"A COMPARATIVE STUDY OF THE EFFECT OF IV KETAMINE WITH IV TRAMADOL ON INTRAOPERATIVE SHIVERING IN PATIENTS UNDERGOING CAESEAREAN SECTION UNDER SPINAL ANAESTHESIA: RANDOMIZED CLINICAL TRIAL"

By

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REG. NO. BA0108005

DISSERTATION

SUBMITTED TO
KLE UNIVERSITY, BELGAUM, KARNATAKA
IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER DEGREE
IN
ANAESTHESIOLOGY

Under the Guidance of

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MAY – 2011

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ACKNOWLEDGEMENTS

First and foremost I would like to thank my guide **Dr. LATA KULKARNI** **MD, DA** Professor, Department of Anaesthesiology, for her constant guidance, valuable suggestions, unparalleled encouragement and co-operation provided to me throughout the course of study. It has been a great pleasure and privilege to work under her. Without her immense professional insight and guidance I could have not completed this study.

I avail this opportunity to thank **Dr. C.S.Sanikop** MD, DA., .Professor and Head, Department of Anaesthesiology, for his keen interest, unparalleled encouragement and co-operation during this study.

I express my sincere gratitude to **Dr. V. D. Patil** **MD, DCH** Principal, J. N. Medical College, Belgaum, **Dr. M. V. Jali** **MD**, Director and Chief Executive, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum for allowing me to utilize the facilities in above institution for the dissertation.

I am deeply indebted to **Dr P.F.Kotur** **MD**, Professor, Department of Anaesthesiology. His stature and knowledge has been highly inspirational all through my career as a post graduate.

I take this opportunity to thank , **Dr. V. K. Dhulkhed** **MD ,** former Professor and Head, Department of Anaesthesiology to whom I extremely grateful. I also thank Professor **Dr. Suresh S.N.MD, Dr. M. G. Dhorigol** **MD,** Associate Professors **Dr. Vandana Gogate** **MD, Dr. Rajesh Mane** **M.D.** and **Dr .Vijay Umarani** **M.D.** for their continuous support..

My special thanks to **Dr.Manjunath C Patil** **MD** , who has helped me out not only as a mentor but also as a friend when it mattered the most.

I also thank Consultant Anaesthesiology **Dr G.C.Mirji** **MD,** Assistant Professors **Dr. Deepak C.J.** **MD, Dr. Kedareshewar** **MD,** for their kind support.

I am thankful to Mr. Dhareshwar, statistician for his help in statistical analysis.

I sincerely thank all my post graduate colleagues for their help in the study.

I thank here all the Staff of Obstetrics and Gynaecology Department, Nursing staff working in labor OT for their continuous support they have rendered, during the course of this study. I am indebted to all my patients who were a part of my study without whom this study would not have been possible.

I convey my heart felt gratitude to my family without whose support and cooperation this study would not have been complete.

Finally, I thank **Almighty** for all the blessings.

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ABBREVIATIONS

ASA American Society of Anaesthesiologist

BP- Blood pressure

BMI- Body mass Index

CO- Cardiac Output

$C0_2$- Carbon Dioxide

CVS- Cardio vascular system

ECG- Electrocardiogram

EEG- Electroencephalogram

GABA-Gama amino butyric acid

Hist- Histamine

HR- Heart rate

Hr- Hour

Inj- Injection

IV- Intravenous

Kg- Kilograms

Mg - Milligrams

Min - Minute

NTS- Nucleus of tactus solitarius

NMDA – N-Methyl-d-Aspartate

RR- Respiratory rate

SAB- Subarachnoid block

TM - Tympanic Membrane

5-HT - 5-Hydroxytryptamine

ABSTRACT

BACKGROUND AND OBJECTIVE

Intraoperative shivering is one of the most common complications of spinal anaesthesia. It is an unpleasant and physiological stressful experience. It occurs in 5 to 65 % of patients recovering from anaesthesia. The main objective of the study was to compare the effectiveness of 0.5 mg/kg IV Ketamine with 0.5 mg/kg of IV Tramadol to reduce the intraoperative shivering in patients undergoing Caesearean section under spinal anaesthesia.

METHODLOGY

The present study was conducted in the department of Anaesthesiology, KLES Hospital and MRC, Belgaum during the period of Dec 2008 to 2009. After obtaining an approval by the ethics committee, patients who gave written and informed consent to participate in this study were included. Only ASA I or ASA II consenting parturients who subsequently developed intraoperative shivering were included. They were randomly allocated into either of the two groups– Group Ketamine or Group Tramadol by computer generated allocation. Intraoperative tympanic membrane temperature was recorded from start of the procedure and then after every 10 minutes interval. Patient was observed for shivering and graded on the following scale -

0- No shivering.

1- Mild fasciculation.

2- Tremors in one group of muscles / one part of the body.

3 - Tremors in more than one group / whole body.

After the onset of shivering IV Ketamine 0.5 mg/kg or IV Tramadol 0.5 mg/kg were given. Antishivering effect of the drug was noted on a 2 minute time interval till 10 minutes. In case of no response for 10 minutes rescue drug Pethidine 0.5 mg/kg IV was given. Patient was noted for any side effects.

CONCLUSION AND INTERPRETATION

The number of patients who stopped shivering (completely improved) within 10 minutes of receiving Ketamine were 28 out of 35 (80 %) , while in Tramadol group only 19 out of 35 patients (54.2 %) improved completely within 10 minutes. Mean grade of shivering at intervals of 2 minutes after injecting the drug was significantly lower in Ketamine group, in which grade of shivering dropped from grade 2 to 0 by 6 minutes, while in Tramadol group it dropped to grade 1 by 10 minutes. The antishivering effect in both the groups commenced by 2 minutes, however peak anti shivering effect of Ketamine was observed at 4 minutes while peak anti shivering of Tramadol was observed at 10 minutes.

In conclusion, Ketamine 0.5 mg / kg IV and Tramadol 0.5 mg / kg IV are useful drugs in controlling shivering in patients undergoing caesarean section under spinal anesthesia. Ketamine was found to be more effective antishivering drug and can be recommended to control shivering under regional anesthesia in patients undergoing caesarean section, keeping in mind the hallucination and sedation as side effects.

Keywords : Ketamine, Tramadol, Intraoperativ shivering, Thermoregulation

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INTRODUCTION

In the year 1956 Pickering wrote: "The most effective system for cooling a man is to subject him to anaesthesia."[1] In practice its importance was still not understood, till mid 1960's when first case of clinical hyperthermia was observed.[1]

The combination of anesthetic induced thermoregulatory impairment and exposure to a cool environment makes unwarmed surgical patients hypothermic. [1]

Regulation of core temperature is achieved by means of behavioral and autonomic mechanism that actively balance heat production and heat loss . These mechanisms are controlled largely from hypothalamus and depend on the input of afferent neurons from various sites within the body.[1]

Surgery and General Anesthesia impair the normal balance between heat production and loss. Anesthestic agents, opioids and sedatives inhibit behavioral and autonomic responses, leaving patients essentially poikilothermic.[2]

Hypothermia during neuraxial anesthesia develops initially from core to peripheral redistribution of body heat. Redistribution of body heat during spinal or epidural anesthesia typically decreases core temperature 0.5-1.0 degree Celsius.[2]

The discovery of importance of temperature monitoring dates back to mid 1600 when Santorio discovered the clinical value of intraoperative temperature monitoring but his efforts were not recognized. After two centuries Wunderlich recognized temperature monitoring as a key parameter.[3]

However, it was in mid 1960 when Intraoperative temperature monitoring became a standard for all anaesthetic procedures. However, it was difficult to monitor temperature intraoperatively because of difficulty in placing probes at unusual sites like nasopharynx and oropharynx which were not tolerated by patients under spinal anaesthesia.[4]

Temperature disturbances is common during both Neuraxial and General Anesthsesia. However, core temperature monitoring still remains rare during regional anesthesia and sometimes substantial hypothermia goes undetected.

Inadvertent hypothermia is associated with numerous adverse outcomes. Although hypothermia may provide protection against ischemia, there is ample clinical evidence that hypothermia causes multiple physiological derangements.[3] Some of them include coagulation abnormalities due to impaired platelet function, wound infection with delayed wound healing due to impaired immunoregulation. Shivering is another complicated response of the body to hypothermia. It is an involuntary, oscillatory muscular activity that can double or triple the oxygen consumption and carbon dioxide production. It is specially disturbing to the mothers during labour and delivery. Vigorous shivering increases the metabolic heat upto 600% above the base level.[4]

Universally lots of attempts have been made to treat shivering rather than prevent it . Various nonpharmacological and pharmacological measures have been studied to control intraoperative shivering.[3.]

Some of the nonpharmacological methods taken to reduce shivering are covering bare parts of the body with surgical drapes or blankets, airway heating and humidification , warming intravenous fluids and active cutaneous warming with insulator. After employing nonpharmacological methods to control shivering, if it still persists then various drugs with antishivering property can be administered.

Some of them are Pethidine, Ketamine, Tramadol, Physostigmine, Nefopam, Ondansetron.[1,2,3.] Pethidine has been shown to be one of the most effective treatments. It is one member of opioid family which has antishivering action. It is due to its central action on alpha adrenoreceptors in the locus coeruleus. One of the other drugs effective against shivering is Tramadol. It is a centrally acting analgesic drug that is a mixture of

two enantiomers which is also thought to possess antishivering action by its action on central adrenoreceptors. It also inhibits the reuptake of neurotransmitters which play an important role in pathway of shivering. But, it has certain side effects which need to considered.[5]

Another widely used drug in the practice of anesthesia is Ketamine. It is a phencyclidine derivative, which is a physiological competitive antagonist at N- Methyl d Aspartate (NMDA) receptor. This receptor activity is responsible for antishivering activity. Both Ketamine and Tramadol are commonly used drugs during perioperative period and are easily available in operating rooms and can be used promptly should the patient shiver.[6] In our study we wish to compare the antishivering efficacy of Ketamine with other drug Tramadol.

It is important that as clinicians we understand the impact of hypothermia and shivering on human body and provide timely intervention. Regional techniques are commonly used for patients undergoing caesarean sections and these women experience shivering frequently. Since shivering can also adversely affect neonatal outcome in addition to the other adverse effects of shivering it is necessary to promptly treat shivering under regional anaesthesia. Hence, in our study we wish to compare the antishivering effects of IV 0.5 mg/kg Ketamine and IV 0.5 mg/kg Tramadol for patients undergoing caesarean sections under spinal anaesthesia.

Thus, working on an old adage, “Prevention is better than cure”,we make an attempt to compare the efficacy and safety of intravenous Ketamine with intravenous Tramadol in controlling shivering in obstetric patients under regional anesthesia for Caesarean sections.

OBJECTIVES

To compare the effectiveness of 0.5 mg/kg of IV Ketamine with 0.5 mg/kg of IV Tramadol to reduce the intraoperative shivering in patients undergoing Caesarean section under Spinal Anaesthesia.

REVIEW OF LITERATURE

Regional anesthesia is safe and popular anesthetic technique for cesarean section, both in elective and emergency situations. One of the most common complications of this technique is shivering. The origin of shivering is unclear and mechanisms have been proposed .[1.]

In the year 1646 Santorio discovered the clinical value of temperature monitoring but it took two centuries before body temperature was recognized by Wunderlich as a key parameter.[1.]

Over the last decade, several studies link the role of general anesthesia as well as regional anesthesia to the occurrence of hypothermia. Shivering may happen as a thermoregulatory response to hypothermia or muscle hyperactivity with tonic or clonic patterns.[2,3.]

Shivering is an accompanying part of regional anesthesia and it leads to various consequences and discomfort to the patient. Proper steps must be taken for its prevention and treatment. As the dictum says, "Prevention is better than cure", it holds true for shivering also and it should be practiced.[3,4.]

Various pharmacological studies and trials have been done to compare the efficacy of routinely used drugs with anti shivering properties in combating intra operative and post operative shivering.[5,6.]

A study was conducted by Engelman et al[7] on 46 ASA grade I pediatric patients scheduled for elective inguinal herniorraphy. They compared the effects of Ketamine and Halothane on temperature and showed that the reduction in body temperature of children treated with Halothane during surgical operations was greater than those receiving Ketamine. They concluded that heat conserving effect of Ketamine could be due to decreased heat loss secondary to peripheral vasoconstriction or due to increased heat

production due to increased metabolism, the mechanism of which is still not elucidated [7.]

In an another study[8] which was conducted to find the efficacy of Ondansetron in patients undergoing orthopedic surgeries given before induction of anesthesia in reducing postanesthetic shivering after general anesthesia, it was found that 8 mg intravenous Ondansetron given during induction of anesthesia prevents post anesthetic shivering without affecting core to peripheral redistribution of heat during general anesthesia.[8.]

Efficacy of Ketamine in preventing postoperative shivering was studied by Dal et al[9] and his colleagues. 90 ASA I/II patients were randomly allocated to receive saline, Ketamine or Pethidine 20 minutes before the end of surgery. Number of patients who subsequently developed postoperative shivering on arrival in the recovery room at 10 and 20 minutes interval were studied They found prophylactic Ketamine (0.5mg/kg) was more effective than Pethidine (20 mg) in controlling postoperative shivering.[9.]

In one studies by Ikeda et al[10], which is unique of its kind, Ketamine was used prohylactically in patients undergoing general anesthesia, to prevent post operative shivering. They compared 0.5mg/kg IV Ketamine with 0.5 mg/kg IV Pethidine which was administered 20 min before extubation. Out of 90 patients three patients in Ketamine group developed shivering > grade 2. They attributed this observation to the dose of Ketamine. It was finally concluded that both drugs were equally efficacious in preventing post operative shivering.[10.]

