbidity and mortality .Nowadays, post ansthesia shivering has become a common phenomenon with the increasing number of surgeries. In fact it occur in 60% of patients during Regional anesthesia and 5-65%of patients on those who recover from general ansthesia(13). Absorption of more irrigating fluids at room temperature makes shivering to be more common during TURP anesthesia (14).

Shivering after spinal anesthesia is due to its effects on central and peripheral thermoregulation it enlarges the inter threshold range by rising the sweating threshold and decreasing the vasoconstriction and shivering threshold thus more heat will be lost and more incidence of shivering will occur after spinal anesthesia than general anesthesia which affects only by impairing central thermoregulation(5,6).

Spinal anesthesia is associated with high incidence of shivering with possible mechanisms of mainly from central thermoregulation disturbance which shows that no significant effect of ambient room temperature on the incidence of shivering(15). Although this incidence is lower in elderly than adults, it can be hazardous to this group of elderly patients with low cardiovascular reserve and frequent co-morbid diseases. Shivering increases O2 consumption, CO2 production, cardiac output, heart rate and hypoxemia. The use of large volume of irrigating fluids usually at room temperature increases hypothermia and shivering in case of TURP procedures(16).

Shivering has many undesirable effects in elderly patients with weak autonomic protective response those patients are common during TURP procedures .undesirable effects such as increased oxygen consumption by 400–500%, increased carbon dioxide production, and patient discomfort (3,5). These side effects increase the load on the cardio respiratory system, especially in elderly patients with low cardio respiratory reserve (3).

Shivering decreases mixed venous oxygen saturation as a result of impaired cardiopulmonary function. In addition, postoperative shivering can increase oxygen consumption up to 5 times, might increase carbon dioxide production, minute ventilation, and hence, cardiac output even

in healthy adults and these complications can lead to cardiovascular and neurological deficits, as well as organ damage. Shivering if not treated, may detrimentally impact patient outcomes, prolong recovery and hospitalization (17,18).

There are many innovative non pharmacological and pharmacological methods used to treat hypothermia to decrease incidence of shivering, from non pharmacological aspects it is ideal to keep patients warm before and during surgery .Additionally pharmacological interventions by using opioids, anti inflammatory drugs, alpha blockers, Pethidine, dexamethasone and others are used(4).

Pethidine has been known as one of the most effective and was thought as a standard antishivering drug(19–21) and considered as a gold standard for the treatment of shivering (11) . Pethidine, an opioid derivative, is frequently recommended for the treatment of post-neuraxial anesthesia shivering. Pethidine is a combined μ- and κ-receptor agonist. Although its mechanism of anti-shivering effect has yet to be fully elucidated, it was indicated in a study in which naloxone was used that pethidine may act via the κ-, rather than μ-opioid, receptors. The antishivering action of pethidine was inhibited by high-dose naloxone, which blocked the μ- and κ-receptors, but not by low dose naloxone which only blocked the μ-receptors. Activation of the κ-opioid receptors decreased the shivering threshold twice as much as the vasoconstriction threshold. However, pethidine probably acts directly on the thermoregulatory centre, and not only through receptor activation but pethidine causes excessive sedation, respiratory depression and post operative nausea and vomiting, which may be stimulated with previously administered opioids or anesthetics(11,12).

A review focus on postoperative shivering, The American society of Anesthesiologist (ASA) guideline recommends Forced air warming from non pharmacological methods and pethidine as pharmacological methods received the highest validation (22)

1.3. Justification of the study

Since shivering mechanism is complex a wide Varity of drugs have been tried and it is open to research different drugs. According to different authors and ASA review pethidine have been thought as a standard and mostly recommended effective antishivering medication but it is not without side effects since it is a strong opioid. Moreover pethidine is not sufficiently available in our setup and it is costy and not easily accessible to our patients so it leads to search another drug which has potent antishivering effect and easily accessible drug.

Dexamethasone have been tested for its effectiveness for prevention of postoperative shivering and study shows that it is effective for prevention of shivering even though there is controversies about its comparability with the recommended standard antishivering medication that of pethidine(3,23,24).

Dexamethasone is cheap, easily accessible and affordable, and commonly used drugs to prevent shivering but there is no study which shows its comparability with the standard antishivering pethidine. This research may give answer for this ambiguity.

Although both are said to be effective on prevention of shivering, as far as my search there was no study conducted on this title in Ethiopia.

In general, if, they are found to be effective to use as either alternative technique or one over other will be recommended.

The result may be used as a base line data for further research, may show possible post spinal shivering prevention modalities for TURP in resource limited settings like ours.

This study was conducted to study the effect of a prophylactic dose of dexamethasone on shivering compared with prophylactic low-dose pethidine in patients underwent TURP under spinal anesthesia.

Chapter Two: Literature review

2.1. Overview

Post anesthesia shivering was first described over fifty years ago with a worldwide incidence of 20-60%.

A study conducted by AnuragTewari.etal conducted a RCT study in 2019 on TURP patients under spinal ansthesia showed that the incidence of shivering was 40%(25,26).

The prevalence of postoperative shivering in Sub-Saharan tertiary hospital after spinal anesthesia is 8.15% with mean time of shivering is between 15 to 25 min with majority of shivering occurring at 20 min(27).

One study conducted in Gonder showed the overall incidence of post anesthesia shivering was 26% and from this 40.4% of patients have mild shivering(Grade 1) ,48.1% of patients have moderate shivering (Grade 2&3) and around 11.5% of patients have severe shivering(Grade 4).and 53.8% was after spinal anesthesia since the incidence is high they recommend the use of antishivering drug prophylaxis(28).

Another study done in Addis Ababa by Zemenu .M showed that the overall incidence of post operative shivering is 29.1% from this majority of patients (60.8%) has Grade 3 shivering.

There are many innovative non pharmacological and pharmacological methods used to treat hypothermia to decrease incidence of shivering, from non pharmacological aspects it is ideal to keep patients warm before and during surgery (4).

In addition to keeping the patients warm by using different important non-pharmacological methods several innovate drugs are used to prevent and treat hypothermia and postoperative shivering, like Pethidine, Ondansetron, Clonidine, Anticholinergics, Opioid agonist, dexamethasone, and Tramadol and pethidine is widely used as the first line therapy (3,4,29,30).

Ketanserin, sufentanil, alfentanil, tramadol, physostigmine, clonidine, magnesium sulphate, Pethidine, dexamethasone, and doxaperam have been used for the treatment of postoperative shivering (31). Among these, Pethidine has been known as one of the most effective and was thought as a standard antishivering drug(19–21,29) and considered as a gold standard for the treatment of shivering (11) and also widely used as the first line therapy (31). However, it might result in nausea and vomiting, delayed gastric emptying, and increased length of recovery stay.

Dexamethasone decreases the incidence of shivering by decreasing the gradient between the core and body temperature via its anti-inflammatory action and inhibition of the release of vasoconstrictors and pyogenic cytokines(32).

2.2. Treatment

Pethidine has a therapeutic effect on PS, and its mechanism is likely to be associated with the activation of κ and μ-opioid receptor, acting principally on the central nervous system. Pethidine is the only opioid that is an agonist at both the μ and κ receptors closely related to the pathogenesis of shivering by reducing the shivering threshold and triggering decreased core temperature, which constitutes its anti-shivering effect.

PS is a very common complication of surgery owing to postoperative pain and post anesthesia hypothermia and is distressing for both patients and clinicians. Hence, effective treatment of PS has become imperative with increasing awareness of the significant benefits of maintaining euthermia intra and after anaesthesia (33). Many therapeutic strategies for treating shivering exist and most are empiric but pethidine is used as standard and first line therapy(21,22,34).