An effort to study postoperative shivering in patients undergoing orthopedic surgeries was made by Ali Seifi et al[11]. They conducted a randomized double blind, comparative study on 60 patients belonging to class ASA I/II undergoing surgeries under general anesthesia. Postoperatively the patients were monitored in PACU for the occurrence of shivering . Patients who had shivering were given IV Tramadol 1mg/kg or Pethidine 0.5

mg/kg. Patients were evaluated for 5 minutes and categorized into three groups : completely improved , partially improved and not improved . 20 patients who were given Tramadol and 16 patient who were given Pethidine improved completely. Based on complex evaluation of data with chi square test they concluded that both Pethidine (0.5 mg/kg) and Tramadol (1mg/kg) were equally effective in controlling postoperative shivering.[11.]

Over the last decade, several studies linking the role of general anesthesia as well as regional anesthesia in predisposing to hypothermia and thus shivering have been conducted. Results suggested that temperature monitoring and management during neuraxial anesthesia is currently inadequate. [11]

Since, perioperative hypothermia is associated with numerous complications, precautions should be taken to reduce heat loss and active warming should be initiated.

Temperature monitoring must be accurate and consistent. Research indicates that during perioperative period when core temperatures changes rapidly at different sites, the relationship between the temperatures measured at various body sites may differ differently.

A study was conducted exclusively by Casey and Smith et al[12] to mark its antishivering actions under epidural anesthesia. 46 parturients undergoing Caesarean section under epidural anesthesia were divided into drug and placebo group. 50 mg of iv Pethidine was compared with saline . Administration of Pethidine showed not only an overall reduction in incidence of shivering from 87% to 35% but also a reduction in severity of shivering [12.]

A comparative study conducted by Yu-Chuan et al[13] on 45 parturients to compare the effect of 0.5 mg/kg Tramadol , 0.5 mg/ kg Meperidine and 15 mg Amitryptyline concluded that both Tramadol and Meperidine showed a faster response in the treatment of post epidural shivering as compared to Amitriptyline[13.]

A study conducted by Talakoub et al[14] was done to compare the efficacy and side effects of Tramadol with Pethidine on post- spinal shivering in caesarean section. 73 ASA I patients were included in the study. Patients were administered 0.5 mg/ kg IV Tramadol and 0.5 mk/kg IV Pethidine when shivering occurred. Shivering was graded and evaluated for 15 minutes. Response rate to Tramadol was 97.2% whereas it was 91.9 % to Ketamine. Based on these results they concluded that both drugs were equally effective in treating post-spinal shivering [14.]

Anne et al[15] conducted a study done on 36 obstetric patients who had episode of shivering intraoperatively undergoing caesarean section under regional anesthesia .They compared two different doses of Tramadol 0.5 ,0.25 mg/kg to Normal saline . Treatment efficacy was evaluated subjectively by patients as no improvement, slight improvement and marked improvement. Side effects such as nausea, vomiting or sedation and Apgar score on the newborn were noted. 80 % of parturients in group T0.5 and 92% in group T0.25 had a control in shivering as compared to 27% in group NS. [15]

They thus concluded that iv Tramadol was quiet effective in controlling shivering during Cesarean section under epidural anesthesia even at low dose of 0.25mg/kg.[15.] There was no increased incidence of side effects in the treatment groups.

A study[16] to compare 0.5 mg/ kg Ketamine, 3 mg Granisetron and combination of both was conducted by O. Sagir et al[16] to find out their prophylactic use in prevention of shivering during regional anesthesia was conducted on 160 ASA I/II patients in which after 15 minutes of giving spinal anesthesia prophylactic dose of one the drugs was given. Shivering was graded subjectively into four different levels. The difference between the various groups was found significant. Result clearly concluded that Ketamine was more effective in preventing shivering during regional anesthesia.[16.]

A study[17] to compare the efficacy of low dose prophylactic Midazolam, Placebo, and a combination of Ketamine and Midazolam was done be Honarmand et al[17.] 120 ASA I and II patients undergoing orthopedic surgeries were included under subarachnoid block. Patients were randomly allocated and were given Saline, 0.5 mg/Kg Ketamine, 75 microgram/ Kg Midazolam and 0.25 mg/Kg Ketamine plus 75 microgram/Kg Midazolam. Results were found to be statistically significant. Based on their results they concluded prophylactic use of Ketamine plus Midazolam was more effective than Ketamine or Midazolam or Saline used alone [17.]

If we restrict ourselves to combat shivering with pharmaceuticals only, recovery will be slower and the patients will be deprived of an important defence mechanism against reduction of core temperatures. If it does occur , it should be treated by warming the patient and then administering medication to the patient to inhibit it.

A Study[18] conducted on 40 patients receiving general anesthesia for orthopedic surgeries were observed for changes in core temperature , vasoconstriction and shivering in younger and older age groups. Mild core hypothermia was associated with postoperative vasoconstriction in 80 % of the younger and 55 % of the older patients. Even mild postoperative hypothermia with core temperature of less than 35.5 degree Celsius initiated shivering [18.]

The effects of regional anesthesia on thermoregulatory control have been studied on human volunteers. Regional anesthesia caused an initial redistribution of heat in the first 30 – 60 minutes, when heat is transferred from the core to periphery. This causes a drop of core body temperature of around 1 degree Celsius. In addition to this redistribution, there is a reduction of threshold of both shivering and vasoconstriction. This results in an expanded inter threshold range over which the core temperature can vary and no efferent thermoregulatory responses are triggered. Even the ability to sense hypothermia is impaired during regional anesthesia because warm input from the lower body overrides the sensation of the core hypothermia .[19.]

In an another observational study temperature changes were monitored by Arkilic et al[20] in 120 patients undergoing neuraxial anesthesia for a variety of operations. On patient arrival in the post anesthesia care unit they recorded various parameters like type of surgery, duration of surgery , whether temperature was recorded intra operatively and whether forced air warming was used . In the post anesthesia care unit, temperature was recorded at tympanic membrane with a thermocouple. They found that in patients admitted to the post anesthesia care unit, 77 % were hypothermic and another 22% had core temperatures below 35 degree Celsius [20.]

Results suggested that temperature monitoring and management during neuraxial anesthesia is currently inadequate.

PHYSIOLOGY OF THERMOREGULATION

Mammals have a remarkable capacity for regulating their core temperature within a narrow physiological range . Temperature of body is regulated by neural feed back mechanisms which primarily operate through the hypothalamus.[1,2].

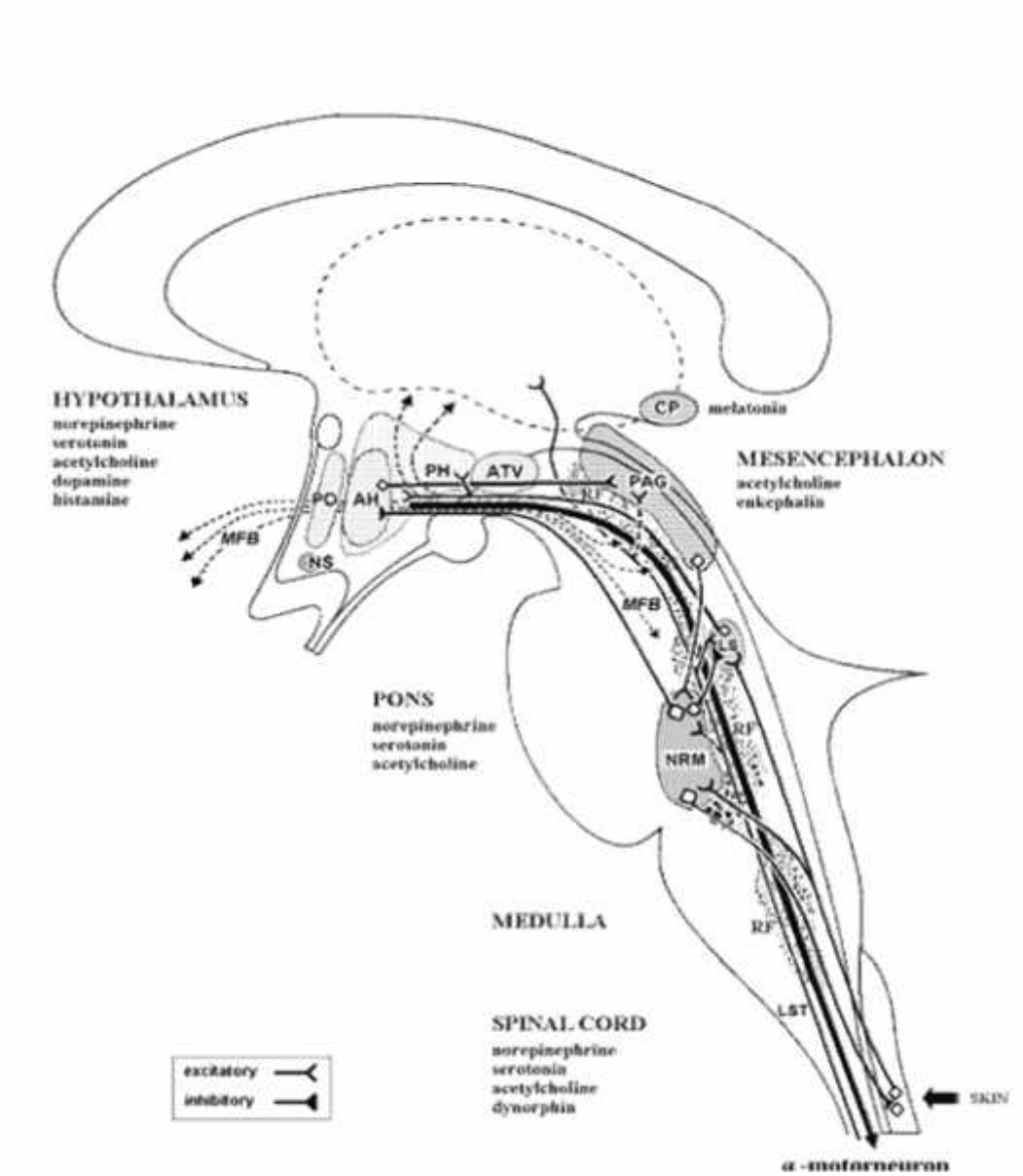
A thermal defence system exists in the humans , which co-ordinates various defences of the body against environmental temperature changes and maintains their temperature within the narrow physiological limit 98 to 100 degree Fahrenheit .[1,2]

Human beings control their central body temperature within a narrow range despite a wide range of environmental temperature. There is also a slight variation in body temperature during menstrual cycle in women with the basal temperature rising after ovulation for the second half of cycle. A constant body temperature is essential for various metabolic processes and enzymatic reaction to occur properly. Central core body temperature of the body is represented by brain , thoracic and abdominal organs and also some deep tissues of the limbs. Next is an intermediate zone which is surrounding the core body. The outermost is the shell layer with a variable depth of 2.5 cm.[3]

Historically, the lateral spinothalamic tract was considered the sole thermoafferent pathway, projecting to the hypothalamic thermoregulatory centers. However, evidence suggests that the majority of these ascending pathways terminate in the reticular formation. Thermosensitive neurons exist at several regions outside the preoptic-anterior hypothalamus including the ventromedial hypothalamus, the midbrain , the medulla oblongata , and the spinal cord . Multiple inputs from various thermosensitive sites are integrated at numerous levels within the spinal cord and brain to provide a coordinated pattern of defense responses.[2]

The temperature-regulating system of mammals is often divided into three components :

1. Thermosensors and afferent neural pathways.
2. Integration of thermal inputs
3. Effector pathways for autonomic and behavioral regulation.
4. The major afferent thermoregulatory structures and the efferent shivering pathway[2]



Thermosensors and Afferent Neural Pathways[2]

A. Spinal cord

The thermosensitivity of the spinal cord and its thermoregulatory significance is beyond doubt. It has the ability to sense and modulate thermal signals .[2]

B. Extrahypothalamic brain stem

Thermosensitive sites that are not associated with defined anatomical structures appear to be dispersed in the lower brain stem. A study in vertebrates concludes that peripheral thermal input to the hypothalamic areas is via the polysynaptic nonspecific reticular areas in the brainstem. [2]

C. Nucleus raphe magnus and Subcoeruleus area

The nucleus raphe magnus in the medulla contains a relatively high percentage of serotonergic thermoresponsive neurons, with a preponderance of warm responsive neurons. The locus subcoeruleus is a circumscribed area in the pons ventromedially to the locus coeruleus , which contains the largest cluster of noradrenergic neurons in the brain. The nucleus raphe magnus and the subcoeruleus area appear to be important relay stations in the transmission of thermal information from skin to hypothalamus. These areas seem to be responsible for the modulation rather than the generation of thermal afferent information. [2]

2. Integration of Thermal Inputs

The preoptic region of the anterior hypothalamus is the dominant autonomic thermoregulatory controller. Much of the excitatory input to warm-sensitive neurons in the preoptic-anterior hypothalamus comes from the hippocampus which links the limbic system (emotion, memory, and behavior) to thermoregulatory responses.

Additionally, the level of activity in preoptic neurons is modulated by arousal state and suprachiasmatic nucleus activity which may explain why changes in body temperature are associated with sleep and circadian rhythms. Thus, warm-sensitive neurons in the preoptic-anterior hypothalamus not only sense core temperature, but also compare local information with thermal and nonthermal synaptic afferents arriving over ascending pathways. [2]

3. Effector Pathways

Multiple inputs are integrated into a common efferent signal to the efferent systems . These effector mechanisms ensure optimal regulation . [3]

The principal defenses against hypothermia in humans include

A. Shivering
B. Nonshivering thermogenesis
C. Skin Vasomotor activity
C. Sweating.

Heat loss is normally regulated by cutaneous vasodilation and vasoconstriction , sweating.[3]

Vasoconstriction decreases cutaneous heat loss and constrains metabolic heat to the core thermal compartment . This usually prevents body temperature from decreasing the required additional 1°C required to activate intraoperative shivering . Thermoregulatory shivering is thus a "last-resort" defense that is activated only when maximal arterio-venous shunt vasoconstriction are insufficient to maintain core temperature. [2,3,4].

Nonshivering thermogenesis is the result of cellular metabolic processes that do not produce mechanical work. Thermoregulatory nonshivering thermogenesis has been demonstrated in the human neonate , but its existence in adult humans is uncertain , as it is not observed in anesthetized adults .[2]

The temperature in the body core depends on the balance between heat production in the core and heat loss in the shell. [18]

HEAT PRODUCTION

Heat production is determined by the metabolic rate of the person and at any given time and is measured in Watts. In an average man under resting conditions, heat production is of order of 50 Watt/m^2, but increases of metabolic rate occur because of food consumption, exercise and other factors. There is no mechanism by which heat production can be reduced to compensate for overheating, but an increase of heat production can be provided by shivering. Such shivering can double the metabolic heat production and a five fold increase in special circumstances.[18]

HEAT LOSS

There are four principal routes of heat loss from the body:-

Radiation	40 %
Convection	30 %
Evaporation	20%
Respiration	10 %

Heat loss from radiation is important and may account for upto 40 % of normal heat loss from the body. Radiation transfers heat energy between two objects which are not in contact, the rate of which depends on the relative temperatures and surface characteristics of the objects.[18]

In convection, the air layer adjacent to surface of the body is warmed by conduction and when it becomes heated it becomes less heated and rises. The resulting convection current carries heat away from the subject.[18]

In Evaporation, heat loss is due to loss of latent heat of vaporization of moisture on the skin's surface. Loss of heat by this route depends on water vapor pressure gradient. Respiration accounts for only 10% of total body heat loss.[5]

All these routes of heat loss lead to a drop in the core body temperature which can trigger shivering.

PERIOPERATIVE TEMPERATURE MONITORING

Temperature monitoring is a very important aspect of perioperative monitoring. Various temperature monitoring devices are in use. They vary according to the type of tranducer used and the site to be monitored. Commonly used transducers are – Thermistors and Thermocouples. A more recent development is monitors that use infrared emission to measure temperature. These are seen commonly in aural canal thermometers, also referred to as tympanic membrane thermometers. Core temperature is the best single indicator of body temperature. [18,19,21.]

Core temperature monitoring is appropriate for most patients undergoing general anesthesia, to facilitate detection and treatment of fever, malignant hyperthermia and hypothermia[18] . The results of various studies show that body temperature if often not monitored in patients receiving regional anesthesia. It is therefore likely that significant hypothermia goes undetected and untreated in many patients. [19.]

Monitoring sites –

Pulmonary artery catheters

These allow the measurements of central blood temperatures, considered as the gold standard for measuring core body temperature. [18,19.]

Esophageal temperature

Usually monitored with a thernistor or thermocouple that is incorporated into an esophaheal stethoscope. It accurately reflects core temperature in almost all conditions. [18.]

Nasopharyngeal temperature

It can be measured with an esophageal probe positioned above the palate , it is reasonably close to brain and core temperature. Because the eardrum is close to the carotid artery and the hypothalamus, tympanic membrane temperature is a reliable measure of core temperature and often is used as a reference for other sites[18]

Bladder temperature

This can be measured with a Foley catheter with an attached temperature thermistor or thermocouple. Although bladder temperature is a close approximation of core temperature , the accuracy of this site decreases with low urine output and during surgical procedures of the lower abdomen. [18]

Axillary temperature

Axillary temperatures are relatively close to core temperature and may be a reasonable choice in selected patients. [18.]

Infrared ear and tympanic membrane thermometers

Infrared ear and tympanic membrane thermometers are based on the fact that objects emit electromagnetic radiation over a range of wavelengths. The intensity of this radiation and the wavelength for which the intensity of emitted radiation is a maximum depends on the temperature of the object. Objects at body temperature primarily emit infrared radiation. The infrared thermometer uses a tube inserted into the ear canal to direct the radiation into an electric signal. Tympanic membrane thermometers are intended to be inserted further into the ear so that they receive radiation only from the tympanic membrane, the temperature of which is more representative of core temperature than the ear canal.[18]

Some of the problems associated with this mode of temperature monitoring are – Measurement is intermittent, poor penetration and obstruction due to impacted wax and obstructions of the ear canal and associated perforation of the tympanic canal. [18,19.]

Careful monitoring of the vital signs including body temperature during surgery are essential to safe anesthetic care. By monitoring temperature we can prevent hypothermia and the risks associated with it like cardiac morbidity, wound infection , surgical bleeding and patient discomfort.[19]

Earlier temperature monitoring was restricted to general anesthesia because these complications were linked to general anesthesia and unfounded belief that regional anesthesia does not alter body temperature. [12]

DRUGS CONTROLLING SHIVERING

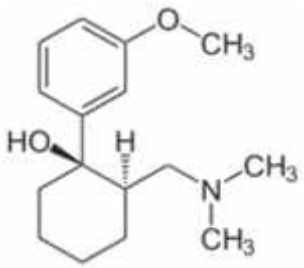
Based on the monoamine theory of thermoregulation laid by Feldberg and Myers in the year 1963 it was discovered the balance of norepinephrine and serotonin (5 Hydroxytryptamine) in the pre-optic-anterior hypothalamus controls the body temperature set point. 5-HT causes shivering and vasoconstriction and a concomitant increase in core temperature , whereas Norepinephrine and Epinephrine lower the normal resting temperature and attenuated the 5-HT induced hyperthermia. Further antishivering properties of various drugs have been studied which come under several classes of drugs like biogenic amines, cholinomimetics, cations, endogenous peptides and NMDA receptor antagonists.[32,33,34,35]

PHARMACOLOGY OF DRUGS

TRAMADOL

Tramadol Hydorcholride is a centrally acting analgesic drug possesses agonist actions at the μ-opioid receptors and also affects reuptake of noradrenaline and serotonin .

STRUCTURE



Tramadol

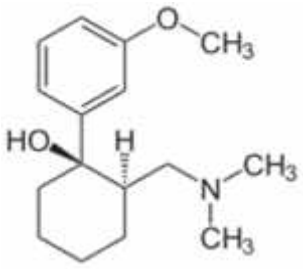
It is a synthetic piperidine analog of the phenantherane alkaloid Codeine. It is an Opioid . Opioids are chemical compounds which act upon one or more of the human opiate receptors , Mu(μ) 1 and 2 receptor. The opioid agonistic effect of Tramadol and its major metabolite(s) are almost exclusively mediated by the substance's action at the μ-receptor. This characteristic distinguishes Tramadol from many other substances of the opioid drug class, which generally do not possess Tramadol's degree of subtype selectivity .It is converted to O-desmethyltramadol which is also responsible for its stereoselective analgesic effect.[4,23,24,33..]

STEREOISOMERS

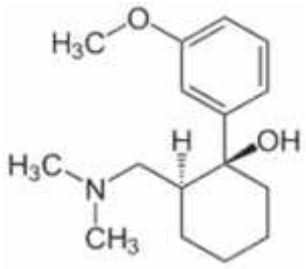
Tramadol [2-(dimethylaminomethyl)-1-(3-methoxyphenyl) cyclohexanol] has two stereogenic centers at the cyclohexane ring. Thus, it may exist in four different

configurational forms:-

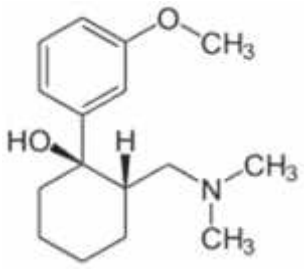
- (1R,2R)-isomer
- (1S,2S)-isomer
- (1R,2S)-isomer
- (1S,2R)-isomer



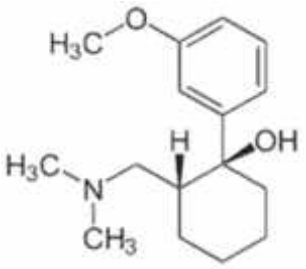
(1*R*,2*R*)-Tramadol



(1*S*,2*S*)-Tramadol



(1*R*,2*S*)-Tramadol



(1*S*,2*R*)-Tramadol

AVAILABILITY

Marketed as the hydrochloride salt. Available for both IV(Intravenous) and IM (Intramuscular) and oral administration[25,26,27,31].

MECHANSIM OF ACTION

Tramadol acts as a μ-opioid receptor agonist, serotonin releasing agent, norepinephrine

reuptake inhibitor, NMDA receptor antagonist, nicotinic acetylcholine receptor antagonist, and M_1 and M_3 muscarinic acetylcholine receptor antagonist.

The analgesic action of tramadol has yet to be fully understood, but it is believed to work through modulation of serotonin and norepinephrine in addition to its mild agonism of the μ-opioid receptor.

It inhibits the reuptake of neurotransmitters which play an important role in pathway of shivering. It is a potent inhibitor of reuptake of 5-HT, Norepinephrine and Dopamine at the synaptic junction. It also facilitates the release of 5-HT. It reduces the neuronal firing rate and hyperpolarizes neurons in concentration dependent manner in locus coeruleus. Locus coeruleus appears to be a proshivering centre that activates heat production. It is also the main noradrenergic nucleus involved in the descending pain control system, which is regulated by 5-HT.

Another centre in brainstem, dorsal raphe nucleus possesses antishivering action which inhibits thermogenesis. A significant amount of norepinephrine exists in nucleus raphe magnus. [2,5,10,25,26,27.]

USES

1. Diabetic neuropathy.
2. Postherpetic neuralgia.
3. Fibromyalgia.
4. Restless legs syndrome.
5. Opiate withdrawal management.
6. Migraine headache .
7. Obsessive-compulsive disorder.
8. Premature ejaculation.

SIDE EFFECTS

Most commonly reported are

1. Nausea , Vomiting,
2. Memory loss,
3. Sweating .
4. Constipation.
5. Drowsiness.

DRUG INTERACTIONS

1. Respiratory depression.
   Common side-effect of most opioids, is not commonly seen with tramadol.
2. With SSRIs, Tricyclic antidepressants, or in patients with Epilepsy, the seizure threshold is further decreased .
3. Dosages of Warfarin may need to be reduced for anticoagulated patients to avoid bleeding complications function.

METABOLISM

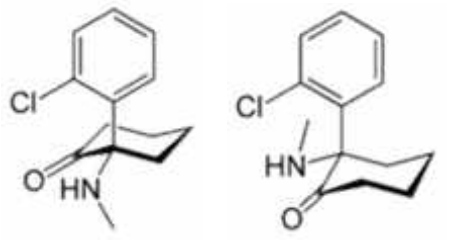
It is metabolized by hepatic cytochrome P450 enzyme systems to a major metabolite . O-Desmethyltramadol . It has significance since it has 200 times the μ - affinity of tramadol, and has an elimination half - life of nine hours, compared with six hours for tramadol itself. In the 6 % of the population that have slow CYP2D6 activity, there is therefore a slightly reduced analgesic effect. Phase II hepatic metabolism renders the metabolites water-soluble, which are excreted by the kidneys. Thus, reduced doses may be used in renal and hepatic impairment[25,26,27,31.].

KETAMINE

Ketamine Hydrochloride is a phencyclidine derivative that produces "Dissociative anesthesia". It produces a cataleptic state in which the subject is separated from the surrounding . It renders the patient non communicative, although wakefulness may be present .

STRUCTURE

Ketamine is a chiral compound and contains two optical isomers or enantiomers. Most pharmaceutical preparations of ketamine are racemic which contain both enantiomers (+) and (-) in equal amounts.



R Ketamine S Ketamine

AVAILABILITY

It is available in intravenous vial.

MECHANISM

Ketamine is a potent anaesthetic agent. It produces "Dissociative anaesthesia", where it stimulates the thalamic and limbic system and inhibits medial medullary reticular formation causing functional and electro-physiological dissociation between thalamus and limbic system . It is a potent analgesic at sub anaesthetic doses and action is mediated by various receptors NMDA , GABA , voltage gated Na and K channels. Ketamine binds competitively to the phencyclidine recognition site on N-methyl- D-aspartate (NMDA) receptors, which is implicated in modulation of central thermoregulatory centres for shivering.

In addition, ketamine may exert effects at other sites including opioid receptors, monoaminergic receptors, and voltage- sensitive sodium and and L-type calcium channels [21.]

METABOLISM

It is metabolized by hepatic microsomal enzymes. The major pathway involves Ndemethylation to form norketamine (metabolite I) , which is then hydroxylated to hydroxynorketamine. These products are conjugated to water-soluble glucuronide derivatives and are excreted in urine.

ROUTES

Ketamine can be given by intravenous , intramuscular , subcutaneous , oral , rectal , nasal , transdermal , epidural , intrathecal routes.

DOSAGES

1. **Induction of General Anesthesia**
   0.5–2 mg/kg IV
   4–6 mg/kg IM
2. **Maintenance of General Anesthesia**
   0.5–1 mg/kg IV with 50% N2 O in O2
   15–45 μg/kg/min IV with 50%–70% N2 O in O2
3. **Sedation and Analgesia**
   0.2–0.8 mg/kg IV over 2–3 min
   2–4 mg/kg IM

USES

1. Pediatric anaesthesia. As the sole anaesthetic for minor procedures or as an induction agent.
2. Asthmatics or patients with chronic obstructive airway disease.
3. In emergency medicine in entrapped patients suffering severe trauma.