Activation of the inflammatory response which leads to release of cytokines during tissue damage at the time of surgery which causes vasodilatation and heat loss makes reduction in body temperature is considered as non thermoregulatory factor cause of post ansthesia shivering(7).Those agents which have anti inflammatory activities ,such as dexamethasone could thus reduce the occurrence of post anesthesia shivering by decreasing the gradient between skin an core temperature(8).

2.3. Pharmacological therapy

Many drugs have been shown to be effective on the prevention and treatment of PS even though the targeted antishivering therapy is complicated and has a wide range of medications(35).

Pethidine is the most common intravenous drug used for treating and preventing shivering, as its equi-analgesic dose is much more efficient than other opioids such as fentanyl, alfentanil, sufentanil or morphine in preventing shivering. Taking the adverse effects into consideration, accumulating studies show that pethidine could increase the incidence of nausea and vomiting and induce respiratory depression. In the systematic quality assessment of published antishivering protocols of Choi, et al a variety of individual and combination treatments were recommended, but skin warming and pethidine use were the most commonly cited strategies(36).

Dexamethasone decreases the incidence of shivering by decreasing the gradient between the core and body temperature via its anti-inflammatory action and inhibition of the release of vasoconstrictors and pyogenic cytokines(32).

2.3.1. Intravenous pethidine

Pethidine has a therapeutic effect on PS and is the most common intravenous drug used for treating and preventing shivering (10).Different studies try to show the effectiveness of pethidine .some of them state like the following bellow .

M, mothal.etal conducted study included 165 patients, randomly allocated to five groups of 33 each. Tramadol in doses of 1, 2 and 3 mg.kg), pethidine 0.5 mg.kg) or normal saline were administered at the time of wound closure and conclude that all three doses of tramadol were effective and comparable to pethidine in preventing post anesthesia shivering.

Ramalingaraju A.V.S, etal conducted a RCT study in which each group included 27 patients. Mean values of central temperature in the recovery room were significantly different between the 2 groups ($p < 0.05$). However, the differences were not significant during surgery but Postoperative shivering was reported in 14.9% and 3.7% of patients in ketamine and pethidine groups, He conclude that Ketamine and Pethidine might reduce postoperative shivering. Pethidine seems to be the most appropriate choice for preventing postoperative shivering.

Mahmood Eydi, etal conducts a study and showed that there was no statistically significant difference between the shivering intensity in both groups. Only regarding the shivering in the first minute after entering the recovery room, there was an obvious difference between ketamine and pethidine groups which was again not statistically significant (P = 0.07) and conclude that ketamine and pethidine are both equally effective in the reduction of postoperative shivering.

Bahman Hasannasab,etal conduct RCT study and showed that three patients (7.5%) of group K, four patients (10%) of group D and one patient (2.5%) of group M experienced shivering (P = 0.39). The interval to the first analgesic requirement significantly prolonged in the groups K and M compared to the group D (P < 0.001). No significant differences were identified in nausea and vomiting among the groups. No significant pharmaceutical adverse effects were observed in our study and conclude that ketamine, doxaperam and meperidine are equally effective in the prevention of postoperative shivering.

Asif Iqbal, etal showed in his study that the three groups did not differ significantly regarding patient characteristics. The numbers of patients shivering on arrival in the recovery room at 15 minutes after operation were significantly less in Group P (7%) and Group G (17%) than in Group S (60%). Groups P and G differ significantly than in Group S ($p<0.05$). However, the difference between Groups P and G was not statistically significant ($p>0.05$) and conclude that the prophylactic use of Granisetron ($40mcg.kg^{-1}$) and Pethidine(25mg) intravenous were found to be effective in preventing postoperative shivering.

2.3.2 Intravenous dexamethasone

Yared, etal(8) conducted a study on patients who underwent cardiopulmonary bypass under general anesthesia and conclude that dexamethasone (0.3 -0.6 mg/kg) was effective in preventing post operative shivering with significant reduction of incidence of shivering from 33.1% to 13.1% (p value=0.001)(7).

Study showed that low dose of dexamethasone (0.15mg/kg) could properly decrease incidence of post operative shivering .In addition .Horn, etal indicated that antishivering effect of dexamethasone is independent of any other factors such as age, type of surgery and duration of ansthesia(30).

Muhammad S,etal (30) conducted a study on patients who underwent ENT procedures under general anesthesia by using 0.15mg/kg of dexamethasone to prevent postoperative shivering and conclude that dexamethasone significantly decreases incidence of shivering from 55%(22/40) to 15% (15/40) as compared with placebo. In line with this there was another study conducted by Kohrsavi, etal(32) showed that 0.15 mg/kg of dexamethasone effectively prevents postoperative shivering by significantly reduces its incidence from 31% to 12% when compared with placebo($p<0.001$).

G AliceVinathi1, etal Showed that dexamethasone, ketamine and tramadol are equally effective in preventing post anaesthesia shivering with no statistically significant difference.

Ali Solhpour MD, etal Conduct a study on effectiveness of prevention of shivering among Pethidine group (P), ketamine with midazolam group (KMi), Pethidine with dexamethasone (PD) and Control group(C). Showed that the incidence of shivering after 30 minutes of spinal anesthesia in groups C, P, KMi, and PD was 64%, 20%, 20%, and 4%, respectively, which was significantly higher in group C compared with other groups (P .0001). Regarding adverse effects, there was no significant difference between groups (P ≥ .2). Axillary temperature significantly increased in the 15th-120th–minute interval in groups P, KMi, and PD (P b .0001) and in group PD was higher than that in other groups. Core temperature decreased in the 15th-120th–minute interval in group PD, lower than that in other groups (P .0001).Conclude that Prophylactic use of meperidine 0.2 mg/kg plus dexamethasone 0.1 mg/kg was more effective than pethidine 0.4 mg/kg as a sole agent or the combination of ketamine 0.25 mg/kg and midazolam 37.5 μg/kg in preventing shivering resulting from spinal anesthesia.

2.3.3 Intravenous Pethidine VS Intravenous Dexamethasone

Masood, etal. took Nineteen cases (47.5%) of placebo group had postoperative shivering, whereas in dexamethasone group only four cases (10%) had shivering and the difference between the two groups was significant. Also in pethidine group, 15 cases (37.5%) had shivering and the difference with placebo group was significant (*P* value = 0.001) and conclude that pethidine and dexamethasone are effective drugs for prevention of postoperative shivering in elective surgery and the effect of dexamethasone in preventing the postoperative shivering is better than pethidine.

Hamideh Gholami, etal conclude that Although statistically there was no significant difference between the three groups of dexamethasone, Pethidine and Normal Saline receivers regarding shivering reduction; clinical complication rate in dexamethasone group was lower compared to Pethidine and Normal Saline groups.

Abd El Azeem, etal states that the incidence and severity of shivering were low in the pethidine and dexamethasone groups compared with the control group ($P < 0.05$), with no significant difference between the pethidine and dexamethasone groups ($P > 0.05$).and concluded that Prophylactic dexamethasone is as effective as pethidine in reducing the incidence and severity of shivering in TURP patients under spinal anesthesia.

This literature review finally revealed that pethidine is the standard drug for both prevention and treatment of shivering and dexamethasone also tested for prevention and treatment of shivering and shows promising effect. But there are controversies in comparability effects of dexamethasone with the standard treatment drug pethidine.