4. To supplement spinal / epidural anaesthesia / analgesia utilizing low doses.
5. Small doses (0.1–0.5 mg/kg·h) as a local anesthetic, particularly for the treatment of pain associated with movement and neuropathic pain.
6. As a co-analgesic , it is most effective when used alongside a low-dose opioid.

SIDE EFFECTS

1. Hallucinations.
2. Dizziness.
3. Light headedness.
4. Nausea.
5. Emergence delirium .
6. Excessive salivation .
7. Increased sympathetic response. Increases Blood pressure, Heart rate , Cardiac output.

PETHIDINE

It is the only opioid which has antishivering property which is one amongst its several non opioid actions. It produces considerable inhibition of 5-HT reuptake in analgesic concentrations. It also possesses non competitive NMDA receptor antagonist activity in the spinal cord .In addition it has anticholinergic effects.

An important contribution made by Takda et al showed that Pethidine can bind to alpha 2 – adrenoreceptor subtype and transduce an agonist action at these sites. These actions are responsible for the antishivering actions in the locus coeruleus . [1,3,4,7].

Pethidine thus possesses antishivering properties that are not shared by pure mu – receptor opioids . The drugs antishivering properties may simply result from the drug's lack of specificity and a fortunate accumulation of pharmacologic actions modulating thermoregulatory shivering . [1,2,7,28,29,230..]

Some of the other drugs which possess antishivering actions-

Nefopam is an analgesic drug with powerful anti-shivering property. It is a potent inhibitor of synaptosomal uptake of 5-HT, norepinephrine, and dopamine, and slightly lowers normal body temperature[1,2,3.].

Ketanserin is anti hypertensive drug which is an antagonist of both 5-HT2 receptors and a1-adrenoceptors It acts indirectly via facilitation of a central presynaptic a2-adrenoceptor mechanism in the lower brainstem [1,2,3].

Ondenstron and Granisetron , 5-HT3 receptor antagonists, known for their antiemetic actions, are currently under investigation for a possible role in the prevention and treatment of postanesthetic shivering [1,2,3,33..]

Physostigmine is effective in preventing of postanesthetic shivering. Physostigmine is a non selective centrally-acting cholinesterase inhibitor. Its analgesic effect are mediated by cerebral cholinergic muscarinic receptors , but serotoninergic receptors and an endorphinergic mechanism may also be involved. Analgesia after intrathecal administration of anticholinesterase is mediated through muscarinic receptors. , There also known is a synergistic interaction with intrathecal μ-opioid and a2-adreneric agonists .Receptors which mediate the thermoregulatory effects are still under study [1,2,3,33,34,35] .

Calcium (Ca2+) and Sodium (Na+) play a functionally opposing role in mediation of body temperature. Excess of Ca2+ into the posterior hypothalamus leads to a decrease in the body temperature while excess of Na+ increases the body temperature. The magnitude of this response depends on the ratio of the cations concentration and may thus define the “setpoint” for body temperature [1,2,3].

Magnesium is a physiologic antagonist of NMDA receptor and was found to stop post anesthetic shivering. The possible physiological role in cold adaptation is due to decrease in the threshold of postanesthetic shivering [1,2,3].

Methylphenidate is effective for prevention and treatment of postanesthetic shivering. It is an analeptic agent that binds presynaptic sites on dopamine, norepinephrine, and 5-HT transport complexes, which in turn block reuptake of the respective neurotransmitters. Activation of the raphe system and the concomitant arousal may explain the impressive anti-shivering potency of methylphenidate. However, experimental evidence for the precise anatomical substrate of methylphenidate's anti-shivering action is lacking [1,2,3,33,35].

PERIOPERATIVE SHIVERING AND ITS CONTROL

Perioperative shivering can be broadly described under neuraxial anaesthesia and post anaesthetic shivering usually following general anaesthesia.

Shivering is an involuntary, oscillatory muscular activity that augments metabolic heat production. It may increase the metabolic heat production up to 600% above basal level. Shivering is elicited when the preoptic region of the hypothalamus is cooled. Efferent signals mediating shivering descend in the medial forebrain bundle. . Thermally-induced changes in neuronal activity in the mesencephalic reticular formation and the dorsolateral pontine and medullary reticular formation exert descending influences on the spinal cord that increase muscle tone. [3]

Spinal alpha motor neurons and their axons are the final common path for both coordinated movement and shivering. A typical cold tremor has a specific rhythm in the form of grouped discharges in the electromyography .The fundamental tremor frequency on the electromyogram in humans is typically near 200 Hz. The basal frequency is modulated by a slow, 4-8 cycles/ min, waxing and waning pattern. During continued cold stimulation of the skin or the spinal cord, motor neurons are recruited in sequence of increasing size, starting with the small gamma motor neurons that are followed by the small tonic alpha motor neurons, and finally, the larger phasic alpha motor neurons. [3]

Abnormal Tremor Patterns

There are three patterns of muscular activity observed in hypothermic volunteers during recovery .The first was a tonic stiffening and appeared to be largely a direct non-temperature dependant effect of anesthesia. A second pattern was overt synchronous tonic waxing and waning pattern. This was the most commonest pattern and resembled that produced by cold induced true thermoregulatory shivering. The third pattern was spontaneous electromyographic clonus which is given below in the diagram [3.]

Shivering can double or even triple oxygen consumption and carbon dioxide production. These large increases in metabolic requirement may predispose patients with existing intrapulmonary shunts, fixed cardiac output, or limited respiratory reserve to a severe compromised state . [2]

Various grades of shivering have been given categorized [9]–

Grades	Clinical Signs
0	No shivering .
1	Mild fasciculation .
2	Visible tremor of one part / one group of body .
3	Gross muscular activity involving more than one part/ entire body

SHIVERING UNDER NEURAXIAL ANAESTHESIA

Autonomic thermoregulation is impaired during regional anesthesia, and is mainly due to intraoperative core hypothermia. This is often perceived by patients which leads to shivering above the level of block. It is seen that shivering threshold is decreased during neuraxial blockade suggesting an alteration in central control. Reduction in threshold is proportional to the number of spinal segments blocked.[1,2,3,32.]

Because neuraxial anesthesia prevents vasoconstriction and shivering in blocked regions, it is not surprising that spinal anesthesia decreases the maximum intensity of shivering.

So the thermoregulatory defenses, once triggered, are less effective than usual during spinal anesthesia. Since core body temperature defenses are triggered at a lower temperature than normal during regional anesthesia so patients do not recognize that they are hypothermic. And because core temperature monitoring remains rare during regional anesthesia, substantial hypothermia often goes undetected in these patients.[1,2,3,18,32.]

POST ANAESTHETIC SHIVERING

Patients report that shivering is remarkably uncomfortable and some even find the accompanying cold sensation worse than surgical pain. Shivering may aggravate postoperative pain simply by stretching surgical incisions. It may occasionally impede monitoring techniques, increases intraocular and intracranial pressures.[2]

Shivering is common in hypothermic patients recovering from anesthesia. Possible explanation for postanesthetic tremor is anesthetic-induced thermoregulatory inhibition which dissipates abruptly , thus increasing the shivering threshold towards normal.[2]

Despite alternative etiologies in some patients, normal thermoregulatory shivering in response to core and skin hypothermia remains by far the most common cause of postoperative shivering. [3]

METHODOLOGY

The present study was conducted in the department of Anaesthesiology, KLES Hospital and MRC , Belgaum during the period of Dec 2008 to 2009.

Study Design:

One year randomized clinical trial.

Source of Data:

Patients undergoing caesarean section under spinal anaesthesia at K.L.E.S. Hospital and M.R.C., Belgaum.

Sample Size:

A total sample size of 70 cases, 35 in group (T) and the other 35 in group(K).

Sample size calculation:

The Sample size was calculated by considering reduction in incidence of shivering 60 % for Tramadol and 90 % for Ketamine with type I error rate , α =0.05 and type II error rate , β=0.02 with a power of 80%, and using formula -

$$N=\frac{2\,(Z\alpha+Z\beta)^2\,p(1-p)}{(P_{1+}\,P_2/2)^2}$$

Inclusion criteria:

1.) Written/ Informed consent.

2.) ASA Grade 1 or 2 .

3.) Patients of both gender ranging 18 to 60 years.

4.) Undergoing Spinal Anaestheisa.

Exclusion criteria:

Patients with-

1. Hyperthyroidism.

2. Cardiopulmonary disease.

3. Known hypersensitivity to the drugs .

Duration of study:

December 2008 – January 2009

Methodology:

After obtaining an approval by the ethics committee, patients who gave written and informed consent to participate in this study were included. A through pre-anaesthetic evaluation was performed by taking history and clinical examination .In all patients age, weight , height , systolic blood pressure , diastolic blood pressure , heart rate and core body temperature (tympanic membrane temperature by infrared thermometer) were recorded. After explaining anaesthetic procedure , written informed consent for surgery and anaesthesia was obtained . Only ASA I or ASA II consenting parturients who subsequently developed intraoperative shivering were included. They were randomly allocated into either of two groups – Group Ketamine or Group Tramadol by computer generated allocation. Intravenous line was secured using 18 Gauge IV cannula . Monitors like Pulse oximeter , ECG , NIBP were attached. Operating room temperature was maintained at 24 degree Celsius. Injection Ranitidine 50 mg IV was given before the start of the procedure . Along with that all patients were preloaded with 500 ml isotonic saline Ringer Lactate. All fluids and drugs were administered at room

temperatures. The studied drugs were prepared as Tramadol 10 mg/ml and Ketamine 10 mg/ml in 10 ml syringes.

Patient was positioned on the operating table. Under strict asepsis 1.8 ml (9mg) of heavy 0.5% Bupivacaine was injected in L2-L3 or L3-L4 subarachnoid space with 23 gauge Quincke spinal needle in left lateral position after confirming free flow of clear CSF. After giving sub arachnoid block, patient was turned supine . A wedge block was placed under the right buttock. Patients were covered with sterile bed sheets. Oxygenation was maintained with Venturi mask at 5 L/Min. After confirming the level of sensory and motor blockade using pin prick and modified Bromage scale respectively, a sensory block of T6-T7 level was achieved. Surgery was then allowed to proceed. Perioperatively blood pressure was monitored using NIBP. IV Ephedrine 3 to 6 mg was given whenever the systolic blood pressure dropped below 20 % of the baseline. After delivery of the baby, injection IV 0.5 mg Methergin or Oxytocin 10 Units (in slow infusion of Normal Saline) was administered.

Intraoperative Tympanic membrane temperature was recorded at the onset of operation (Time TO), and at every 10 Min from the start till the end of the procedure.

Patient was meticulously observed for shivering . The onset time was graded according to the following scale as per Dal et al[8]–

0 - No shivering.

1 - Mild fasiculation .

2 - Tremors in one group of muscles / one part of the body.

3 - Tremors in more than one group / whole body.

After the onset of shivering grade 1 or above parturients were administered either 0.5 mg/kg IV Ketamine or 0.5 IV mg/kg Tramadol depending upon the random allocation. Patients did not know which drug was being administered. Anti shivering effect of the

administered drug was observed and recorded at an interval of every 2 minutes (S0, S2, S4, S6 , S8 and S10) from the start of shivering till 10^{th} minute. In case of no improvement after 10 minutes, drug was regarded as ineffective. Rescue drug Pethidine (0.5 mg/kg IV) was used in such a case.[11] The response to antishivering drugs were observed and recorded by anesthesia colleague not involved in the study.

Patient was observed for any side effects. One of the known side effects of the drug administered was sedation which we graded according to the following scale.[5,6]

0 - No sedation.

1 - Mildly sedated - Easily arousable.

2 - Heavily sedated .

APGAR score was also recorded at 1 and 5 minutes after delivery of the baby.

Statistical analysis :

The Sample size was calculated based on previous studies by considering reduction in incidence of shivering 60 % for Tramadol and 90 % for Ketamine with type I error rate , α =0.05 and type II error rate , β=0.02 with a power of 80%.

Demographic and Parametric data were analysed by student unpaired –t test. Non-parametric data was analysed by using Mann Whitney U Test. P value of less than 0.05 is considered significant.

TRAMADOL

KETAMINE

SUB ARACHNOID BLOCK

SPINAL SET

TYMPANIC MEMBRANE THERMOMETER

RESULTS

The present study was conducted in the Department of Anaesthesiology , K.L.E.S. Hospital and M.R.C., Belgaum during the period Dec 2008 to Dec 2009. 70 patients who underwent Caesarean Section under spinal anaesthesia were observed for intraoperative shivering and divided into two groups, Group T(n=35) and Group K(n=35). At the onset of shivering, Grade1 and above drug 0.5 mg/kg Ketamine or 0.5 mg/kg Tramadol were administered intravenously and effects observed and recorded. The following are some of the observations made in our study .

Table 1 - Demographic data.

Table 1

PARAMETER	**Group K (Mean ± S.D.)**	**Group T (Mean ±S.D.)**	**p VALUE**
Age (in yrs)	24 ± 2.36	25 ± 2.36	0.3630
Weight (in kg)	61 ± 10.0	60 ± 9.90	0.9336
Height (in cm)	157 ± 5.42	156 ± 7.4	0.8371

Demographic data were comparable in both the groups.

Average age in group Ketamine was 24 years, in group Tramadol was 25 years.

Average weight in group Ketamine was 61 kgs, in group Tramadol was 60 kgs.

Average height in group Ketamine was 157 cms, in group Tramadol was 156 cms.

Table 2 -Baseline Hemodynamic Parameters

Parameter	Group K (Mean ± S.D.)	Group T (Mean ± S.D.)	p-Value
Systolic Blood Pressure (in mm of Hg)	120.2286 ± 7.59	121.0286 ± 7.67	0.6623
Diastolic Blood Pressure(in mm of Hg)	70.94286 ± 7.80	71.05714 ± 7.94	0.9517
Heart Rate(Beats per min)	87.77143 ± 10.91	87.77143 ± 10.91	1.0000
Temperature(Degree k Farenheit)	97.34 ± 0.46	97.42 ± 0.52	0.5147

Baseline hemodynamic parameters and Temperature parameters are depicted in the table given above.

Baseline hemodynamic parameters and Temperature parameters were comparable in both groups.

Preoperative temperature in the group Ketamine was 97.34 degree Fahrenheit in group Tramadol it was 97.42 degree Fahrenheit.

Systolic Blood pressure was 120 mm Hg in group Ketamine , 121 mm Hg in Group Tramadol.

Diastolic Blood Pressure was 70 mm Hg in group Ketamine , 71 in mm Hg in group Tramadol.

Heart Rate was similar 87 beats per min in both Ketamine and Tramadol group.

Table 3- Mean tympanic membrane temperature at various time intervals

	TIME INTERVAL												
Group	Preop 0 min	10 min	20 min	30 min	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min	120 min
Group K (n=35)	97.34	97.34	97.13	96.94	96.79	96.87	96.93	97.03	97.23	97.13	97.17	97.26	97.40
Group T (n=35)	97.42	97.36	97.17	97.05	96.98	96.83	96.88	96.90	96.94	96.98	97.00	96.90	96.87

Mean temperature at the end of the surgery in group Ketamine was 97.40 degree Fahrenheit whereas it was 96.87 degree Fahrenheit in group Tramadol.

The minimum temperature recorded in Ketamine group was at 40 minutes(96.79 degree Fahrenheit) after start of surgery , whereas in Tramadol group it was at 50 minutes(96.83 degree Fahrenheit) after onset of the surgery.

Table 4 - Mean Time of onset of shivering in two groups.

Table 4

Group K	34.04
Group T	33.14

Mean onset time of shivering was 34.04 minutes in group K and 33.14 in group T.

Table 5 - The median grade of shivering observed in the two groups at various time intervals is given in table below.

Table 5

TIME (Minutes)	**GROUP K (n = 35)**	**GROUP T (n = 35)**	**p- VALUE**
0	2	2	0.5890
2	1	1	0.4593
4	1	1	0.2088
6	0	1	0.0365
8	0	1	0.0325
10	0	1	0.0281

Median grades of shivering at intervals of 2 minutes are shown in the table above. Shivering in group K dropped from grade 2 to 0 by 6 minutes while in group T it dropped to only grade 1 by 10 minutes.

Results of the data observed from our study showed that the difference in anti shivering effect is significant after S6. However, the difference is significant after the sixth minute (T6).

The effect has been graphically illustrated. P values are statistically significant in Group K as compared to Group T .(<0.05) at 6 minutes.

Table 6 - Number of patients showing peak antishivering effect observed clinically at different time intervals. –

Table 6

TIME (minutes)	**GROUP** K (n = 35) Number of patients	**GROUP** T (n = 35) Number of patients
0	1	0
2	4	3
4	14	3
6	4	5
8	4	4
10	8	19

Peak anti shivering effect of Ketamine was observed at 4 minutes. Peak anti shivering of Tramadol was observed at 10 minutes .

Table 7 - Shows the efficacy of the two drugs in reducing shivering over 10 minute period.

Table 7

Drug	Shivering Completely Reduced
Ketamine	28 / 35 (80.0%)
Tramadol	19 / 35 (54.2)

In the Ketamine group, number of the patients who had complete cessation of shivering were 28 out of 35 (80%).

In the Tramadol group , number of the patients in whom shivering completely stopped were 19 out of 35 (54%).

Side effects

1.) Sedation

Table 8- Comparison of sedation (Complication of drug) in the two groups.

Table 8

Drug	Incidence	Mean ± S.D.	P value
Group K	24 /35 (69%)	0.94 ± 0.68	<0.0001
Group T	4/35 (11%)	0.140± 0.36	

P – value <0.05 significant (0.0001 being highly significant)

Table 9

Number of patients who developed sedation

Group	Grade 1 (Mild)	Grade 2 (Heavy)
Ketamine	24 (48.5%)	7 (20 %)
Tramadol	4 (11 %)	0 (0%)

24 out of 35 patients (68.5 %) in Ketamine group developed sedation.7 out of 35 patients(20%) developed grade 2 sedation (Heavy sedation) and

17 out of 35 patients (48.5 %) developed grade 1 (Mild sedation- easily arousable) wheraas no sedation was observed in 11 patients (31.5 %).
4 out of 35 (11 %) developed grade 1 (Mild sedation) in Tramadol group., P value being significant (<0.0001).

2.) Other complications –

Table 10- Incidence of other side effects –

Table 10

Number of patients who developed hallucinations-

Side effects	Group K	Group T
Hallucinations	2/ 35 (6%)	0 (0%)
Nausea / Vomiting	0 (0%)	8/ 35 (23%)

Incidence of hallucinations in group K was 6% (2 out of 35) , whereas in group T it was 0%.
Incidence of Nausea / Vomiting was 0 % in group K , whereas in group T it was 23% (8 out 35).

Apgar Scoring -

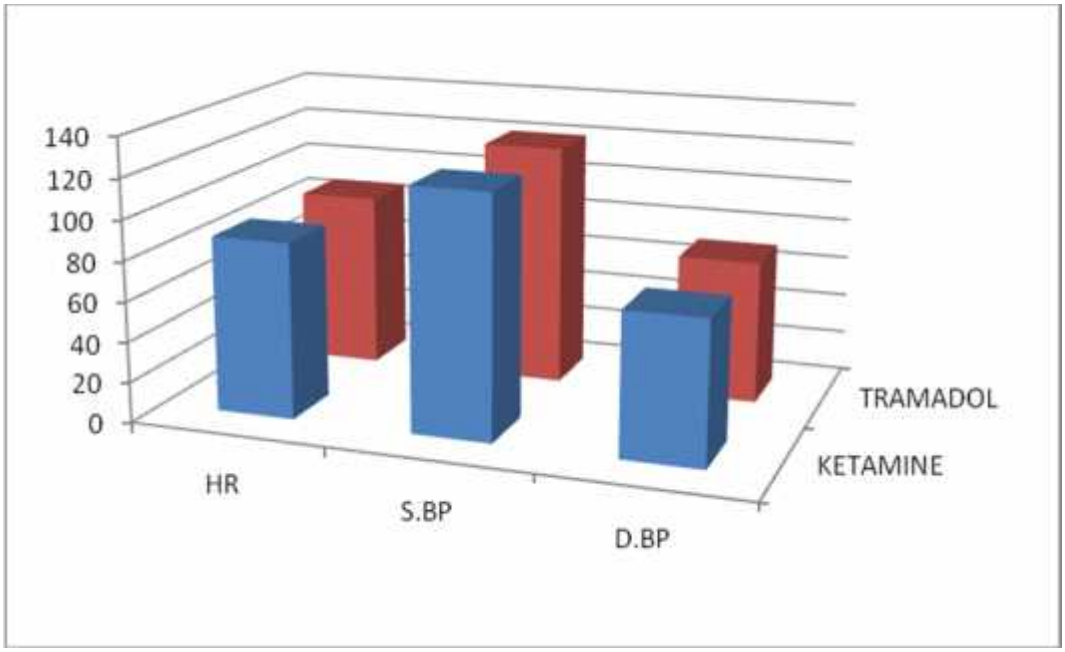
Table 11

TIME	Group K (Median ± S.D.)	Group T (Median ± S.D.)	P - value
1 MIN	7 ± 0.56	7 ±0.61	0.0404
5 MIN	8 ± 0.56	8 ± 1.51	0.7690

Apgar scores in group K at 1 and 5 minutes were 7 and 8 respectively.
Whereas apgar score in group T at 1 and 5 minutes were also 7 and 8 respectively.

GRAPHS

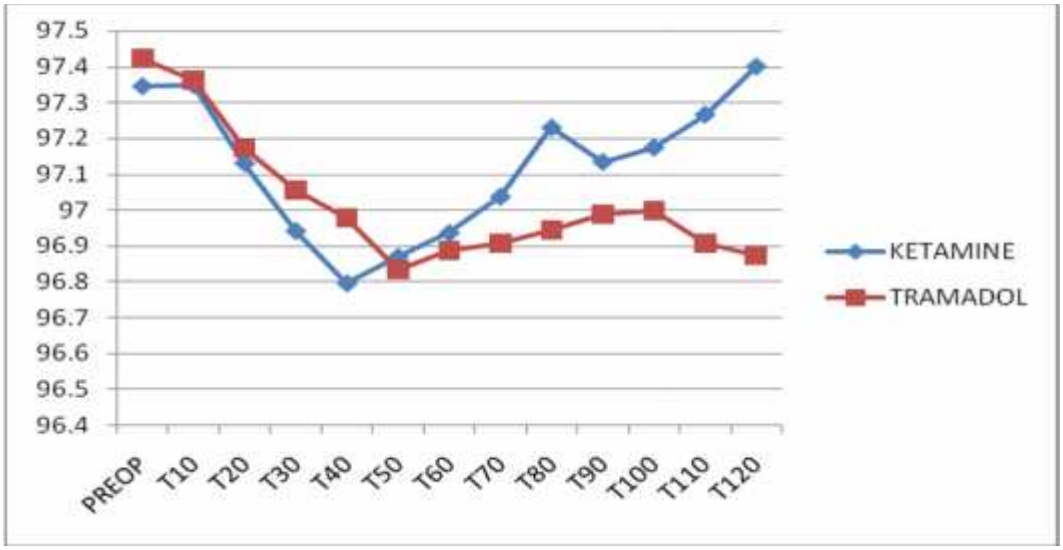
Graph 1 showing baseline hemodynamic parameters .
Graph 1



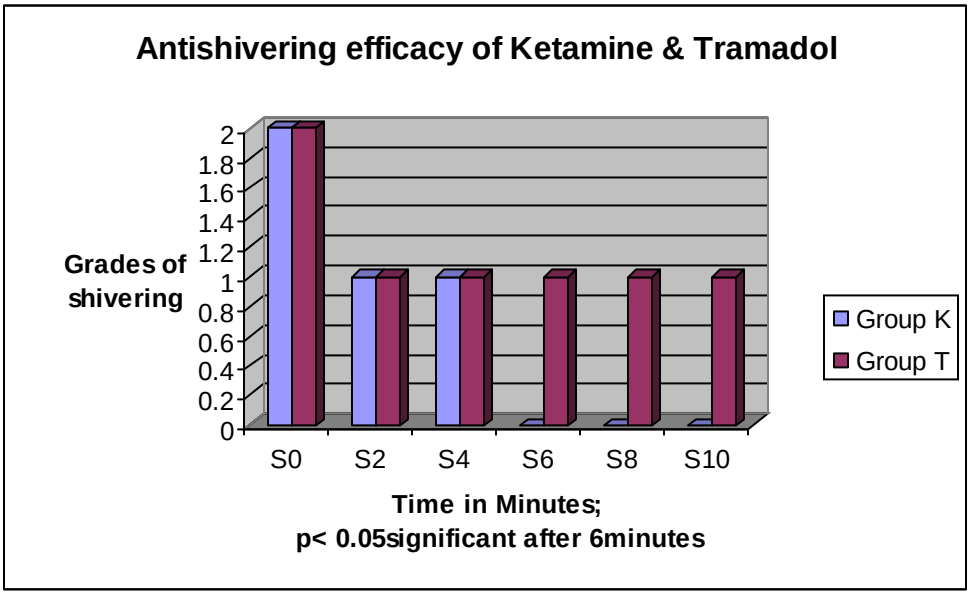
S. BP- Systolic BP D. BP- Diatolic BP HR – Heart Rate.

Graph 2

Comparison of Tympanic Membrane temperature at various intervals in both the groups including baseline temperatures.

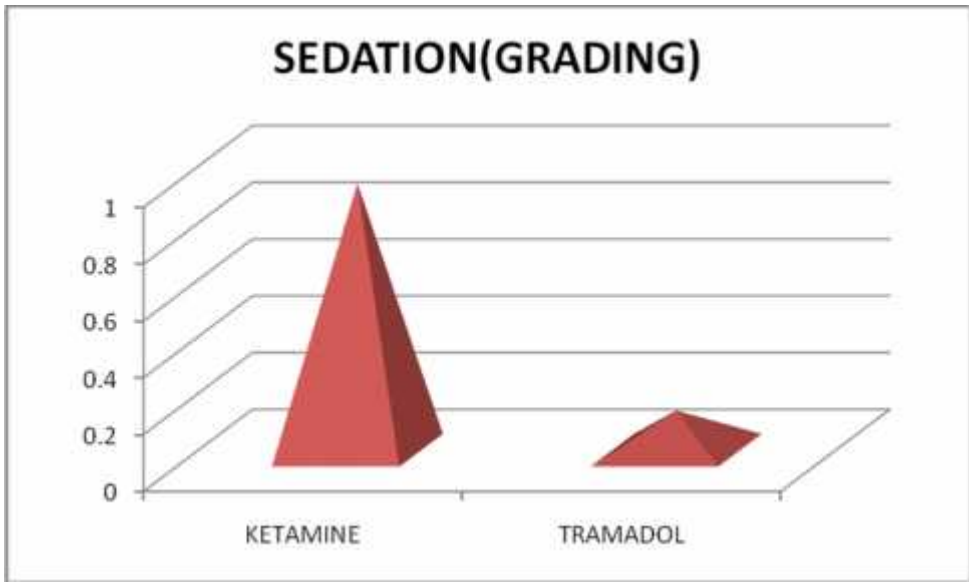


Graph 3 : Action of drugs



Graph 4

Sedation



DISCUSSION

The mechanism of shivering under regional anesthesia is not fully understood and is still a topic of interest amongst researchers. Possible contributing factors are a decrease in core temperature and misinformation from receptors. A decrease in core temperature may be due to peripheral vasodilatation as a result of sympathetic blockade, increased cutaneous blood flow, and subsequent increased heat lost via skin. Cold operating room conditions and cold anesthetic fluid administered lead to a further drop in body temperature. Combination of all these factors make unwarmed surgical patients hypothermic [2,3.]