So that the aim of this study was to compare the effect of dexamethasone and pethidine for prevention of post spinal anesthesia shivering for patients who undergoing TURP procedure.

Research hypothesis

HA1: There is statistically significant difference in incidence of shivering between the groups

HA2: There is statistically significant difference in severity of shivering between groups

HA3: There is statistically significant difference in time to 1st onset of shivering between groups

HA4: There is statistically significant difference in consumption of rescue medication between the groups.

Chapter Three: OBJECTIVE

3.1 General objective

To compare intravenous dexamethasone and pethidine for prevention of post spinal anesthesia shivering for patients who underwent transurethral resection of the prostate at Dagmawi Minilik second hospital from October 26 to January 24/ 2020.

3.2 Specific objective

To compare the incidence of shivering between the groups

To compare the severity of shivering between the groups

Compare the time to first onset of shivering between the groups

Compare total anti shivering medication consumption between the groups

Chapter four: METHODS

4.1. Study area and period

Dagmawi Minilik referral hospital : is one of the oldest hospital in the country located in north east Addis Ababa in Yeka Sub City and it was established in 1910.The hospital provides health services with a surgical bed capacity of 135 from the attachment population of about one million and six hundred thousand people. Surgery department is one of the major departments and it has five wards with separate male and female wards in each, two referral clinic and one operation room which contains three major operation tables and one intensive care unit .The department conducts General,Urologic,Gynacological,Ortopaedics, Ophthalmologic ,Cardiothoracic and Emergency surgery.

The study was conducted at Dagmawi minilik referral hospital, Addis Ababa, Ethiopia from October 26 –January 24/2020

4.2. Study design

An institutional based Prospective cohort study was conducted

4.3. Population

4.3.1 Source population

Elective surgical patients who underwent TURP procedures under spinal anesthesia at Dagmawi Minilik second hospital.

4.3.2 Study population

Elective surgical patients who underwent TURP procedures under spinal anesthesia at Dagmawi Minilik second hospital during the study period.

4.4. Inclusion and Exclusion criteria’s

4.4.1 Inclusion criteria

ASA 1 and ASA2 patients

Patients scheduled for transurethral resection of the prostate under spinal anesthesia

4.4.2 Exclusion criteria

A history of sensitivity to the drugs of the study

Patients having opioid and steroidal premedication

Having neuromuscular disease or neurologic disturbance

Baseline body temperature <36.5 and >38 degree centigrade

Having uncontrolled diabetes mellitus

Patients who needs blood transfusion

Taking a2 blocking drugs

Failed spinal

4.5. Variables

4.5.1 Dependent variable

Incidence of shivering

Severity of shivering

Time to first onset of shivering

Total consumption of anti-shivering medication

4.5.2 Independent variable

Body temperature

Room temperature

ASA status of the patient

Hemodynamic parameters like RR, TO, MAP and SPO2

Duration of the procedure

Types of drugs used

Amount of irrigating fluid used

Amount of Blood loss

Site of spinal ansthesia given

4.6. Operational definition

Spinal Anaesthesia: is the administration of local ansthetic in to the subarachnoid space to cause anesthesia.

Postoperative period: The time period when patient admitted to recovery room to the first 30minute.

Post Anaesthesia Care Unit: is the room in which the patients are admitted to be followed by nurses for brief period of time after anesthesia and until they transfer to ward.

Shivering: is abnormal and uncontrolled movement of one or a group of muscles

GRADES OF SHIVERING

Shivering grade using a four-point scale (3)

Grade 0: no shivering,

Grade 1: piloerection or peripheral vasoconstriction but no visible shivering,

Grade 2: muscular activity in only one muscle group,

Grade 3: muscular activity in more than one muscle group but not generalized and

Grade 4: shivering involving the whole body or generalized shivering

Cystoscopy: endoscopic observation of the bladder

Nausea : sensation of vomiting

Vomiting: explosion of vomitus

Hypothermia : Temperature measurement of less than 35 degree centigrade

4.7. Sample size and sampling technique

4.7.1 Sample size

The sample size was calculated from the data of the primary out come in a preceding pilot study using incidence of shivering as primary outcome variables .The incidence of shivering was used to estimate the sample size and the observed incidence of shivering from the pilot study was equal for both groups and it was (p1=p2=50%) then by using a double proportion formula based on primary outcome variables and used a priori power analysis (G Power version 3.01) by taking 80 % power, alpha 5%, and 10% added for loss to follow up.

Let $P=\frac{P1+rP2}{1+r}$

$$n1=\frac{[Z\frac{\alpha}{2}\sqrt{\left(1+\frac{1}{r}\right)P\left(1-P\right)}+Z\beta\sqrt{P1\left(1-p1\right)+\frac{p2\left(1-p2\right)}{r}}]^2}{(p1-p2)^2}$$

- Where r is the allocation ratio of group 2 to group1, i.e.n2:n1 (n2=r n1).

- P1=is proportion in pethidine group
- P2=is proportion in dexamethasone group
- $Z\frac{\alpha}{2}$ =is the quintile of the standard normal distribution for type one error
- Zβ=is the quintile of the standard normal distribution for type two error/power
- n1 =sample size for pethidine group
- n2=sample size for dexamethasone group

Overall it yields 32 patients to be enrolled per group.

The results of that pilot study were not included in the present analysis, and none of the patients from the pilot study were included in the present study.

4.7.2 Sampling Technique

Convenient sampling techniques was used .All patients who underwent TURP procedures under spinal ansthesia during the study period who fulfilled the inclusion criteria were included. Since we have homogenous population and same study area and factors which can make difference in the outcome is excluded by the exclusion criteria so being a convenient sampling doesn't affect the study that much. Moreover when doing situational analysis in the study area it gives almost near to our expected sample so all the patients in the study period had a chance to be included in the sample.

4.8. Data collection

Before data collection, training was given for data collectors with a brief short lecture about severity of shivering and practical session when appropriate. Data was collected by using pretested questionnaires. All patients who was scheduled for TURP and fulfilled inclusion criteria and volunteer to took part in the study was thoroughly assessed before surgery by history taking, and chart review following informed consent. On the morning of the surgery data collector instruct the patient on how to self report sense of shivering and other adverse effects. After obtaining oral informed consent, standard monitoring NIBP, Pulse oxymetry, ECG were attached, temperature probe attached, and Base line Axillary temperature and Room temperature recorded and then every 10min until the end of the surgery. Then each patient had spinal anesthesia between L3-L4 levels with 2-3 ml of 0.5% Bupivacaine using 20 or 21 -Gauge spinal needle based on the anesthetists preference. After this, the patients

were repositioned in supine position and level of sensory block was assessed and tested by pinprick sensation. Additional necessary intraoperative data were recorded.

Most of Msc students try to prevent shivering by administering available antishivering medications immediately after spinal ansthesia is given since it is common during TURP procedures and most of patients are complaining discomfort which is stressful for both the patient and the ansthesia provider .In the study hospital they uses 25 mg of Pethidine or 4mg of dexamethasone depending on the decision of anesthetist in charge.