In our study we decided to standardize some of these possible factors by maintaining operating room temperatures at 24 degree Celsius , administering intravenous fluids and drugs at room temperatures and by covering the patients with sterile thick cotton bed sheet. All these measures were also adopted in other studies mentioned in the literature. [2,3,4.]

Research indicates that during perioperative period when core temperatures changes rapidly at different sites, the relationship between the temperatures measured at various body sites may differ. A recent survey found infrared tympanic membrane monitoring to be the preferred route of temperature monitoring. For these reasons we decided to monitor tympanic membrane temperature intraoperatively.[3]

In the present study we made a record of the tympanic membrane (core) temperature before start of the surgery and at every 10 minutes interval for duration of the surgery.

In our study we found that both Ketamine (0.5 mg/kg) and Tramadol (0.5 mg/kg) were effective in reducing intraoperative shivering under spinal anesthesia for patients undergoing caesarean section.

Ketamine (0.5 mg/kg) was found to be more effective in preventing shivering than Tramadol (0.5 mg/kg).

The number of patients who stopped shivering (completely improved) within 10 minutes of receiving Ketamine were 28 out of 35 (80 %). In the Tramadol group only 19 out of 35 (54.2%) improved completely within 10 minutes.

Median grades of shivering at intervals of 2 minutes after injecting the drug was significantly lower in Ketamine group in which grade of shivering dropped from grade 2 to 0 by 6 minutes while in Tramadol group it dropped to 1 by 6 minutes. The antishivering effect in both the groups commenced by 2 minutes of administration however, by 4 minutes Ketamine had exerted its clinical peak effect in 14 parturients whereas in group Tramadol the similar effect was observed by 10 minutes in 19 patients.

Results of the data observed from our study showed a close association between the efficacy of both drugs in terms of fall in degree of shivering which appeared almost similar upto the sixth minute (T6) of the drug administration. However, after six minutes (T6) the drugs showed a variable response. A considerable difference was observed (p value 0.0365), Ketamine being more efficient.

Efficacy of Ketamine in preventing postoperative shivering was studied by Dal and his colleagues in 90 patients with a double blind study using Normal Saline , 0.5 mg/kg Ketamine and 20 mg Pethidine prophylactically in preventing post operative shivering in patients who under went general anaesthesia. Results clearly showed that prophylactic 0.5 mg/kg Ketamine and 20 mg Pethidine were more effective in controlling postoperative shivering than the placebo. There was no statistical diference between Ketamine and Pethidine in preventing post operative shivering. They described that the NMDA receptor antagonist is likely to modulate shivering at a number of levels and also that it modulates noradrenergic and serotonergic neurons in locus coeroleus. They described antishivering effect of Ketamine by non shivering thermogenesis either by action on hypothalamus or by beta adrenergic effect of norepinephrine.

Several pharmacological properties of Ketamine viz kappa opoiod agonism , blocking of amine uptake in descending inhibitory monoaminergic pain pathway , having local anaesthetic action and interaction with muscarnic receptors could be contributory according to them. [8]

A comparative study by O Sagir et al[16] in controlling shivering in patients undergoing urological surgeries under sub arachnoid block was conducted using Ketamine (0.5 mg/kg), Ketamine (0.25 mg/kg) plus Granisetron (1.5 mg) , Granisetron (3 mg)and Saline as placebo in a prospective double blind randomized study in 160 ASA I and II patients.

Number of patients who had shivering with Ketamine alone were 0, whereas with Ketamine plus Granisetron were 7. With Granisetron alone 6 patients had shivering while with Placebo 22 had shivering. This result was statistically significant between Ketamine and all other groups (p value < 0.0001) Thus, they concluded that 0.5 mg/ kg Ketamine was more effective in preventing shivering during regional anesthesia. [16]

Unlike their study, in our study shivering was controlled only in 80 % of the patients by 0.5 mg/kg Ketamine intraoperatively .We did not use Ketamine prophylactically as we wanted to study the response time of antishivering action of Ketamine and Tramadol.

Honamand A and Safavi et al[17] made a comparative study of prophylactic study of midazolam (75 mcg/kg), Ketamine (0.5 mg/kg) and Ketamine (0.25 mg/kg) plus Midazolam (37.5 mcg/kg) and Saline as placebo. Their results showed combination of Ketamine and Midazolam more effective than Ketamine or Midazolam alone in preventing shivering during regional anesthesia. Ketamine alone showed 76.7 % reduction in the incidence of shivering.[17]

Our study also showed 80 % control of shivering intraoperatively although we did not use Ketamine prophylactically.

A study conducted by Talakoub et al[14] was done to compare the efficacy of Tramadol with Pethidine on post- spinal shivering in caesarean section. 73 ASA I patients were

included in the study. Patients were administered 0.5 mg/ kg IV Tramadol and 0.5 mk/kg IV Pethidine when shivering occurred. Shivering was graded and evaluated for 15 minutes. Time elapsed from treatment to cessation of shivering was 2.5 ± 1.07 min in Tramadol group whereas in our study the response time from administration of Tramadol to cessation of shivering was 6 minutes although the antishivering action started in 2 minutes. [14]

Our incidence of reduction of shivering for Tramadol group was much lower compared to there study viz 54.2 %.

Anne et al[15] used 0.25 mg/kg , 0.5 mg/kg of Tramadol along with Normal Saline for post spinal shivering during regional (subarachnoid / epidural) undergoing caesearean section similar to our study. They concluded that antishivering effect of Tramadol was better with 0.25 mg/kg (92 % of patients) than 0.5 mg /kg (83 % of patients). We used 0.5 mg /kg of Tramadol in our pilot study which showed 60 % reduction.[15]
According to them it is highly likely that antishivering effect was mediated by serotonergic or noradrenergic neuronal activity .

Ali Seife[11] et al did a comparative study of Tramadol and Pethidine for post operative shivering and concluded that Tramadol and Pethdine are equally effective for controlling postoperative shivering, Tramadol being more superior as there is minimal sedation and less hemodynamic disturbances. They have made a remark in their discussion that in literature some papers believe that Pethidine is the most efficacious antishivering medication while others say that Tramadol is superior to Pethidine , though De Witte[1] published that they have similar post operative anti shivering properties. As such we have used 0.5 mg/kg Pethidine as a rescue drug.[11.]

Another study by Yu-Chan Tsai et al[13] was done to compare Tramadol, Amitritpline, and Meperidine in post epidural anaesthetic shivering in parturients .Patients were divided in to three groups and were administered 0.5 mg/kg Tramadol, 0.5 mg/kg

Pehidine and 20 mg Amitriptline. Response seen to Pethidine was 93 % and 87 % to Tramadol whereas only 13 % in Amitriptline group. Time elapsed from administration of the drug to cessation of shivering was 5 minutes in Tramadol group whereas 4 minutes in Pethidine group.[13]

Casey et al[12] studied iv Mepeirdine or saline in a randomized double blind study in patients undergoing caesarean section under epidural anesthesia and found anti shivering effect within 2 minutes of drug injection that persisted through out the study period and they observed significant decrease of incidence and severity of shivering from 87 to 35 % and 3.5 to 0 % respectively but their patients were drowsy at 2 and 5 minutes .

Anti shivering action of Meperidine may be partially mediated by kappa opioid receptor other than mu receptor .Other possible mechanisms have been explained by action on preoptic – anterior hypothalmic neurons, dorsal raphe nucleus neurons, locus coeruleus and spinal cord[2].

SIDE EFFECTS

In our study it was observed that 68.5 % patients in Ketamine group developed sedation out of which 20 % developed grade 2 sedation. However 48.5 % developed grade 1 (Mild sedation- easily arousable) whereas no sedation was observed in 11 patients (31.5 %). Ketamine is a drug known to cause sedation without any respiratory depression.

4 out of 35 (11 %) developed grade 1 (Mild sedation) in Tramadol group. Also in other studies tramadol was found to be a weak sedative.[5]

Hallucination is a well known side effect of Ketamine. In our study 2 out 35 patients experienced hallucination intraoperatively. They were treated by iv 0.05 mg/kg.

Midazolam. Such hallucinations was not observed in other studies as mentioned by Dal et al[9]. However, Ketamine is reported to produce hallucination in other studies[22].

Vomiting is a known side effect of Tramadol. In our study, 8 patients out of 35 vomiting before the end of the operation. They were treated with Inj. 8 mg IV Ondansetron.

Talakoub et al[9] have reported vomiting in 19.4 % of patients and Yu – Chuan et al[13] have reported 3 out of 15 patients.

Apgar scores of the newborn children were found to be similar at both 1 minutes and 5 minutes in both Ketamine and Tramadol groups being 7 at 1 mnutes and 8 at 5 minutes and both the drugs Ketamine 0.5 mg/kg and Tramadol 0.5 mg/kg appear safe to be used in patients undergoing caesarean section.

We have not done a double blind study which can be a limitation of our study.

Intraoperative shivering during regional anesthesia especially in parturients undergoing caesarean section needs to be treated actively as shivering is not only trouble some but also increases the oxygen demand which can adversely effect both maternal and fetal outcome. Ketamine and Tramadol both being easily available in perioperative set up, are found to be useful drugs for their antishivering effect.

By virtue of application of this knowledge, combating shivering with drugs only may not be the most successful approach. We should rather nip the "Evil in the bud" and prevent hypothermia which would reduce the incidence of shivering, which was done in our study by covering the patient and maintaining the operation theatre temperature. Use of warming devices like hot air blowers can give additional benefits which were not used in our study.

CONCLUSION

In conclusion, Ketamine 0.5 mg / kg IV and Tramadol 0.5 mg / kg IV are useful drugs in controlling shivering in patients undergoing caesarean section under spinal anesthesia.

Ketamine was found to be more effective antishivering drug and can be recommended to control shivering under regional anesthesia in patients undergoing caesarean section, keeping in mind the hallucination and sedation as side effects.

SUMMARY

The present study was carried out in the Department of Anaesthesiology , KLES Prabhakar Kore Hospital and MRC, Belgaum after obtaining an approval from institutional ethics committee and written and informed consent .

The study included 70 ASA grade I and II patients posted for caesarean section under spinal anesthesia . A thorough pre anesthetic evaluation was done and the basal core temperature (Tympanic Membrane) was recorded. Patients were randomly allocated by computer generated method into two groups – Group Ketamine and Group Tramadol. Sub arachniod block was administered with 1.8 ml of 0.5 % heavy Bupivacaine. Those patients who subsequently developed intraoperative shivering were given either 0.5 mg/kg Ketamine or 0.5 mg/kg Tramadol at the onset of shivering.
The core body temperature was recorded at 10 minute interval from the start till the end of the procedure.

We observed that there was a fall in the temperature in both the groups and the least temperatures were recorded at 60 minutes in Ketamine group (96.93 degree Fahrenheit) whereas the least temperature in Tramadol group was noted at 50 minutes (96.83 degree Fahrenheit) , but the difference was insignificant.

Shivering was graded at 2 minutes interval and the response of the administered drugs were noted . Median of grades of shivering at intervals of 2 minutes after injecting the drug was significantly lower in Ketamine group in which grade of shivering dropped from grade 2 to 0 by 6 minutes while in Tramadol group it dropped to 1 by 10 minutes.
Results of the data observed from our study showed a close association between the efficacy of both drugs upto the sixth minute (T6) of the drug administration. However , after six minutes (T6) the drugs showed a considerable difference ($p < 0.0365$).
The number of patients who stopped shivering (completely improved) within 10 minutes of receiving Ketamine were 28 out of 35 (80 %) and 7 out of 35 partially improved (20%). In the Tramadol group only 19 out of 35 (54.2%) improved

completely within 10 minutes whereas 16 out of 35 (45.8 %) showed partial improvement.

Vomiting is a known side effect of Tramadol . It was observed in 8 patients out of 35 who were given Tramadol.

Hallucination is a well known side effect of Ketamine . In our study 2 out of 35 patients experienced hallucination intraoperatively .

Apgar scores of the newborn children were found to be similar at both 1 minutes and 5 minutes in both Ketamine and Tramadol groups.

So based on the results obtained , we conclude that Ketamine is more effective in controlling intraoperative shivering in patients under spinal anaesthesia.

BIBLIOGRAPHY

1. De Witte J, Daniel Sessler. Perioperative shivering. Anesthesiology 2002; 96: 467-84.

2. Larry J. Crowley, Donal J. Buggy. Shivering and neuraxil anesthesia. Regional Anesthesia and Pain Medicine Volume 33 No 3 May – June 2008:241-252.

3. Bhattacharya P, Bhattacharya L, Jain R, Aggarwal R. Post Anaesthesia shivering (PAS): A Review. Indian J. Anaesth.2003; 47(2): 88 – 93.

4. Miller RD Temperature monitoring: in Miller's Anaesthesia 6th Ed. Edited by Daniel I. Sessler. Philadelphia; Elsevier Churchill Livingstone; 2005.

5. DeWitte JL, Kim J, Sessler DI. Tramadol reduces shivering. vasoconstriction and sweating threshold . Anesth Analg 1998;87: 173-9

6. Eberhart Et al. Independent Risk Factors for Postoperative Shivering. Anesthesia Analgesia 2005 ; 101 :1849 – 57.

7. Engelman RD, Lockhart HC. Comparisons between temperature effects of Ketamine and Halothane anaesthesia in children. Anesth Analg 1972; 51(1):98 -101.

8. Powell R, Buggy D. J. Ondansetron Given Before Induction of Anesthesia Reduces Shivering After General Aneasthesia. Anesthesia Analgesia 2000;90: 1423-7.

9. D. Dal, A.Kose, M. Honca, S.B.Akinci, E.Basgul, U.Aypar. Efficacy of prophylactic Ketamine in preventing postoperative Shivering. BJA 95(2): 189-92(2005).

10. Ikeda T, Kazama T, Sessler DI, Toriyama S, Niwa K, Shimada C, et al . Induction of anaesthesia, with Ketamine reduces the magnitude of redistribution hypothermia . Anesth Analg 2001; 93: 934-8.

11. Ali Seifi et al. A Comparative study of the effect of Tramadol and Pethdine on Post operative shivering. The Internet journal of Anesthesiology.2008; 16:2.

12. WF Casey et al. Intravenous Meperidine for control of shivering during caesarean section under epidural anaesthesia. Can J A 1998, Volume 35,128-133.

13. Yu-Chuan Tsai, Koung- Shing Chu. A comparison of Tramadol, Amitryptline, and Meperidine for Post Epidural Anesthetic Shivering in Parturients. Anesthesiology Analgesia 2001; 93:1288-92.

14. R. Talakoub, Sh. Noori Meshkati. Tramadol versus Meperidine in the treatment of shivering during spinal anesthesia in cesarean section. JRMS 2006; 11(3): 151-155.

15. Anne Miu Han Chan, Kwok Fu Jacobus, Edwin Wai, Gordon Siu. Control of shivering under Regional anesthesia in obstetric patients with Tramadol. Can J ANESTH 1999 / 46: 3 /pp 253-258

16. O. Sagir, Gulhas, H.Toprak, A.Yucel, Z.Beggac, Ersoy. Control of shivering during regional anesthesia: prophylactic Ketamine and Granisteron. BritishJ Anaesthesia 2008.June2008.

17. Honarmand A, Safavi MR. Comparison of prophylactic use of midazolam, ketamine, and ketamine plus midazolam for prevention of shivering during regional anaesthesia: a randomized double-blind placebo controlled trial. BritishJAnaesth.2008 Jul11.

18. Steven R. Insler, Daniel I. Sessler. Perioperative Thermoregulation and Temperature Monitoring. Anesthesiology Clinics 24(2006) 823-837.

19. Steven M. Frank , Judy m. Nguyen et al . Temperature Monitoring Practices During Regional Anesthesia. Anesthesia Analgesia 1999;88: 373-7.

20. Cem F Arkilic, Ozan Akca et al. Temperature Monitoring and Management During Neuraxial Anesthesia: An Observational Study. Anesthesia Analgesia 2009;91: 662-6.

21. Nader El-Gamal, Nabil et al .Age- Related Thermoregulatory Differences in a Warm Operating Room Environment. Anesth Analg 2000;90:694-8.

22. Stoelting KR .Pharmacology and physiology in anesthesia practice. 3rd Ed. Philadelphia: Lipincott Raven ; 1999.

23. Sharma Dr et al, Ketamine and shivering. Anaesthesia 1990; 45: 252-3.

24. Dorsch AJ Dorsch ES. Understanding anaesthesia equipment. 5 Ed. Pennsylvania . Williams and Wilkins 1994.

25. Guyton AC, Hall JE. Text book of medical physiology 9th Ed. Philidelphia : WB Saunders ; 1996..

26. Bhatnagar S, Saxena A, Kannan TR, Punj J . Tramadol for post operative shivering. A double blind comparison with Pethidine. Anesth Intensive care 2001;29: 149-54.

27. Iwashita H, Matsukawa T, Sessler DI. Hypoxemia decreases the shivering threshold in anesthesised patients with isoflurane . Anesth Analg 1998; 87:1408-11.

28. Burke HH, Aisner J, Fortner CL, Wiernik PH. Mepiridine for the treatment of shaking chills and fever. Anesthesiology 1980; 140:483-88.

29. Alfonsi P, Sessler DI, Dumanoir B. The effects of Meperidine and Sufentanil on the shivering threshold in postoperative patients. Anesthesiology 1998; 89: 43-48.

30. Jhi JW, Shung T, Shih Cl. A comparison among nalubphine , meperidine and placebo for treating post anesthethic shivering, Anesth Analg 1999;88:686-689.

31. DeWitte J, Deloof T, Housmans PR. Tramadol in the treatment of post anesthesia shivering . Acta Anaesthesiol scand 1997; 41: 506-10.

32. Vassilieff N, Rosnercher N, Sessler DI. The shivering threshold during spinal anesthesia is reduced in elderly. Anesthesiology 1995; 83:1162-66.
33. Powell RM, Buggy DI. Ondansetron given before induction of anesthesia reduces shivering after general anesthesia. Anesth Analg 2000; 90:1423-7.
34. Joris J , Banache M, Bonnet F, Sessler DI. Clonidine and Ketanserin both are effective treatment for postanesthetic shivering. Anesthesiology 1993; 70: 532-9.
35. Horn EP, Standl T, Sessler DI. Buschs C , Schulte J. Physostigmine prevents postanesthetic shivering as does meperidine or clonidine .Anesthesiology 1998;88:108-13.

KETAMINE															
S.NO	IP. NO	AGE(Yrs)	HEIGHT(Cn	WEIGHT(Kg	BASE LINE VALUES			TEMPERATURE (DEGREE FARENHEI							
					HR	S.BP	D.BP	PREOP	T10	T20	T30	T40	T50	T60	T70
1	304458	26	155	52	87	130	80	98.2	98.2	98	97.9	97	97.4	98.1	98
2	303716	24	164	62	90	126	86	97.4	97.3	97	96.8	97.2	96.9	96.8	97.2
3	304157	26	155	64	98	129	70	98.4	98.4	98.1	98	98.3	98	97.6	98.2
4	307754	21	152	50	96	120	64	97.4	97	97.2	97.3	96.9	97.6	97.7	97.4
5	305797	22	158	55	94	124	66	97	96.6	96.4	97	97	97.2	97	97.3
6	306224	25	164	51	97	128	70	98	98	97	97.4	97.6	97.2	97.4	97.8
7	306803	23	164	80	94	126	78	97	96.4	96.2	96.6	97	97.2	97.3	97.2
8	307365	24	162	50	98	122	76	97	97	96.2	96.1	97	97.2	97.4	97
9	307765	24	154	52	97	120	70	97.4	97.4	97	97.2	97.4	96.8	96.6	97.4
10	304428	28	152	56	80	126	80	97	97	97	96.6	96.6	96.6	96.8	97
11	301516	25	166	76	90	122	76	97.2	97	97.2	96.8	96.6	97.4	97.2	97.4
12	305565	23	160	50	84	124	80	97	97.6	97.8	96.8	96.6	96	97	97
13	305210	23	158	50	80	110	70	97	96.6	96.8	96	96.8	96.6	96.8	97
14	302216	29	160	55	76	120	60	97.2	97	96.8	96.6	96	96.2	96.6	96.6
15	296743	25	150	76	80	110	60	97	97	97.2	97	96.6	96.6	96.4	96.4
16	300090	23	155	55	86	118	74	98.1	97.8	96	96.8	96.8	97.2	97.1	97
17	300453	25	150	51	80	126	78	97	97	97	96.8	96.4	96	96	96.2
18	320121	22	166	56	70	110	60	97.4	97	96.6	96.4	96	97	97	97.2
19	306451	29	155	56	78	120	76	97.6	97.6	97.4	97.5	97.4	97.6	97.4	97.8
20	306255	23	166	82	80	110	78	97.6	97.4	96.8	96.6	97	97.6	97.8	97.8
21	321450	26	154	61	78	130	64	97	97	97.2	96.6	96	96	96.4	96.5
22	209458	22	156	55	70	126	70	97.4	97.2	97	96.6	96.2	96	97.2	97
23	323659	28	156	60	90	110	60	98	97.6	98	96.4	96.1	97.2	97.8	97.9
24	323660	27	160	76	87	126	74	97.2	97.2	97.4	97.2	97	97.6	96.2	95.8
25	294510	28	159	70	110	110	60	97.2	97.2	96.4	96.4	96	96.1	96.1	96
26	306111	24	151	53	78	106	64	97.8	97.6	97.5	97.3	97.2	96.6	96.5	96.2
27	306419	25	155	60	90	116	64	97.4	97.4	97.4	97.2	96	95.6	95	95.6
28	304221	26	160	60	80	112	80	96.6	96.4	96.2	96	95.8	95.6	96.4	96.4
29	204458	20	151	56	90	124	80	97.4	97.2	97.4	97	96.2	95.8	95.6	
30	209458	23	148	60	88	112	78	96.4	96.2	96	95.6	95.6	96.2	96.6	96.4
31	302115	28	150	66	72	110	65	97.2	97.6	97.2	97	96.4	96.2	96.4	96.5
32	306665	28	152	70	82	120	60	97	98	97.9	97.8	97.5	97.6	96.7	96.7
33	307745	25	151	62	110	130	70	97.2	97.9	97.6	97.3	97.4	97.5	97.6	97.3
34	294558	24	160	65	114	134	80	97.2	99	98.7	98.3	98.1	98	98.1	98
35	203458	22	166	86	98	121	62	98.2	98.4	98	98.1	98.2	98.2	98.2	98.1

T)					SHIVERING							APGAR SCORE		SEDATION
T80	T90	T100	T110	T120	ONSET(mir	S0	S2	S4	S6	S8	S10	1 MIN	5 MIN	
97.9	98	98	98.2		40	2	1	1	0	0	0	7	9	1
97	97.2	97.3	97.1	97.3	10	3	2	1	0	0	0	8	8	1
98.2	97.8	98.2			20	2	1	1	1	1	1	8	8	2
97.8	97.6	97.2			15	3	2	1	0	0	0	8	8	1
97.4	97.4	97			10	2	1	0	0	0	0	7	7	1
97.8	97.6				20	2	2	1	0	0	0	7	7	0
97.4	97.2	97.4			10	2	2	1	0	0	0	8	8	2
97.2	97.2				15	2	2	1	0	0	0	8	9	1
97	97.4	97.2	97.2	97.4	20	3	2	2	1	0	0	8	8	0
97	97.2	97			20	2	1	1	0	0	0	8	8	1
97.3	97.1	97			40	2	1	1	1	0	0	7	8	1
97.3	97.3	97.2			60	2	1	1	1	1	0	8	8	1
97.2	97.2				30	3	2	1	0	0	0	8	8	1
96.6					30	2	1	1	1	1	1	9	9	0
96.6					20	2	1	1	1	1	0	8	8	2
97.2					20	3	2	1	1	0	0	8	8	1
97					20	2	1	0	0	0	0	8	8	0
97.2					30	2	1	1	0	0	0	8	9	1
97.6					25	2	1	1	1	1	0	7	9	2
97.8	97.6				30	2	1	1	0	0	0	7	9	0
97	96.6				35	2	1	1	1	1	1	7	9	1
97.3	96.9	96.2			45	2	1	1	1	1	1	7	9	1
98	97.6	97.8	98.1	97.5	35	2	1	1	0	0	0	8	9	1
96	96.6	97			60	2	1	1	0	0	0	7	9	1
97.2					60	2	2	1	0	0	0	7	9	2
96.4	95.6	96.6	97		45	2	1	1	1	1	1	7	9	1
					40	2	1	1	1	1	1	7	8	1
96.8					64	2	1	1	1	0	0	7	9	2
					50	2	1	0	0	0	0	7	9	0
96.3	96.5				60	2	2	2	1	1	1	7	9	2
96.7	96.5				40	2	1	1	1	1	0	7	9	1
96.8	97	97.2			30	1	1	0	0	0	0	7	8	0
97.3	97	96.5	96		60	1	0	0	0	0	0	7	8	0
98.2					80	2	2	2	2	2	1	7	8	0
98.1					20	1	1	1	0	0	0	8	9	1