The occurrence of shivering was assessed in all groups by using the same structured questionnaires for the group and also severity of shivering was assessed by using Mathew, etal classification of severity of shivering as (3):

Grade 0	No shivering observed
Grade 1	One or more of piloerection; peripheral cyanosis without
	Other cause, but without visible muscular activity
Grade 2	Visible muscle activity confined to one muscle group
Grade 3	Visible muscle activity in more than one muscle groups
Grade 4	Gross muscular activity involving the entire body

The time to the first onset of shivering and total antishivering medication consumption of each patient was recorded. At the times of shivering assessment, the axillary temperature, the room temperature, the heart rate, the mean arterial blood pressure, respiratory rate, SPO2 and antishivering medication requirement was assessed. Any postoperative adverse events such as nausea, vomiting, shivering was recorded and informed for treatment. Patients are followed for 30 minutes at PACU to observe the incidence of shivering and other side effects.

All data's was coded by the investigator to identify patients on the questionnaire and the completed questionnaires were kept in a secured location.

4.9. Data quality control

To assure the reliability and validity of the data, questionnaire was pretested before the actual data collection. Training and orientation about the objectives and relevance of the study, each

items included in the study tools and the whole process of data collection was provided for data collectors and supervisors. Verbal informed consent was obtained from the patients. During data collection, regular supervision and follow up was undertaken. Supervisors had checked each questionnaire daily with further cross check by principal investigator for completeness and consistency of data.

4.10. Data analysis and interpretation

Data entered into SPSS version 20 for analysis. The data was tested for normality using the Shapiro–Wilk normality test and homogeneity of variance were tested by Levene's test for normally distributed quantitative data.

Independent sample t-test statistics and Mann-Whitney U test were used for quantitative data that was distributed normally and non normally respectively.The comparisons of categorical parameters were analyzed using chi-square test. Data presented as mean ±SD for normally distributed, median ± IQR (25th–75th percentile) for non- normally distributed and categorical data was presented as numbers and frequencies (percentages). P-values <0.05 was considered statistically significant.

4 .11 Ethical consideration

Ethical clearance was obtained from the department ethical clearance committee before the start of the study. Official support letter was written to Hospitals and Addis Ababa Heath Bureau and permission for data collection was sought from the responsible authorities. The purposes and the importance of the study were explained verbal and verbal informed consent was obtained from each participant. Confidentiality was maintained at all levels of the study by avoiding identifiers and using codes to identify patients. The participant's involvement in the study was on a voluntary basis, participants who were not willing to participate in the study and those who wish to quit their participation at any stage were informed they are allowed to do so without any restrictions.

4.12 Dissemination of the result

The results of the study will be presented to department of Medical Anesthesia as part of partial fulfilment of master's degree in Ansthesia and will be presented for those who are in need of the result for presentation or for further research. It will be sent to reputable national and international journals for publication.

Chapter five: RESULTS

5.1 Demographic and Perioperative characteristics

Sixty four (64) patients were participated in the study based on whether they received intravenous Dexamethasone as exposed group and those who received intravenous Pethidine as a positive control (standard treatment) group.

There was no significant difference between the groups with regard to Age, Baseline room temperature, Baseline body temperature, Baseline MABP, Baseline Heart rate, and Baseline oxygen saturation (p value >0.05).

Both groups were comparable in terms of perioperative factors like ASA status, Duration of surgery, level of spinal anesthesia given and drugs used, types and amount of irrigating fluid used and amount of blood loss with no significant difference between the groups (p value > 0.05).

Table 1 Demographic and Baseline parameters of patients who underwent elective TURP procedures under spinal anesthesia in Minilik referral hospital Addis Ababa, 2019/2020

	Pethidine group	Dexamethasone group	P value
Age (year)	63.9±16..9	63.7±13.8	0.97
Baseline room temperature	21±1,1	21±1.6	0.37
Baseline body temperature	36.1±0.8	36±0.7	0.38
Base line MABP	94.3±12	92.3±15	0.57
Base line heart rate	81.5±12.9	77.5±10.4	0.18
Base line saturation	96±1.5	96.3±1.1	0.31
Values are presented by: Mean ±SD ,Independent sample t-test and p value <0.05 is statistically significant			

Both room temperature and body temperature were measured throughout the procedure and at the PACU for 30 min until discharge and there was the reduction of mean body temperature within the groups but the difference was not statistically significant (p>0.05) between the group.

All timely measured parameters were comparable between the groups throughout the time with no statistically significance difference between the groups as analyzed by independent sample t-test with p value>0.05.

5.2. Comparison between groups in terms of incidence of shivering

This research result showed that the overall incidence of shivering was 7(21.9%) in the pethidine group and 14(43.8 %) in the dexamethasone group with no significance difference between the groups with p value greater than 0.05.

Table 2, Incidence of shivering and comparisons between the groups

Variable	Total	Pethidine Group	Dexamethasone Group	P –value
Shivering				
YES	21(32.8%)	7(21.9)%	14(43.8%)	0.11
NO	43(67.2%)	25(78.1%)	18(56.2%)	

Values are presented by: numbers and percentages, chi-square test and p value <0.05 is statistically significance.

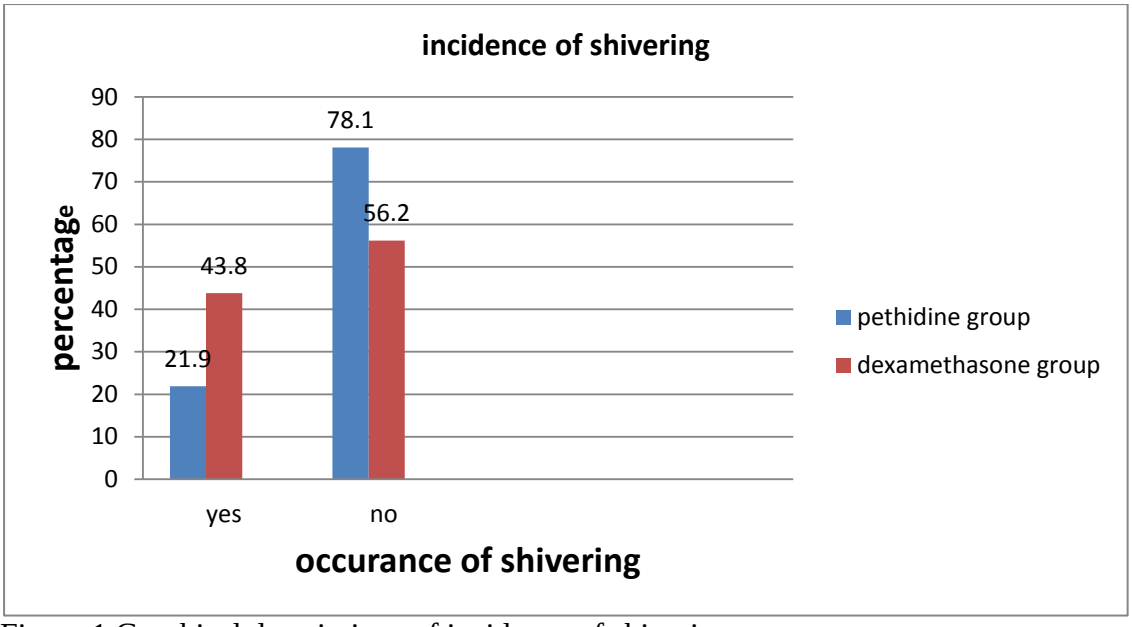

Figure 1 Graphical descriptions of incidence of shivering

5.3. Comparison between groups in terms of Severity of shivering

The result showed that the severity of shivering in Dexamethasone group was significantly reduced but it is not statistically significance between the groups. This showed that four patients (12.5%) had Grade 2 shivering and three patients (9.4%) had Grade 3 shivering while in Dexamethasone group 4 patients (12.5%) had Grade 1shivering,6 patients (18.8%)and 4 patients (12.5%) had Grade3 shivering .from the results we revealed that Grade 2 shivering is common for the two groups.

Table 3 Comparison of the severity of shivering between the groups

Grades of shivering	Pethidine group	Dexamethasone group	P value
Grade 1	0(0%)	4(12.5%)	
Grade 2	4(12.5%)	6(18.8%)	0.29
Grade 3	3(9.4%)	4(12.5%)	
Values are presented by: numbers and percentages , chi-square test and p value <0.05 is statistically significant			

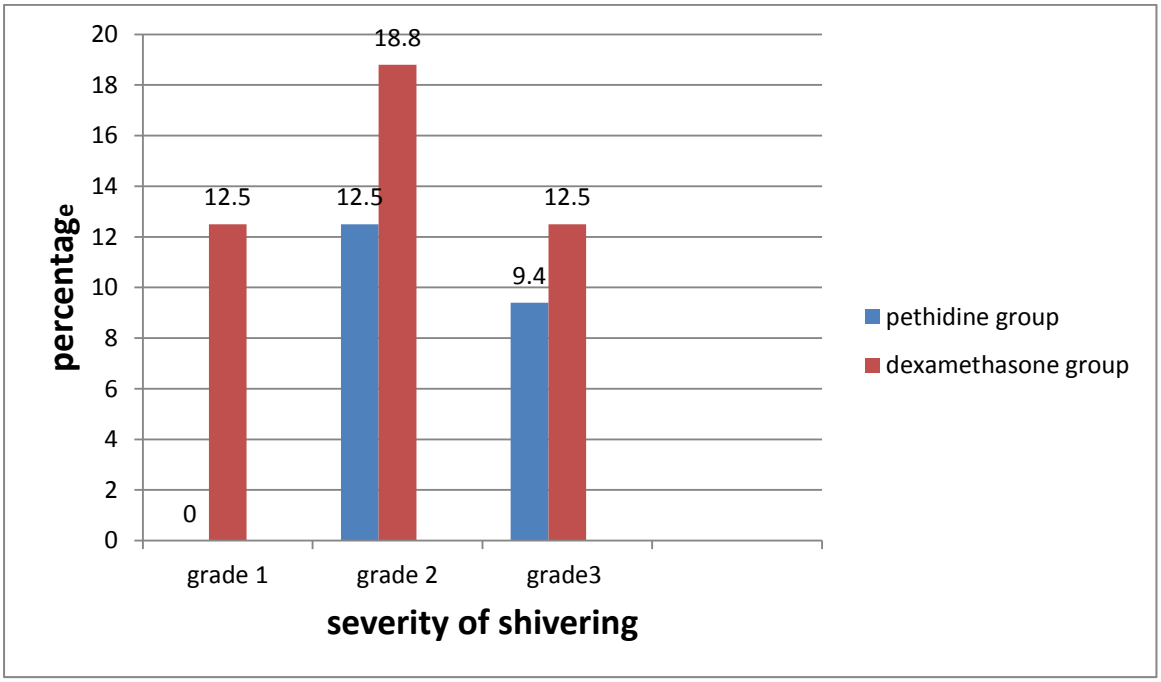

Figure 2 Graphical representation of severity of shivering

5.4. Comparison between groups in terms of time to first onset of shivering

Independent sample t-test revealed that the mean time for first onset of shivering was comparable between dexamethasone (65minute) and pethidine (81minute) group (p=0.23).

Table 4 Comparisons of mean time for 1st onset of shivering between groups

	Mean time for 1st onset of shivering Dexamethasone group	P value
Pethidine group	81±13 minute	
Dexamethasone group	65±43 minute	0.234

Values are presented by: Mean and SD, independent t-test and p-value<0.05 is statistically significant

5.5. Comparison between groups in terms of antishivering medication consumption.

The Mann-Whitney test revealed that the median consumption of antishivering medication was comparable between dexamethasone (54.2 mg) and pethidine (68.8mg) group (p>0.05).

Chapter 6: Discussion

This study showed that dexamethasone was as effective as that of pethidine as a prophylaxis for prevention of post spinal ansthesia shivering for patients underwent TURP in terms of reducing incidence and severity of shivering, had comparable time to first onset of shivering and median dose of antishivering medication consumption.

In this study factors like age, room temperature, perioperative body temperature ,type and duration of surgery ,amount of blood loss and total fluid intake which were considered as a risk factor for perioperative hypothermia and shivering(27–29,37) were comparable between the groups (>0.05).

Body temperature of the patients in the two groups was recorded in the operation theater and in the PACU and compared between groups and was found to be statistically insignificant different (p>0.05).

In this study the mean axillary temperature was lower during intraoperative time compared to baseline score in both groups .The decrease in body temperature between the two groups was not significantly different (P>0.05).There might have a clinical significance for this difference and could be due to anesthetic impairment of thermoregulatory center, decreased metabolic heat production, core to peripheral redistribution of heat and heat transfer through an exposed surgical wounds.

We found that the incidence of shivering was 14(43.8%) and 7(21.9%) for dexamethasone and pethidine group respectively (p=0.064).

This was in line with a study conducted by Yared, etal(8) on patients who underwent cardiopulmonary bypass under general anesthesia and conclude that dexamethasone (0.3 -0.6 mg/kg) was effective in preventing post operative shivering with incidence of 13.1% .while the result of this study show that the incidence of shivering in dexamethasone group was 43.8% and this discrepancies in the incidence rate might be because of different population and different modalities of anesthesia techniques. In this case both spinal anesthesia and TURP procedures increase the incidence of shivering by preventing both central and peripheral thermoregulation during spinal anesthesia while it only inhibits central thermoregulation in case of general anesthesia, In their cases they use small dose opioiates.lorazepam and neostigimine which have antishivering effect and they were doing re

warming to maintain body temperature which may lead to decrease incidence of shivering in their study .Moreover the use of large dose of dexamethasone (0.6mg/kg) in their study and smaller dose of dexamethasone (0.1mg/kg) in our case may gave better explanation for the discrepancies in incidence of shivering.

In agreement with this study there was another RCT study conducted by Muhammad S,etal (30) on patients who underwent ENT procedures under general ansthesia by using 0.15mg/kg of dexamethasone to prevent postoperative shivering and conclude that dexamethasone significantly decreases incidence of shivering from 55%(22/40) to 15% (15/40) as compared with placebo while it was 43.8% in this study and the discrepancies may be due to the use of other medications which have antishivering effect like fentanyl and neostigimine even though used the same dose of dexamethasone. In line with this there was another study conducted by Kohrsavi, etal(32) showed that 0.15 mg/kg of dexamethasone effectively prevents postoperative shivering by significantly reduces its incidence from 31% to 12% when compared with placebo($p<0.001$).

There is also another study which is done in 2003 by Essam E, etal performed on patients undergoing heart valve replacement surgery and it become clear that premedication with 100 mg dexamethasone would lead to reduction in post operative shivering.

Also in line with this study there was another study conducted by Farzi double blind RCT which enrolled 250 patients in two groups dexamethasone (0,25mg/kg) and placebo and conclude that dexamethasone reduced the incidence of post operative shivering(40% compared with 16.7%) (p value<0.001).

Study showed that low dose of dexamethasone (0.15mg/kg) could properly decrease incidence of post operative shivering .In addition .Horn, etal indicated that antishivering effect of dexamethasone is independent of any other factors such as age, type of surgery and duration of ansthesia(30).

This result revealed that comparatively equal incidence of shivering in pethidine group of patients which is 21.9 %(7) in our study and 20%(10) in pethidine group with RCT study conducted by Alisolhpour MD, etal in 2016 which enrolled 200 patients in four groups 50 for each group who underwent elective urologic and orthopaedic procedures under spinal ansthesia the grouping was as Control group (saline),pethidine group(0.4 mg/kg),ketamine

0.25mg/kg plus midazolam 3.75 micro gram/kg(KMI),and pethidine 0.2mg/kg plus 0.1 mg/kg dexamethasone (PD) group and the study showed that the incidence of shivering was 56%(28) in Control group ,20%(10) in pethidine group ,20%(10) in KMI group and 4%(2)in PD group .This also revealed the significant effectiveness of shivering when we use it in combination and this indicates that both are effective in prevention of shivering (13).

Also Vinthai G, etal conducted a study to compare the effectiveness among dexamethasone (0.6mg/kg), ketamine (0.5mg/kg) and tramadol (1mg/kg) and finally the study conclude that dexamethasone .ketamine and tramadol all are equally effective in preventing post ansthesia Shivering with no statistically significant difference but dexamethasone is with less complication.

In this study the overall incidence of post spinal ansthesia shivering was 32.8% .This is in line with the RCT study conducted in Egypt, El Menoufia University, in 20l6 by Abd El Azeem A,etal which was 31.1% and these discrepancies might be due to a different study design and the difference in perioperative management and their study showed that no statistical significant difference found between dexamethasone and pethidine group in terms of incidence of shivering ($p>0.05$).this might be due to utilization of the same dose of drugs and same population with same ansthesia techniques(3) .

In contrast to this study S, Morteza, H, etal (29)conducted a study on 135 patients to compare the effect of dexamethasone (0.6mg/kg),pethidine(0.5mg/kg),and ketamine(0.5mg/kg) for prevention of post anesthesia shivering after general ansthesia and the result of the study showed that the incidence of shivering was 31.1%(14/45) in dexamethasone group,11.1%(5/45) in pethidine group and 37.8%(17/45) in the ketamine group(=0.012) and conclude that pethidine is the most appropriate choice of treatment and preventing post operative shivering. This difference is might be due to different in study design and different population with different types of ansthesia, when compared with the result shown by this study in terms of incidence of shivering in the dexamethasone group and pethidine group which was 43.8% and 21.9% respectively in this study and the decrease in incidence of shivering in both groups in their study may be attributed to the use of other drugs which uses fentanyl.neostigmine and others which have antishivering effects in their study and larger dose of dexamethasone than this study ,this may explain better for the reduction in incidence of shivering in both groups in their study.

Another study which is in contrast with this study was conducted by Masood EntezariasI, etal, RCT study on dexamethasone for prevention of postoperative shivering comparison with pethidine and concludes that both dexamethasone and pethidine are effective drugs for the prevention of post operative shivering in elective surgery and the effect of dexamethasone is better than pethidine in prevention of post operative shivering.

In contrast to our study a RCT study in Iran by Gholami, etal in 2018 .on comparison of the effect of dexamethasone and pethidine for prevention of postoperative shivering after spinal ansthesia which enrolled 66 patients 22 patients as control group(saline),pethidine (0.5mg/kg)and dexamethasone (0.6mg/kg) demonstrated that the incidence of shivering was 72.7%(16) in the dexamethasone group,45.5% in the pethidine group while it was 50%(11)in the placebo group with no statistically significant difference among the groups (p value=0.149).and concluded that even though there were no statistical significance difference among the groups in reduction of the incidence of shivering clinical complication rate in dexamethasone group was lower when compared to pethidine and pethidine is better in prevention of post spinal ansthesia shivering. But this may be due to difference in the study population and study design and their sample size which is relatively small as they try to explain as limitation of their study.

The severity of post spinal ansthesia shivering was another interest of this study. It was compared between the groups and the difference was not statistically significant (p=0.289).

This is in line with the result of a randomized double blind study conducted by Abd EL Azeem, etal showed that severity of post spinal ansthesia shivering was not significantly different between dexamethasone and pethidine groups (p>0.05).

The number of shivering patients with grade 2 and 3 in our study was 4 and 3 respectively in pethidine group and 6 and 4 respectively in dexamethasone group while grade 1 shivering was seen in 4 patients in dexamethasone group. This is in line with a study conducted by Abd EL Azeem, in their study 6 patients developed grade 1 shivering and one patient had grade 2 shivering in pethidine group and five patients had grade 1 shivering and one patient had grade 2 shivering in dexamethasone group while no patients was develop grade 3 shivering and this might be due to the different study design, and difference in perioperative patient management.

This study also showed that the mean time for first onset of shivering was 81 minute in pethidine group while it was 65 minute in dexamethasone group but it was not significant statistically(p value>0.05).

The study also showed that the median dose of tramadol consumption is lower in dexamethasone group which were 54.2 mg while it was 68.8 mg in the pethidine group which shows that clinically dexamethasone is better by directly decreasing opioid consumption and indirectly by decreasing opioid side effects like nausea, vomiting and pruritus even though side effects were not observed in both groups in this study.

Limitation

Since it is not RCT study and there may be confounding factors which may have contribution effect for shivering directly and indirectly are not controlled.

Limited availability of similar studies for comparison

RCT studies used for comparison

Strength of the study

Comparable study groups in terms of socio demographic distributions, perioperative factors that affect study outcome and the same surgical procedure so that the difference observed may be due to exposure factors.

Chapter 7: Conclusion and Recommendation

7.1. Conclusion

Based on the finding of this study we conclude that dexamethasone (4mg) is equally effective as pethidine (25mg) that of standard antishivering drug as a prophylaxis for prevention of post spinal anesthesia shivering by decreasing both the incidence and severity of shivering and had comparable mean time to first onset of shivering and median consumption of rescue medication consumption.

7.2. Recommendation

For Ansthesia professionals

We recommend the use of dexamethasone (4mg) as an alternative of standard antishivering drug that of pethidine as a prophylaxis for prevention of shivering for patients undergoing TURP procedures under spinal ansthesia.

For Ansthesia department and Researchers

We recommend conducting further strong RCT study to know the true incidence of shivering and best drugs for prevention of shivering and on different population groups.

Reference

1. McVary K. Epidemiology and pathophysiology of benign prostatic hyperplasia - UpToDate [Internet]. UpToDate. 2019. Available from: https://www.uptodate.com/contents/epidemiology-and-pathophysiology-of-benign-prostatic-hyperplasia

2. Kim EH, Larson JA, Andriole GL. Management of Benign Prostatic Hyperplasia. 2016;

3. El Bakry AEA, Ibrahim E. Prophylactic dexamethasone or pethidine for the prevention of postoperative shivering during transurethral resection of the prostate under spinal anesthesia. Ain-Shams J Anaesthesiol. 2016;9(3):349.

4. Alijanpour E, Banihashem N, Maleh PA. Prophylactic Effect of Oral Clonidine and Tramadol in Postoperative Shivering in Lower Abdominal Surgery. 2016;137–47.

5. Elmawgood AA. Efficacy of prophylactic use of hydrocortisone and low dose ketamine for prevention of shivering during spinal anesthesia. Egypt J Anaesth [Internet]. 2012;28(3):217–21. Available from: http://dx.doi.org/10.1016/j.egja.2012.04.002

6. Buggy DJ, Crossley AWA, Le L. Thermoregulation , mild perioperative hypothermia and post- anaesthetic shivering. Br J Anaesth [Internet]. 2000;84(5):615–28. Available from: http://dx.doi.org/10.1093/bja/84.5.615

7. Yared JP, Starr NJ, Torres FK, Bashour CA, Bourdakos G, Piedmonte M, et al. Effects of single dose, postinduction dexamethasone on recovery after cardiac surgery. Ann Thorac Surg [Internet]. 2000 May;69(5):1420–4. Available from: https://www.ncbi.nlm.nih.gov/pubmed/10881816

8. Yared JP, Starr NJ, Hoffmann-Hogg L, Bashour CA, Insler SR, O'Connor M, et al. Dexamethasone decreases the incidence of shivering after cardiac surgery: a randomized, double-blind, placebo-controlled study. Anesth Analg [Internet]. 1998 Oct;87(4):795–9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/9768772

9. Park B, Lee T, Berger K, Park SM, Choi K-E, Goodsell TM, et al. Efficacy of

Nonpharmacological Antishivering Interventions: A Systematic Analysis. Crit Care Med [Internet]. 2015 Aug;43(8):1757–66. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26186477

10. Dal D, Kose A, Honca M, Akinci SB, Basgul E, Aypar U. Efficacy of prophylactic ketamine in preventing postoperative shivering. 2005;95(2):189–92.

11. Kaparti L. A Randomised Trial Comparing Efficacy , Onset and Duration of Action of Pethidine and Tramadol in Abolition of Shivering in the Intra Operative Period. 2014;7–9.

12. Fern L, Misiran K. Comparison of dexmedetomidine , pethidine and tramadol in the treatment of post-neuraxial anaesthesia shivering Comparison of dexmedetomidine , pethidine and tramadol in the treatment of post-neuraxial anaesthesia shivering. South African J Anaesth Analg [Internet]. 2015;1181:1–6. Available from: http://dx.doi.org/10.1080/22201181.2015.1013323

13. Solhpour A, Jafari A, Hashemi M, Hosseini B, Razavi S, Mohseni G, et al. A comparison of prophylactic use of meperidine , meperidine plus dexamethasone , and ketamine plus midazolam for preventing of shivering during spinal anesthesia : a randomized , double-blind , placebo-controlled study ☆. J Clin Anesth [Internet]. 2016;34:128–35. Available from: http://dx.doi.org/10.1016/j.jclinane.2016.03.036

14. El H, Moawad S. Egyptian Society of Anesthesiologists Efficacy of intrathecal dexmedetomidine in prevention of shivering in patients undergoing transurethral prostatectomy : A randomized controlled trial. Egypt J Anaesth [Internet]. 2015;31(2):181–7. Available from: http://dx.doi.org/10.1016/j.egja.2015.01.001

15. ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES , SCHOOL OF GRADUATE STUDIES DEPARTMENT OF ANESTHESIA Efficacy of Meperidine versus Tramadol as a treatment agent on post spinal anaesthesia shivering , hemodynamic stability and therapeutic side effects i. 2017;

16. Resection T, Turp P. The Effect of Low-dose Intrathecal Fentanyl on Shivering during Spinal. 2014;2(September):31–5.

17. A.V.S DR. Post Operative Shivering: Prophylactic Effects of Ketamine and Pethidine, A Comparative Study in Tertiary Care Hospital. IOSR J Dent Med Sci. 2017;16(03):12–5.

18. Nazir A, Dar FA, Javed T. A Comparative Study ; Prophylactive Intravenous Ketamine and Tramodol in Preventing Intraoperative Shivering in Patients Undergoing Elective Lower Limb Surgery Under Spinal Anaesthesia. 2014;

19. Entezariasl M. The effect of granisetron , ondansetron , and pethidine in preventing postoperative shivering : controlled clinical trial. :1–15.

20. Kim YA, Kweon TD, Kim M, Lee HI, Lee YJ, Lee K. Comparison of meperidine and nefopam for prevention of shivering during spinal anesthesia. 2013;64(3):229–33.

21. Iqbal A, Ahmed A, Rudra A, Wankhede RG, Sengupta S, Das T, et al. Prophylactic Granisetron Vs Pethidine for the Prevention of Postoperative Shivering : A Randomized Control Trial. 2009;53(June):330–4.

22. Choi K-E, Park B, M. Moheet A, Rosen A, Lahiri S, Rosengart A. Systematic Quality Assessment of Published Antishivering Protocols. Anesth Analg. 2016 Sep 1;124:1.

23. Gholami H, Moradi Y, Khazaei Z, Tehrani S. A comparison of the effect of dexamethasone and pethidine for prevention of shivering after spinal anesthesia in caesarean section : randomization clinical trial A comparison of the effect of dexamethasone and pethidine for prevention of shivering after s. 2018;(September).

24. Vinathi GA, Latha VS. Efficacy and Potency of Dexamethasone In Comparison With Ketamine and Tramadol in the Prevention of Post-Operative Shivering. IOSR J Dent Med Sci. 2018;17(4):66–72.

25. Tewari A, Dhawan I. Use of oral tramadol to prevent perianesthetic shivering in patients undergoing transurethral resection of prostate under subarachnoid blockade. 2014;8(1):1–6.

26. Tewari A, Dhawan I, Mahendru V, Katyal S, Singh A, Narula N. A comparative study evaluating the prophylactic efficacy of oral clonidine and tramadol for perioperative shivering in geriatric patients undergoing transurethral resection of prostate.

2014;30(3):340–4.

27. Luggya TS, Kabuye RN, Mijumbi C, Tindimwebwa JB, Kintu A. Prevalence , associated factors and treatment of post spinal shivering in a Sub-Saharan tertiary hospital : a prospective observational study. BMC Anesthesiol [Internet]. 2016;1–5. Available from: http://dx.doi.org/10.1186/s12871-016-0268-0

28. Tawuye Yimer H, Hailekiros AG. Magnitude and Associated Factors of Postanaesthesia Shivering Among Patients Who Operated Under General and Regional Anesthesia, Northwest Ethiopia: A Cross Sectional Study. J Anesth Clin Res. 2015;6(11):6–10.

29. Morteza S, Tabaei H, Morovati L, Koushki AM. A comparative study on the prophylactic effects of ketamine , dexamethasone , and pethidine in preventing postoperative shivering. 2012;(March):175–81.

30. Hossain MS, Rashid MM. Dexamethasone for Prevention of Postoperative Shivering : A Prospective Clinical Study. 2019;10(02):81–4.

31. Ramalingaraju AVS, D SR, Neethika M. Post Operative Shivering : Prophylactic Effects of Ketamine and Pethidine , A Comparative Study in Tertiary Care Hospital . 2017;16(3):12–5.

32. Article O. Treatment of Postoperative Shivering with Dexamethasone : A Prospective. 2002;27(1):15–7.

33. Park SM, Mangat HS, Berger K, Rosengart AJ. Efficacy spectrum of antishivering medications: meta-analysis of randomized controlled trials. Crit Care Med [Internet]. 2012 Nov;40(11):3070–82. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22890247

34. Vanderstappen I, Vandermeersch E, Vanacker B, Mattheussen M, Herijgers P, Van Aken H. The effect of prophylactic clonidine on postoperative shivering. A large prospective double-blind study. Anaesthesia [Internet]. 1996 Apr;51(4):351–5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/8686824

35. Controlling NN. Physiology and Pharmacology. 2002;(2).

36. Lopez MB. Postanaesthetic shivering – from pathophysiology to prevention. 2018;25(1):73–81.

37. Eberhart LHJ, Döderlein F, Eisenhardt G, Kranke P, Sessler DI, Torossian A, et al. Independent risk factors for postoperative shivering. Anesth Analg. 2005;101(6):1849–57.

Annex one: Information sheet to get permission for the research

Introduction

This information sheet is prepared to explain the research project that you are asked to join by a research investigators.

The research team includes Msc students, two senior advisors from AAU and Two anesthetists for data collection from Dagmawi minilik referral Hospital.

Name of Principal investigator: - Belete Destaw

Advisor's name: - Mr.:- Eyayalem Melese

Mr.:- Suleiman Jemal

Name of sponsor: - AAU

Name of organization: - AAU, college of Health sciences, anesthesia department

This information sheet is prepared by the above mentioned investigator.

Risk

There is no any risk or harm that you will face by participating in this research. Any personal information recorded will not be copied and transferred to other bodies. No need of writing participants' name but by a code. Every piece of information will be kept confidentially.

Benefits

There is no incentive or payment to be gained by taking part in this project. The information collected from this research project will be kept confidential and only accessed by the researcher and research assistant only. This research project will be reviewed and approved by ethical committee of the department. If you want to know more information, you can contact the committee through the address below.

1. Belete Destaw - principal investigator
   Department of anesthesia, Addis Ababa University
   Tel: +25178834744
2. Eyayalem Melese – advisor
   Department of anesthesia, Addis Ababa University
   Tel:
3. Suleiman Jemal – advisor
   Department of anesthesia, Addis Ababa University

ANNEX 2: Informed consents

Data collectors will read the Following Paragraph for the Selected Person:

"To conduct our study, I would like to ask you some question which may take about 5 to 10 minutes in three different times. As your participation is very important to the outcome of the study we kindly request you to give us your sincere and truthful answer. All the information that you and other patients going to provide us will remain confidential and you don't need to mention your name."

Are you willing to participate in the interview? Yes - continue), No - (thank & stop here)

Signature -_____ Date _____

Signature of the interviewer certifying that consent has been obtained verbally.

Questionnaire

It is prepared to collect data on "comparison of the effectiveness of intravenous Pethidine and intravenous Dexamethasone for prevention of post spinal shivering for patients undergoing Transurethral resection of the prostate in Dagmawi minilik referral hospital from October 26, 2020 to January 24, 2020

I. English version questionnaire

Department of Anaesthesia College of Medicine and Health Sciences, AAU

Questionnaire identification number_____

Greeting

Hello, I am_____. I am working in the research team of Addis Ababa university Department of Anaesthesia.

The purpose of this questionnaire is to gather information about "comparison of the effectiveness of intravenous Pethidine and intravenous Dexamethasone for prevention of

post spinal shivering for patients undergoing Transurethral resection of the prostate in Dagmawi minilik referral hospital. The research will be beneficial to those underwent TURP for prevention of post spinal shivering with effective antishivering drug with less side effects .We will ask you some questions which will take few minutes in three different times. The answer to those questions is confidential. We will not write your name in the questionnaire.

You can refuse to respond to any of the questions and you can interrupt at any point in the interview. Do I have your permission to continue? 1. If yes, continue to the next page 2. If no, skip to the next participant

Informed consent Certified by

Interviewer: Code _____Name_____ signature_____

Date of interview _____Time started _____ Time completed_____

Result of interview: 1. Completed 2. Respondent not available 3. Refused 4. Partially completed

Supervisor (Checked): Name _____ Signature _____Date_____

Annex Three: Questioner

EFFECTIVNESS BETWEEN INTRAVENOUS DEXAMETHASONE(0.1mg/kg) AND PETHIDINE(25mg) FOR THE PREVENTION OF POST SPINAL ANSTHESIA SHIVERING FOR PATIENTS UNDERGOING TRANSURETHERAL RESECTION OF THE PROSTATE AT MINILIK SECOND HOSPITAL FROM October 26 to January 24/ 2020

Section-1; Socio demographic characteristics

No	Questions	Response
101	Age Age in a year_____	-----
102	ASA status of the patient	ASA 1 ASA 2 ASA 3 ASA 4
103	Room temperature	Base line …. Then every 15 min after operation started 15min….. 30min 45min 1hr …. …….
104	Allergy to any of the following drugs	Local anesthetics Pethidine Others (specify….)
105	Does the patient has preexisting medical problem	1. Yes 2. No If yes specify _____

Section-2; Hemodynamic parameters

No	Questions	Response
201	Baseline parameters	Body Temperature 1. Axillary……. 2. Tympanic ….. HR---------- MAP---------- SPO2---------- RR----------
202	Hemodynamic parameters after SA is given	Body TO HR MAP SPO2 RR At 1 min- ---- ------ ----- ----- …… After 1 minute Every 10 minute 10 min ---- ------- ----- ----- …… 20min ----- ------ ---- ----- …… 30min ----- ----- ---- ---- ……. 40min ---- ------ ----- --- ……. 60min …… …….. …… …. ……. At the time of ------ -------- ------ ---- …… ….. Discharge to PACU
203	Hemodynamic parameters at PACU	Body TO MAP PR SPO2 RR At reception …….. …… …. ….. ….. Every 10 minute 10m ……. ….. ….- …… …. 20min ------ ---- ---- ……. …. 30min- ------ ---- ---- ……. …. At time of ----- ----- --- ……. ….. Discharge
204	Hemodynamic parameters after discharge from PACU	Every 1hr until SA wears of Body To MAP PR SPO2 RR AT 1hr ……. …… …… …… …… At 2hr ……. ……. …… ……. …….

Section .3 Shivering and Severity of Shivering

301	Is shivering occur	Yes no
302	If answer yes answer question number 302	Intraoperative Postoperative
303	How Is the severity of the shivering according to grading.	Grade 0------ Grade 1-------- Grade 2------ Grade 3……. Grade 4…….
304	Time to 1st onset of shivering	At <10min 10-20 min 20-30 min 30-40min 40-50min 50-60min b/n 1hr and 2hr >2hr
305	Is other antishivering medication used	YES NO If Answer yes what medication used and its dose Pethidine dose….. Tramadol dose…….. Ketamine dose……. Others(specify),,,,,,,,, dose….

Section .4 Spinal Ansthesia related factors

401	Site of spinal anesthesia given	1 .L2/L3 2 .L3/L4 3,,Below L4 4,,Above L2
402	Type of drug used	Bupivacaine alone Bupivacaine with Fentanyl Bupivacaine with Pethidine

		Others (specify)…….

Section .5 Surgical related factors

501	Duration of surgery	Less than 1hr Between 1hr and 2hr Greater than 2hr
502	Amount of blood loss	Less than 500ml Between 500m1 and 1000ml Greater than 1000ml
503	Irrigating fluid	Warmed fluid Cold fluid
504	Amount of irrigating fluids used	Less than 500ml Between 500ml and 1000ml Greater than 1000ml

Section .6 Associated side effects

601	Any observed side effects	Nausea yes no	Vomiting yes no	Pruritus yes N o

Annex Four Grades of shivering

Shivering will be graded by using a scale similar to that validated by Tsai and Chu.

Grade 0: no shivering,

Grade 1: piloerection or peripheral vasoconstriction but no visible shivering,

Grade 2: muscular activity in only one muscle group,

Grade 3: muscular activity in more than one muscle group but not generalized and

Grade 4: shivering involving the whole body or bed shaking

Grade 1 is considered as mild,

Grade 2 as moderate

Grades 3 and 4 as severe shivering