TRAMADOL															
S.NO	IP. NO	AGE(Yrs)	HEIGHT(Cm	WEIGHT(Kg	BASE LINE VALUES			TEMPERATURE (DEGREE FARENHEI							
					HR	S.BP	D.BP	PREOP	T10	T20	T30	T40	T50	T60	T70
1	303535	26	155	52	87	130	80	97.6	97.6	97.4	97.2	97	96.8	97	97.2
2	304102	22	164	62	90	126	86	98	98	97.2	96.8	96.8	96.9	96.8	97.2
3	345354	24	155	64	98	129	70	98	98	97.6	97.4	97	97.6	97.6	97.2
4	305755	24	152	50	96	120	64	97.6	97.6	97.2	97.3	96.9	97	97.4	97.4
5	304445	26	158	55	94	124	66	98	97.9	97.7	97	97	97.2	97	97.3
6	312191	25	164	51	97	128	70	97.4	97.4	97	97.4	97.6	97.2	97.4	97.4
7	312197	23	164	80	94	126	78	97	96.4	96.2	96.6	97	97.2	97.3	97.2
8	304781	26	156	50	98	122	76	97.4	97.4	97.4	97	97	96.8	97	97
9	313347	24	154	52	97	120	70	97	97	97	97.2	97.4	96.8	96.6	97.4
10	313521	20	152	56	80	126	80	97	97	97	96.6	96.8	96.6	96.8	96.7
11	317116	25	160	76	90	122	76	97	97	96.8	96.6	96.6	96.6	96.8	97
12	315772	24	160	50	84	124	80	97.2	97.2	97	96.6	96.4	96.2	96.2	96.2
13	313217	25	158	50	80	110	70	97.4	97.4	97	97	96.8	96.4	96.4	96.4
14	309343	22	160	55	76	120	60	98.2	98	97.8	97.7	97.4	97	96.4	96.4
15	3133117	28	155	56	80	130	60	98	98	97.8	97.8	97.6	97	96.6	96.4
16	201594	23	155	55	86	118	74	97	97	97	96.6	96.8	96.4	96.8	97.2
17	320733	26	150	51	80	110	78	99.1	99.1	98.4	98.6	98.4	98.2	98.2	97.6
18	320902	23	166	56	70	110	60	97.7	97.5	97.4	97	97.2	97.1	96.8	97
19	294516	28	156	60	78	130	76	97	96.8	97	97.2	97	96.8	96.8	96.4
20	323309	28	166	82	80	124	82	97.2	97.2	97	96.8	97	97	97.2	97
21	312209	26	154	56	78	130	64	97.2	97.2	97	97.6	97.2	96.6	96.6	96.4
22	324060	26	156	55	70	126	70	97.4	97	97.2	97.1	97.2	97	97.1	97.2
23	323604	33	156	60	90	110	60	97	97.2	97	96.9	96.6	96.6	96.5	96.6
24	216654	27	160	76	87	126	74	97.2	97.4	97.6	97.1	97.1	97	97	96.6
25	323668	26	156	70	110	110	60	97	97.2	96.8	96.6	96.4	96.6	97	96.6
26	323668	24	151	53	78	106	64	97	97	97.2	97.4	97.2	97	97.2	96.8
27	345651	25	155	60	90	116	64	97.4	97.4	97.4	97.2	97.4	97	96.6	96.6
28	325115	26	160	60	80	112	80	96.6	96.6	96	96	96.2	96.2	96.2	96.2
29	334545	27	151	70	90	124	80	98	97.6	97	96.6	96.6	96.6	96.6	96.7
30	294596	24	148	60	88	112	78	97	97	97	96.6	96.6	96.4	96.2	96.7
31	219876	28	150	66	72	110	65	97	97	97.2	97	96.6	96.6	97	97
32	328631	26	152	70	82	120	60	98.2	98	97.6	97.5	97.6	97.4	97.4	97.4
33	216888	25	151	62	110	130	70	97	97	97	96.6	96.5	96.6	96.6	97
34	294444	27	160	65	114	134	80	97	96.6	96.8	97	96.6	96.4	97	97.2
35	296589	22	166	86	98	121	62	98	98	97.4	97.4	96.8	96.4	97	97.2

T)					SHIVERING							APGAR SCORE		SEDATION(
T80	T90	T100	T110	T120	ONSET	S0	S2	S4	S6	S8	S10	1 MIN	5 MIN	
97.2	97.2	97.3	97.3		40	3	2	2	2	2	0	7	9	0
97	97.2	97.3	97.1	97.3	10	3	2	1	1	0	0	7	8	0
98	97.4	97.2			30	2	1	1	1	1	1	7	8	0
97.8	97.6	97.6			30	3	2	2	1	0	0	7	8	0
97.4	97.4	97			30	2	2	2	1	0	0	6	8	0
97.4	97.3	97.4			15	2	2	1	1	0	0	6	8	0
97.2	97.2	97			25	2	2	2	1	1	1	6	9	0
97.2	97.2				30	2	2	2	2	2	2	6	9	0
97	97.4	97.2	97.2	97.4	20	3	2	2	1	1	1	8	8	1
96.5	97.4	97.5			30	2	2	1	1	1	0	7	8	1
97	97				25	2	1	1	1	0	0	8	8	0
96.3	96.2	96.6			30	1	1	1	1	1	1	8	8	0
96.2	96.4				20	2	2	2	2	2	2	7	8	0
96.4	96.4	96.3	96.8		20	2	1	1	1	1	1	7	8	0
96.4	96.4				20	2	2	1	1	1	0	7	8	0
97	97	97.2	97.1		20	2	1	1	1	1	1	7	9	0
97.6	97.4				20	2	1	0	0	0	0	7	9	0
97.2	97	96.8	96.7		70	2	1	0	0	0	0	7	8	0
96.8	97	97			30	1	1	1	1	1	1	7	9	0
97.2	96.8	96.8			25	1	1	1	0	0	0	7	0	0
96.2	96.6	96.7			25	2	1	1	1	1	1	8	9	0
97.1	97.2				30	2	2	1	0	0	0	7	9	0
97	97	97.2	97.4		60	1	1	1	1	1	1	6	8	0
96.4	96.6	96.8	96.6	96.2	60	2	1	1	1	1	2	8	8	0
96.4	97.2	97	97		45	2	1	1	0	0	0	7	9	0
97	97	96.4	96.8		30	2	2	2	1	1	0	8	9	0
96.8	97	97			15	2	1	1	0	0	0	7	8	0
96.4	96.6	96.6	96.6	96.6	60	2	1	1	1	1	1	7	9	0
96.7	96.6	96.6	96.6		60	2	1	1	1	1	1	7	9	0
97	97	97.2			50	2	1	1	0	0	0	8	9	0
97	97	97	96.6		30	2	1	0	0	0	0	7	8	1
97.3	97.3	97.3			34	2	1	1	1	1	1	7	8	1
97	97	97.2			30	2	1	1	1	1	1	8	9	0
97					60	1	1	1	1	1	1	8	8	0
97	96.6	96.8			45	2	2	1	1	1	1	7	9	0

INFORMED CONSENT FORM

A study, **"A COMPARATIVE STUDY OF THE EFFECT OF IV KETAMINE WITH IV TRAMADOL ON INTRAOPERATIVE SHIVERING IN PATIENTS UNDERGOING CAESEAREAN SECTION UNDER SPINAL ANAESTHESIA: RANDOMIZED CLINICAL TRIAL".** is being conducted by Dr. Ankush Kaushal, post graduate in anaesthesiology at J. N. Medical College Belgaum, Karnataka. Under guidance of **Dr. Lata Kulkarni** Prof. Dept. of Anaesthesiology, J. N. Medical College, Belgaum, under K.L.E.'s academy of Higher Education, Belgaum.

Respected _____ we request you to participate in our study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you are suppose to answer to the best of your knowledge.

Your participation in this study is voluntary. Your decision whether or, not , to participate in the study will not affect your relationship with J.N.M.C. If you decide to participate you are free to withdraw at any point of time. The purpose of the study is to compare the effectiveness of ketamine with tramadol in controlling intraoperative shivering in patients undergoing spinal anaesthesia.

Objective of the study :

Objective of my study is to compare the effectiveness of iv Ketamine with iv Tramadol in reducing shivering in patients undergoing spinal anaesthesia.

Procedure involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history then you will be clinically examined in detail

and investigated accordingly. You will receive one of the two study drugs (Inj. Tramadol , Inj. Ketamine) if there occurs shivering in spinal anesthesia .

Benefits and Risks:

Shivering during operation is very uncomfortable and distressing for the patient . Drug Tramadol used in our study is very effective in controlling shivering and is not known to produce any side effects.

Low dose Ketamine will also be used to control shivering as part of study . This drug used in very low dosage will not produce side effects.

Voluntary participation / Withdrawal

Taking part in the study is voluntary. You may choose not to enroll yourself in this study . Your decision will not change present or future health care services offered to you at K.L.E.S. Hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Confidentiality:

All information collected about me during the course of the study will be kept confidential to the extent permitted by law. The code numbers will identify you in this study records and the information from this study may be published but your identity will be confidential in any publication.

Financial Incentives for participation :

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

In the event of injury, related to the study, treatment will be made available at KLES Hospital & MRC, Belgaum. No reimbursement, compensation or free medical care will be given, by law. If you are injured, you may contact Dr. Ankush Kaushal at Department of Anaesthesiology, KLE's Hospital & MRC or by Ph. No. 9844415920.

Queries/ Contact details :

If you have any queries, in future or in case of study related injury or illness, you may contact. Dr. Ankush Kaushal at Department of Anaesthesiology, KLES Hospital & MRC, Ph No. 0831-2473777 or on phone 9844415920.

If you have any queries about your rights as a study subject, you may call Dr. V.D. Patil. Principal and Chairman. J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Ph. 0831-2473777 at J.N. Medical College, Belgaum.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY:

I, Mr./ Mrs. _____

voluntarily agree to take part in this study, by signing this consent form I am not giving up my legal rights. I may withdraw at any time. I am signing after having read, or been read to me in the vernacular language including risks and the benefits and having all queries cleared.

Signature of the participant :_____

Witness name: _____

Signature of the participant :_____

Date :_____

Place :_____

Signature of Investigator :_____

K.L.E.SOCIETY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELGAUM-590010 (KARNATAKA-INDIA)
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Fax No. +91 (0)831 – 2470759

Ref. No. : MDC/DOME/2158

Date: 7/10/2008

To,

Dr. Ankush Kaushal,
Postgraduate student in
Department of Anaesthesiology,
J.N.Medical College,
Belgaum.

Dear Dr. Ankush Kaushal,

The JNMC – Institutional Ethics Committee on Human Subjects Research met on 6th October, 2008 to consider your application for approval of the research project **"A COMPARATIVE STUDY OF THE EFFECT OF IV KETAMINE WITH IV TRAMADOL ON INTRAOPERATIVE SHIVERING IN PATIENTS UNDERGOING SPINAL ANAESTHESIA: RANDOMIZED CLINICAL TRIAL".**

After review of the documents submitted by you and satisfactory explanations provided to the members, the committee has provided approval date through October 5th, 2009 at which time the study will be reviewed by the committee.

If you have any questions concerning the above, please feel free to contact the committee office.

Sincerely,

(Dr.V.B.Patil)
Chairman,
JNMC Institutional Ethics Committee on
Human Subjects Research

PROFORMA

"A COMPARATIVE STUDY OF THE EFFECT OF IV KETAMINE WITH IV TRAMADOL ON INTRAOPERATIVE SHIVERING IN PATIENTS UNDERGOING CAESEAREAN SECTION UNDER SPINAL ANAESTHESIA: RANDOMIZED CLINICAL TRIAL"

Name : IP.No.:

Age (in years) : Sex:

Weight: Height:

Address: Date:

PRE ANAESTHESTIC EVALUATION :

Chief Complaints :

Past History :

1.Diabetes mellitus/Hypertension/ Asthma/ Tuberculosis :

2.Drug Therapy :

3. Previous Anaesthetic procedure/Previous Surgeries :

Family History :

General Physical Examination:

Pallor: Icterus: Cyanosis: Clubbing:

Lymphadenopathy : Edema :

Vitals:

Pulse rate : Respiratory rate:

Temperature :

Airway Assessment :

Mouth Opening : Teeth:

Jaw Movement: MP Grading:

Systemic Examination:

CVS:

RS:

CNS:

SPINE:

Investigations:

Hb**%**: Urine Routine:

Any other:

ASA STATUS: Grade 1 / 2

Diagnosis:

Proposed Surgery:

Inclusion Criteria:

1.) Written/ Informed consent.

2.) ASA Grade 1 or 2 .

3.) Patients of both gender ranging 18 to 60 years.

4.) Undergoing Spinal Anaestheisa.

Exclusion Criteria:

1.) Hyperthyroidism

2.) Cardiopulmonary disease.

3.) Alcohol or substance abuse**.**

4.) Hypersensitivity to drug**.**

ANESTHETIC PROCEDURE:

After having met all the inclusion and exclusion criteria and obtaining written and informed consent , patients will be randomly divided into two groups Group T(Tramadol) and Group K(Ketamine)of 35 patients each by computer generated randomization. A through PAE will be performed by taking history and clinical examination. In all patients basal heart rate , weight, height, respiratory rate and blood pressure will be recorded .Routine investigations Hb, Urine analysis and EKG, Chest x-ray will be recorded. Tympanic membrane temperature will be recorded preoperatively by using infrared thermometer. Intravenous line will be secured with IV cannula. Monitors like Pulse Oximetry, ECG , NIBP will be attached. All preloading fluids are to be given at room temperatures maintaining Operating room temperatures at 24 deg C. Subarachnoid block will be instituted with 0.5 % Bupivacaine in all cases . Intraoperative Tympanic membrane temperature will be recorded at the onset of procedure (TO), and at 10 Min interval till the end of the procedure .Eligible patients will be divided in two groups K, T . Randomization will followed with Strict protocol. Should the patient develop shivering, it should be graded accordingly -

0 - No shivering

1-Mild fasiculation .

2.-Tremors in one group of muscles/one part of the body

3.-Tremors in more than one group /whole body.

Anti shivering effect will also be observed and recorded at 2 minutes interval until the shivering ends or till 15 minutes after which drug will be labeled ineffective. Improvement will also be assessed and graded on the same scale .In case of no improvement 0.5 mg/kg of Pethidine will be used .

A record of assessment of the sedation of the patient has to be made –

0- No sedation .

1-Mildly sedated / easily arousable

2-Heavily sedated .

Apgar score recordings over 1 and 5 min will also be noted in case of parturients who where given drug before the delivery on baby .

Observations:

Readings were recorded in the following manner :

DRUG Adminstered : _____ .

Group: _____ .

Variable	S0	S2	S4	S6	S8	S10
Shivering						

Variable	Preop	T10	T20	T30	T40	T50	T60	T70	T80
Temperature									

Variable	T90	T100	T110	T120	T130	T140	TEND
Temperature							

Side Effects -

Variable	Grading		
Sedation	0	1	2

Any other side effects noted._____ .

Signature of staff in charge: