"A COMPARISON OF ORAL TRAMADOL AND ORAL TAPENTADOL FOR PREVENTION OF PERIOPERATIVE SHIVERING DURING SUBARACHNOID BLOCK IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF PROSTATE-A RANDOMIZED CONTROL TRIAL"

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In

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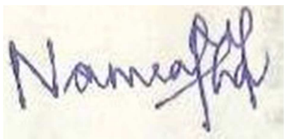

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ABBREVIATIONS

TURP-Transurethral resection of prostate

ASA-American society of Anaesthesiologists

IV-Intravenous

Tab-Tablet

MAC-Minimum alveolar concentration

MRC-Medical research center

SAB-Subarachnoid block

BMI-Body mass index

MINS-Minutes

CBT-Core body temperature

ST-Skin temperature

SG-Sedation score

SS-Sedation score

P.R-Pulse rate

R.R-Respiratory rate

SpO_2 - Arterial saturation of oxygen

ABSTRACT

Background and objectives

Shivering, a frequent complication in these procedures, can lead to various adverse effects. While opioids like tramadol are effective for shivering, they have side effects. Tapentadol offers potential benefits due to its dual mechanism of action and fewer side effects, but its efficacy for preventing shivering in this context has not been previously studied. The study aims to assess the effectiveness of oral tapentadol in preventing shivering during TURP in elderly patients under spinal anesthesia.The study investigates the efficacy of oral tapentadol in preventing shivering during TURP procedures in elderly patients under spinal anesthesia.

Methodology

We conducted a randomized controlled trial to compare the efficacy of tapentadol versus tramadol in preventing shivering during subarachnoid block for TURP surgery in male geriatric patients aged 50-80 years with ASA grades 1 and 2. Patients were randomly assigned to the tramadol group (n=75) or the tapentadol group (n=75) using a sealed-envelope method. The tablets were given with sips of water 90 minutes before surgery.

Body temperature (both forehead and tympanic), shivering, and sedation levels were monitored every 5 minutes for the first hour and subsequently every 10 minutes for the remainder of the observation period. Blood pressure, heart rate, respiratory rate, and oxygen saturation were continuously monitored throughout the surgical procedure.

Results

There was no significant difference in mean duration of surgery between both the groups. There were no significant differences in core body temperature between the groups at any recorded time point. While skin temperature showed significant changes within each group over time, no significant differences were observed between the two groups at any time.

Similarly, no significant differences were observed in shivering grade or sedation scores between the groups at any time point. However, within each group, sedation scores increased over time. The majority of participants in both groups did not require additional interventions or experience any side effects.

Conclusion

Both oral Tramadol and oral Tapentadol are equally effective in prevention of perioperative shivering in patients undergoing TURP under subarachnoid block.

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INTRODUCTION

Transurethral resection of the prostate (TURP) is the treatment of choice for benign prostatic hyperplastic disease in elderly patients. The subarachnoid block is preferred as the anesthesia method for TURP due to several advantages over general anesthesia, including effective post-operative pain relief and diminished surgical stress response.

Furthermore, it enables anesthesiologists to assess the consciousness level of patients and notice early clinical signs and symptoms of TURP syndrome. [1,2]

Perioperative shivering is a frequent and significant problem observed in patients undergoing urological procedures during subarachnoid block.[3] It manifests as involuntary, oscillatory muscle contractions that increase metabolic heat production. The incidence of perioperative shivering ranges from 40% to 70%, typically occurring around 20 minutes after subarachnoid blockade.[12] Shivering is highly unpleasant, sometimes surpassing surgical pain. It has various physiological consequences, including increased oxygen consumption, hypoxemia, hypercarbia, lactic acidosis, and elevated intracranial and intraocular pressures. Moreover, shivering can disrupt monitoring techniques, leading to potential measurement inaccuracies.[6-8]

Postanaesthetic shivering has a multifaceted and intricate mechanism involving various contributing factors. It encompasses both thermoregulatory and non-thermoregulatory elements. The elevated occurrence of postanaesthetic shivering is primarily associated with intraoperative hypothermia. This condition arises due to heat dissipation from the body surface and redistribution of heat away from vital organs towards the skin surface of the body.

The exact cause of postanaesthetic shivering is a complex mechanism with multiple contributing factors. Both thermoregulatory and non-thermoregulatory factors play roles in perioperative shivering. The increased occurrence of shivering after anesthesia is associated with intraoperative hypothermia, caused by heat loss from the body surface and the redistribution of heat away from vital organs towards the skin surface.[9-11]

Maintenance of normothermia and prevention of shivering is advisable during the perioperative period to minimize adverse consequences. So, different pharmacologic interventions have been identified and studied considering their role in modulation of shivering. Opioids have demonstrated significant anti-shivering properties and are used frequently for the management of postanaesthetic shivering.[10] The untoward complications like drowsiness, respiratory depression, pruritus, nausea, and vomiting have limited their use. Oral formulation of Tramadol is being extensively used and is a cheap but effective drug formulation without clinically significant side effects. [13-16]

Tapentadol is an FDA-approved central-acting analgesic with combined actions of μ receptor agonism and inhibition of noradrenaline reuptake. Oral preparation of Tapentadol is associated with an opioid-sparing effect contributing to the reduction of typical opioid-related side effects and resulting in better patient acceptance and compliance. [17,18]

An extensive literature search did not reveal any study determining the effectiveness of oral Tapentadol as an antishivering agent during subarachnoid blockade. So, through this study we analyze the antishivering attributes of oral Tapentadol and compare its effects with oral Tramadol during the perioperative period in geriatric patients.

OBJECTIVE OF THE STUDY

Aim of the study

- To assess the comparative effectiveness of oral Tramadol and oral Tapentadol in the prevention of perioperative shivering in patients undergoing TURP under subarachnoid block

Objective of the study

- To compare oral Tramadol and oral Tapentadol as a premedicant in the prevention of perioperative shivering following subarachnoid block in patients undergoing TURP.

REVIEW OF LITERATURE

Perioperative shivering following subarachnoid block is a common and undesirable complication. Many medications both oral and parenteral have been recommended to prevent shivering. Oral opioids like Tramadol have been extensively studied and used during the preoperative period. In this study, the newer opioid derivative oral Tapentadol is compared with oral Tramadol as a premedicant to prevent perioperative shivering.

While the exact mechanism of postanaesthetic shivering remains uncertain, disrupted central thermoregulation due to hypothermia is considered a primary contributing factor. During the subarachnoid block, several factors contribute to hypothermia, including vasodilation secondary to sympathetic blockade, distribution of heat from the core to peripheries, and infusion of cold intravenous fluids. Shivering, characterized by involuntary oscillatory muscle activity, serves to increase heat production. It is initiated by cooling of preoptic hypothalamus area. Traditionally, it is thought that a central pathway for shivering descends from the mamillary region. Spinal α motor neurons and their axons act on the same pathway for shivering and its associated coordinated movements. [5, 15]

Tramadol profoundly decreases 5-hydroxytryptamine uptake and increases its stimulated efflux in the pons and midbrain's raphe nucleus dorsalis. During cold adaption periods, the nucleus raphe magnus functions as an anti-shivering centre, triggering loss of heat and suppressing heat production. The reason behind its inhibitory effect on shivering is that it extends into the hypothalamus and farther

down a pathway to the spinal cord, where it presynaptically inhibits posterior horn cells.[16]

Tewari et al. studied use of oral formulation of Tramadol as an antishivering agent in patients posted for urological procedures under subarachnoid block. The incidence of shivering found to be only 7.5% and onset of shivering was delayed with a shorter duration.A dose of 1mg/kg of oral Tramadol was safe and did not cause respiratory depression [17,18]. A study conducted by Lakhe et al. demonstrated antishivering properties of Tramadol without any untoward effects. It was found that prophylaxis with 0.5mg/kg intravenous Tramadol reduced the incidence of shivering by 46.7%. Previous reports have documented a shivering incidence to be ranging from 8.8% to 16% with Tramadol.[11]

In another study, Nain P et al. compared oral Tramadol and oral Gabapentin to prevent perioperative shivering in 150 adults undergoing orthopedic procedures. The incidence of shivering among Tramadol group (18%) and Gabapentin group (20%) was statistically similar. Both medications significantly reduced the perioperative shivering incidence when compared to the control group. Nausea and vomiting were higher with Tramadol but sedation was significantly lesser in comparison to Gabapentin.[25]

Tapentadol is a central acting analgesic that has demonstrated promising results in treating both nociceptive and neuropathic pain. Its analgesic effects stem from combined action: agonism at μ opioid receptors and inhibition of noradrenaline reuptake. Compared to morphine, Tapentadol exhibits 50 times lesser affinity for μ receptors and is twice less potent as analgesic. Despite being a weak serotonin

reuptake inhibitor, this action does not contribute significantly to its analgesic efficacy.[19,20]

Iyer et al. assessed the effectiveness of oral Tramadol and oral Tapentadol for pain management in 60 adult patients following cardiac surgery. Their findings indicated that oral Tapentadol offers superior gastrointestinal tolerance compared to other opioids. Post-operative nausea and vomiting occur with an incidence ranging from 12% to 38% .[13] Furthermore, Tapentadol can be administered to geriatric patients without requiring dose adjustments.[21]

In one clinical trial carried out by Saini et al., the effectiveness of Clonidine and Tapentadol when taken orally in managing perioperative shivering and providing postoperative pain relief was evaluated. Administration of 100mcg oral Clonidine and 50mg oral Tapentadol 60 minutes before subarachnoid block significantly decreased the occurrence of shivering in comparison with the placebo group ($p<0.05$). Additionally, both medications prolonged postoperative analgesia without causing hemodynamic fluctuations or adverse effects. Oral Tapentadol was associated with significantly lower intraoperative sedation levels when compared to oral Clonidine.[22]

In a prospective double-blinded trial, Bindal et al. examined the efficacy of orally administered Tramadol and Tapentadol as preemptive treatments to alleviate bladder discomfort due to catheterization and alleviate the response to surgical stress in geriatric population undergoing TURP. The study demonstrated that oral Tapentadol significantly decreased the incidence of discomfort in the bladder in the early postoperative period, particularly at 2 hours. Additionally, cortisol levels were notably lower in the Tapentadol group. Complications such as dry mouth and nausea were noticed exclusively in the Tramadol group. [23]

Roulet et al., in their literature review, compared the safety profiles and pharmacological effectiveness of Tapentadol and Tramadol. Both Tapentadol and Tramadol exhibit a combined mode of action, acting as mu receptor agonists and possessing mono aminergic properties. Tapentadol is 2 times as potent as Tramadol and 2-3 times less potent than Morphine. Unlike Tramadol, Tapentadol doesn't rely on activation by specific enzymes (cytochrome P450) or have pain-relieving metabolites. This reduces potential variability in pain control seen with Tramadol due to genetic variations in these enzymes. Tapentadol's unique metabolism makes it less likely to interact with other medications that use the same enzymes as Tramadol, potentially reducing the risk of unintended side effects. Due to its stronger opioid action, Tapentadol carries a higher risk of constipation and respiratory depression compared to Tramadol.[24]

BASIC SCIENCE

THERMOREGULATION

Thermoregulation is the maintenance of physiologic core body temperature by balancing heat generation with heat loss. A healthy individual will have a core body temperature of 37 +/- 0.5°C, the temperature range needed for the body's metabolic processes to function correctly.

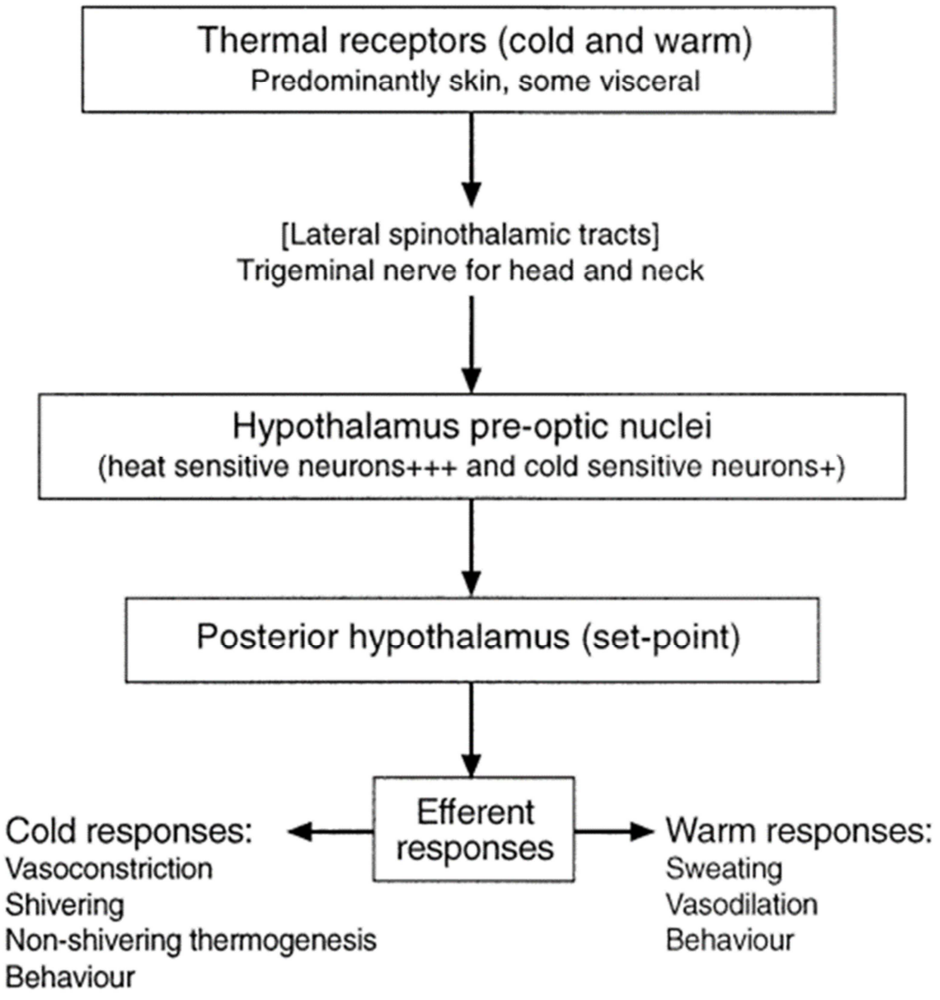


Fig 1: THERMOREGULATORY PATHWAY

Afferent thermal signals play a crucial role in our perception of temperature and in regulating our body's response to changes in temperature.

1. Types of Receptors:

- Thermally sensitive receptors in the skin and mucous membranes mediate thermal sensation and contribute to thermoregulatory reflexes.
- Cold-specific receptors are innervated by type A-δ nerve fibers, whereas warm receptors are innervated by type C nerve fibers.

2. Peripheral vs. Central Receptors:

- Peripheral cold sensing receptors are more effective than central cold thermoreceptors.
- Central thermoreceptors are active only when the temperature falls below the set point.
- The hypothalamus, spinal cord, thoracic and abdominal tissues, and skin surface contribute to the total thermal inputs to the central regulating system.

3. Response of Cold Receptors:

- Cold receptors respond to both long-term, gradual decreases in temperature and sudden, transient changes in environmental temperature.

4. Transmission of Thermal Sensation:

- The anterior spinothalamic tract in the spinal cord transmits most of the thermal sensation to the brain.

- No single tract is responsible for transmitting the entire thermal sensation. To completely abolish thermal sensation, the entire anterior spinal cord should be abolished.
- In mammals, the spinal cord acts as a primary thermoregulatory control because it senses and modifies thermal signals before they reach the hypothalamus.

5. Brain Stem Relay Stations:

- Areas in the brain stem, such as the sub-ceruleus and the raphe magnus nucleus, serve as relay stations for transmitting thermal information from the skin before it reaches the hypothalamus.

CENTRAL INTEGRATION – THE HYPOTHALAMUS

The anterior hypothalamus is responsible for integrating afferent thermal information, while the posterior hypothalamus controls the pathways to effectors.

Within the pre-optic area of the hypothalamus, there are temperature-sensitive and insensitive neurons. Temperature-sensitive neurons can be further categorized into heat-sensitive and cold-sensitive neurons. Heat-sensitive neurons increase their firing rate in response to higher environmental temperatures, leading to increased heat loss mechanisms. Conversely, cold-sensitive neurons increase their firing rate when the pre-optic area of the hypothalamus is cooled.

The posterior hypothalamus integrates peripheral cold signals with heat-sensitive stimulation from the pre-optic area, initiating effector responses.

Four neural mechanisms dominate autonomic thermo-regulation for heat production at warm skin temperatures:

i. Central detection of warmth

ii. Peripheral detection of cold

iii. Central inhibition of the metabolic response to cold

iv. Inhibition of thermoregulatory sweating by cooling core temperature.

In humans, the 'set-point' temperature, typically ranging from 36.7°C to 37.1°C, refers to the temperature range where there is no effector response. This set-point, also known as the 'thermoneutral zone' or 'inter-threshold range', represents the range at which metabolic rate increases.

The thermoregulatory responses include:

i. Vasomotor responses, consisting of vasoconstriction and piloerection in response to cold, and vasodilation in response to heat

ii. Shivering and increased metabolic rate.

When the hypothalamic thermostat detects a body temperature that is too cold, signals are sent from the hypothalamus to the cerebral cortex, creating the sensation of feeling cold. This leads to changes in behavior, such as increased movement, seeking warmer environments, or adding more clothing.

Autonomic responses are triggered once the body temperature falls outside the set-point temperature range, typically between the vasoconstriction and sweating thresholds of 36.7–37.1°C. During general anesthesia, this range widens from

approximately 0.4°C to about 4.0°C. Each response has its specific threshold (activation temperature), gain (rate of response increase as deviation from normal increases), and maximum intensity of response.

EFFERENT RESPONSES

Efferent responses integrate multiple inputs into a common signal for effector systems. In both animals and humans, effector mechanisms are activated in a coordinated manner for optimal regulation. Key defenses against hypothermia in humans include skin vasomotor activity, non-shivering thermogenesis, shivering, and sweating.

Heat loss is primarily regulated by cutaneous vasodilation or vasoconstriction, with sweating and shivering as major responses to heat regulation. Shivering serves as a "last resort" defense, activated only when other compensatory mechanisms and maximal vasoconstriction are inadequate to maintain core temperature.

Non-shivering thermogenesis is a metabolic process observed particularly in neonates, not involving mechanical work.

Shivering is involuntary muscular activity that can increase metabolic heat production by up to 600%. It occurs when the preoptic region of the hypothalamus is cooled, and its efferent pathway arises from the posterior hypothalamus. Changes in muscle tone during shivering are due to temperature-induced alterations in neuronal activity in specific brain regions.

In heat balance and shivering, the processes leading to core hypothermia in regional and general anesthesia are similar. Initial hypothermia in regional anesthesia

results from heat redistribution from the core to the periphery. However, patients receiving spinal or epidural anesthesia struggle to reestablish core temperature equilibrium due to impaired peripheral vasoconstriction. Shivering in these patients generates relatively little heat, as it is confined to the small muscle mass above the block.[38]

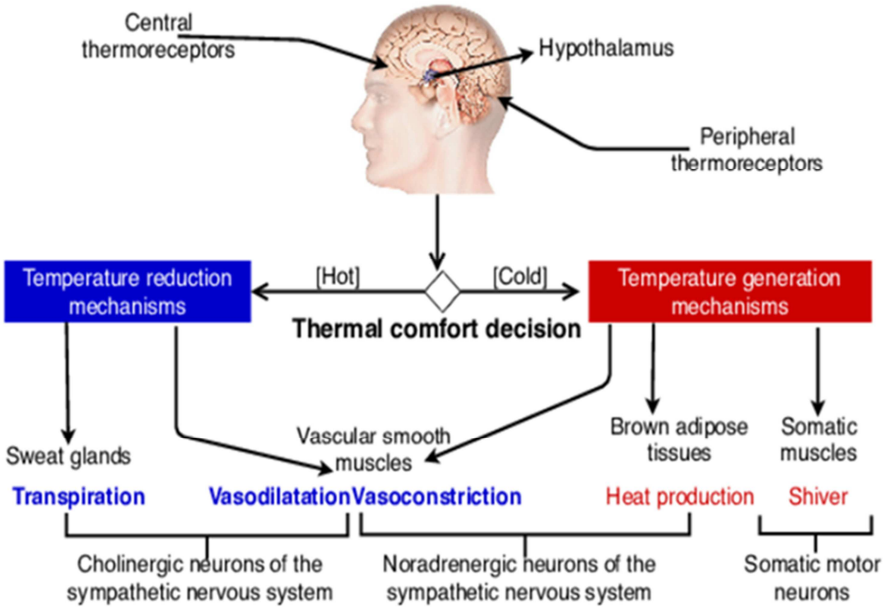


FIGURE: MECHANISM OF THERMOREGULATION

EFFECTS OF ANAESTHESIA ON THERMOREGULATION

Hypothermia occurs in a characteristic 3-phase pattern.

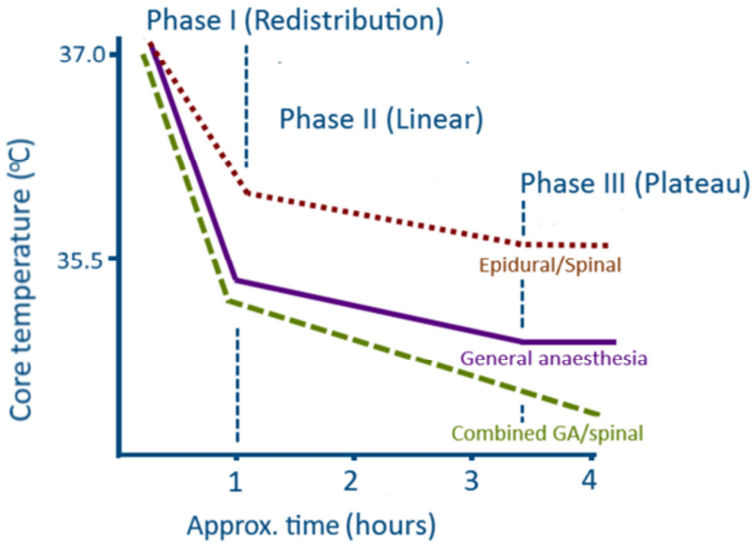


FIGURE: PHASES OF HYPOTHERMIA

Phase 1: A rapid decrease in core temperature of 1.0–1.5°C occurs within the first 30–45 minutes of anesthesia. This is due to vasodilation and other effects of general anesthesia. Vasodilation disrupts the normal vasoconstriction, leading to a core-to-peripheral temperature gradient and the redistribution of body heat from the core to peripheral tissues. Additionally, general anesthesia lowers the threshold for thermoregulatory vasoconstriction, allowing core temperature to drop significantly before the vasoconstrictor response is triggered.

Phase 2: Following Phase 1, there is a gradual, linear decrease in core temperature of approximately 1°C over the next 2–3 hours of anesthesia. This decline

is attributed to heat loss through radiation, convection, and evaporation, which exceeds heat gain determined by metabolic rate. Major surgeries exacerbate heat loss through evaporation due to the increased surface area of exposed tissue.

Phase 3: This phase represents a plateau in core temperature where heat loss is balanced by metabolic heat production. It occurs when anesthetized patients become sufficiently hypothermic to trigger the altered threshold for vasoconstriction, limiting the core-to-peripheral heat gradient.

Redistribution during spinal or epidural anesthesia primarily affects the lower half of the body, resulting in a milder initial core hypothermia of approximately 0.5℃ compared to general anesthesia.

Unlike in general anesthesia, spinal or epidural anesthesia does not lead to a plateau phase because vasoconstriction is blocked. Consequently, patients undergoing long procedures with combined general and epidural anesthesia are at a higher risk of greater hypothermia.

Regional anesthesia decreases the threshold for shivering and vasoconstriction below the block level, likely due to decreased afferent input from peripheral thermal centers. Initial hypothermia occurs as cooler peripheral blood redistributes to the core, induced by vasodilation from regional anesthesia. However, vasoconstriction above the block level can partially compensate. The highest risk of heat loss is during combined regional and general anesthesia.[38]

CONSEQUENSES OF PERIOPERATIVE HYPOTHERMIA

Perioperative hypothermia affects various aspects of patient outcome:

(i) Pharmacological Effects:

Hypothermia alters drug metabolism and distribution, prolonging drug action. It decreases hepatic blood flow, leading to increased plasma drug concentrations, especially for drugs like propofol and fentanyl. Hypothermia reduces the MAC of volatile anesthetics and prolongs neuromuscular blockade.

(ii) Coagulopathy:

Hypothermia impairs plasma coagulation, diminishing enzyme activity and clotting factor synthesis. It causes platelet sequestration and inhibition of platelet aggregation, increasing bleeding risk. There's a reversible impairment of platelet function, further contributing to bleeding risk.

(iii) Blood Loss and Transfusion Requirement:

Each 1°C decrease in core temperature increases bleeding incidence by 16% and transfusion requirement by 22%.

(iv) Surgical Site Infections:

Hypothermia impairs tissue oxygenation and wound healing, increases the risk of surgical site infections. It diminishes immune system function, decreasing defense against pathogens.

(v) Delayed Discharge from Post-Anesthesia Care Unit (PACU):

Hypothermic patients require longer recovery times and prolonged PACU stays.

Even when not required by discharge criteria, hypothermic patients take approximately 40 minutes longer to be fit for discharge from PACU.

Recovery duration is about 90 minutes longer in hypothermic patients, increasing perioperative costs.[37]

PERIOPERATIVE TEMPERATURE MONITORING

Perioperative temperature monitoring is essential for managing thermal balance and preventing complications. Body temperature varies across regions: deep thoracic, abdominal, and core temperatures are typically cooler than peripheral areas and skin surface. Core temperature, tightly regulated, is the best indicator of thermal status.

Core temperature monitoring (e.g., tympanic membrane, pulmonary artery, distal esophagus, nasopharynx) is vital for detecting intraoperative hypothermia and preventing overheating. Other sites (e.g., mouth, axilla, bladder, rectum, skin surface) are used when core monitoring isn't feasible, each with its limitations.

Both core and mean skin-surface temperature measurements are necessary for assessing anesthetic effects and estimating mean-body temperature.

Thermometers

Thermometers have evolved significantly over time. Mercury-in-glass thermometers, once widely used, have become obsolete due to their slow response time, bulkiness, and the biohazard posed by spilled mercury. They are now mainly used for laboratory calibration purposes.

In clinical settings, electronic thermometers have gained popularity. Thermistors and thermocouples are the most common types. Thermistors are temperature-sensitive semiconductors, while thermocouples rely on the current generated by joining dissimilar metals. Despite their accuracy and cost-effectiveness, both devices require calibration to correct for non-linear signals.

Another type of thermometer, infrared sensors, has gained popularity in recent years. They detect infrared energy emitted by all surfaces above absolute zero degrees, allowing temperature measurement without physical contact. This feature is particularly useful for measuring high-temperature surfaces like molten lava or metals. Infrared thermometers are accurate, relatively inexpensive, and can measure core temperature when used on the tympanic membrane.

Monitoring Sites

Monitoring body temperature is crucial during anesthesia, guided by the ASA standards. It is recommended when significant changes in body temperature are intended, expected, or suspected. Core temperature monitoring is essential for patients undergoing general anesthesia lasting more than 30 minutes or major surgery with neuraxial anesthesia. However, it is typically unnecessary during mild or moderate sedation or peripheral nerve block procedures.

Various sites can be used for core temperature monitoring, with common choices being the nasopharynx, distal esophagus, tympanic membrane, and pulmonary artery. While pulmonary artery temperature is the most accurate, it's seldom used. Nasopharyngeal and distal esophageal probes are commonly utilized, with proper insertion depths crucial for accuracy. Tympanic membrane probes are less reliable due to positioning challenges. Alternative "near-core" sites include the axilla, bladder, rectum, forehead, oral cavity, and sublingual area. Axillary temperature monitoring is most accurate when the probe is positioned over the axillary artery.[35]

PREVENTION AND TREATMENT OF TREATMENT OF SHIVERING

a) Prewarming: Redistribution of body heat during neuraxial anesthesia causes hypothermia. Sympatholysis leads to peripheral vasodilation, redistributing warm-core blood to the skin. Pre-anaesthetic cutaneous warming reduces this heat loss by increasing peripheral tissue heat content and reducing the core-to-peripheral tissue temperature gradient. Studies show that a brief 15-minute prewarming, along with intraoperative warming, prevents hypothermia and shivering in patients undergoing elective caesarean delivery under neuraxial anesthesia.

b) Intraoperative Warming: Forced-air warming, warm intravenous fluids, and ambient operating room temperature control are common methods to prevent intraoperative hypothermia. Forced-air warming units distribute heated air to the body surface, increasing skin temperature and reducing the core-to-peripheral tissue temperature gradient. This method effectively transfers heat to the body and minimizes heat loss from the skin.

c) Pharmacotherapy: Various drugs are utilized to treat shivering post-anesthesia. Tramadol, alpha agonists, opioids, magnesium sulfate, steroids, and serotonin antagonists are among them. These drugs modulate central thermoregulatory control mechanisms to control shivering[35].

TRAMADOL

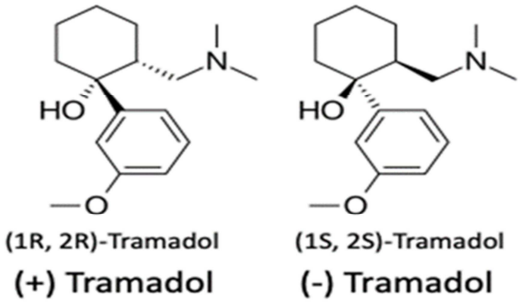
Tramadol is a centrally acting analgesic,it affects the central nervous system to relieve pain. Tramadol consists of two enantiomers.

1. (+) - Tramadol: This enantiomer is primarily responsible for tramadol's analgesic effects. It works as a weak μ-opioid receptor agonist.
2. (-) - Tramadol: This enantiomer has weaker affinity for opioid receptors and doesn't contribute significantly to tramadol's analgesic effects.

Additionally, Tramadol is metabolized in the liver to its active metabolite, (+)-O-desmethyltramadol (M1), which also acts as a μ-opioid receptor agonist. This metabolite contributes to Tramadol’s analgesic activity.

By acting as agonists of the μ-opioid receptor, both (+)-Tramadol and (+)-O-desmethyltramadol contribute to pain relief by altering the perception of pain in the central nervous system.

Chemical structure of Tramadol



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

MECHANISM OF ACTION: Tramadol operates through both opioid and non-opioid pathways. It acts as an agonist, mainly at μ-opioid and gamma-aminobutyric acid (GABA) receptors, and it inhibits serotonin (SSRI) and norepinephrine (SNRI) reuptake. Tramadol is a racemic mixture of (+) and (−) enantiomers, each with distinct affinities for opioid receptors and different impacts on serotonin and norepinephrine reuptake.

ROUTES OF ADMINISTRATION: Tramadol is available as drops, capsules, and sustained-release formulations for oral intake, suppositories for rectal use, and solutions for intramuscular, intravenous and subcutaneous injection.

PHARMACOKINETICS:

After oral administration, Tramadol is rapidly and almost completely absorbed. Sustained-release tablets release the active ingredient over a period of 12 hours, reach peak concentrations after 4.9 hours and have a bioavailability of 87–95% compared with capsules.

Distribution: The volume of distribution of Tramadol is reported to be in the range of 2.6-2.9 L/kg.

Metabolism: Tramadol is mainly metabolised by O- and N-demethylation and by conjugation reactions forming glucuronides and sulfates.

Route of elimination: Tramadol and its metabolites are mainly excreted via the kidneys.

Half-life: Tramadol has a half-life of 5-6 hours while the M1 metabolite presents a half-life of 8 hours.

PHARMACODYNAMICS:

Apart from analgesia, Tramadol may produce a constellation of symptoms (including dizziness, somnolence, nausea, constipation, sweating and pruritus) similar to that of other opioids.

a) Central Nervous System: At therapeutic doses, Tramadol has no effect on heart rate, left-ventricular function or cardiac index. Orthostatic hypotension has been observed. Tramadol produces respiratory depression by direct action on brain stem respiratory centers.

b) Tramadol depresses the cough reflex by a direct effect on the cough center in the medulla. Tramadol causes miosis and seizures have been reported in patients receiving tramadol within the recommended dosage range.

c) Gastrointestinal System: Tramadol causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased.

d) Endocrine System: Opioids may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Increase in serum prolactin and decreases in plasma cortisol and testosterone.

e) Cardiovascular System: Tramadol administration may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of drugs such as phenothiazines and other tranquillizers, sedative/hypnotics, tricyclic antidepressants or general anesthetics.

USES: -Acute and chronic pain

-Postoperative shivering

ADVERSE EFFECTS:

a) Central nervous system: depression, Seizure, Anxiety, Low-grade coma

b) Cardiovascular system: Inhibition of calcium channels, Palpitation, Mild hypertension Cardiopulmonary arrest, Sinus tachycardia, Dominant S and R wave, Right axis deviation, QTC prolongation, QRS widening, Complete or incomplete RBBB, Brugada pattern

c) Gastrointestinal system: Nausea and vomiting, Acute liver failure, Vacuolization in tubular cells

d) Respiratory system: Respiratory depression ARDS, increase of apneic threshold, Decrease in total CO2 sensitivity

e) Renal system: Renal failure, Renal histopathologic changes

f) Endocrine system: Hypoglycemia/hyperglycemia, Declined hepatic gluconeogenesis

g) Musculoskeletal system: Rhabdomyolysis, Increased creatine phosphokinase

h) Serotonin Syndrome

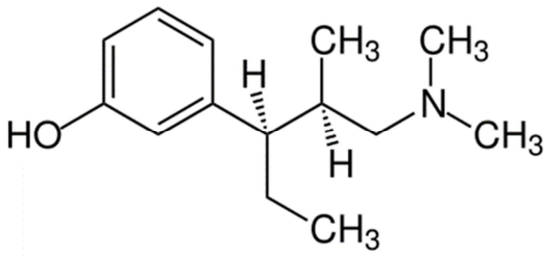
DOSE: When taken orally Tramadol is used at a dose of 50–100 mg every 4–6 hours. Maximum dose of Tramadol is 400 mg/day.

DRUG INTERACTIONS: Tramadol interacts with the drugs such as MAO inhibitors, antidepressants, blood thinners, digoxin, ketoconazole, rifampin, erythromycin, quinidine and medications that cause drowsiness. Tramadol interacts with alcohol and increases the CNS side effects like dizziness, sleepiness, lack of concentration, thinking and judgment behavior.

TAPENTADOL

Tapentadol is a centrally-acting synthetic analgesic with a dual mechanism of action.

CHEMICAL STRUCTURE OF TAPENTADOL



MECHANISM OF ACTION: Tapentadol is believed to have two main mechanisms of action. Tapentadol is a selective mu-opioid receptor (MOR) agonist: it binds to MOR with an affinity greater than or equal to ten-fold affinity compared to delta- and kappa-opioid receptors. Tapentadol also inhibits noradrenaline reuptake, thereby increasing noradrenaline levels and activating alpha-2 receptors to promote analgesia. Tapentadol is a weak serotonin reuptake inhibitor; however, this action does not contribute to its analgesic effect.

PHARMACOKINETICS:

Absorption: The mean absolute bioavailability after single-dose administration of Tapentadol in a fasted state is approximately 32% due to extensive first-pass metabolism. Maximum serum concentrations of Tapentadol are typically observed at around 1.25 hours after dosing.

Volume of distribution: Tapentadol is widely distributed throughout the body. Following intravenous administration, the volume of distribution (Vz) for tapentadol is 540 ± 98 L.

Protein binding: The plasma protein binding is approximately 20%

Metabolism: Tapentadol is mainly metabolized by Phase II pathways, and only a small amount is metabolized by Phase I oxidative pathways; thus, drug metabolism mediated by cytochrome P450 system is of less importance than phase II conjugation. The major pathway of Tapentadol metabolism is conjugation with glucuronic acid to produce glucuronides. After oral administration, approximately

70% of the drug, of which 55% is the O-glucuronide metabolite and 15% is the sulfate metabolite, is excreted in urine. About 3% of the dose was excreted in urine as the unchanged parent drug.

Route of elimination: Tapentadol and its metabolites are 99% excreted via the kidneys

Half-life: The terminal half-life is about four hours after oral administration

PHARMCODYNAMICS: Tapentadol is an opioid agonist that exerts physiological effects commonly caused by the opioid drug class. These effects include miosis, reduced gastrointestinal motility, and peripheral vasodilation. Tapentadol produces respiratory depression by reducing the responsiveness of the brain stem respiratory centers to both increases in carbon dioxide tension and electrical stimulation. Tapentadol has a high potential for misuse and abuse, which can lead to the development of substance use disorder. Abuse of Tapentadol poses a risk of overdose and death, which increases with alcohol or other central nervous system depressants.

DOSE: Tapentadol is available as 25, 50, 75, and 100mg tablets. The recommended maximum dose is 600 to 700 mg daily for an adult without significant contraindications. The immediate-release and extended-release formulations are equipotent. At present, there is no commercially available intravenous preparation.

ADVERSE EFFECTS: Tapentadol produces different central and peripheral adverse effects. Peripherally, Tapentadol may cause nausea and vomiting because of its effects on the gastrointestinal tract. Centrally, Tapentadol may cause headaches, dizziness, and somnolence. It is less likely to cause life-threatening situations

associated with delirium, neuromuscular rigidity, and hyperthermia when combined with selective serotonin reuptake inhibitors (serotonin syndrome).

MEDICAL USE: Tapentadol is used for the treatment of moderate to severe pain for both acute (following injury, surgery, etc.) and chronic musculoskeletal pain. It is also specifically indicated for controlling the pain of diabetic neuropathy when around-the-clock opioid medication is required. Extended-release formulations of Tapentadol are not indicated for use in the management of acute pain.

DRUG INTERACTIONS:

Combination with serotonin receptor agonists may lead to potentially lethal syndrome. Combination with monoamino oxidase inhibitors may also result in an adrenergic storm. Use of Tapentadol with alcohol or other sedatives such as benzodiazepines, barbiturates, nonbenzodiazepines, phenothiazines, and other opiates may result in increased impairment, sedation, respiratory depression and death.

MATERIALS AND METHODS

This research was conducted from March 2023-Fenruary 2024 on male patients, aged 50-80 years, with ASA grade-I and grade-II who were receiving TURP under Subarachnoid Block at KLE's Dr. Prabhakar Kore Hospital and MRC, Belagavi.

SAMPLE SIZE AND RANDOMIZATION

The minimum sample size formula based on two proportions is

$$n = \frac{(z_\alpha + z_\beta)^2 \bar{p}(1-\bar{p})}{d^2}$$

where p_1 and p_2 are the proportions of the two groups.

$$p = \frac{p_1 + p_2}{2} \text{ and } d = p_1 - p_2$$

zα is linked with the level of significance and zβ is linked with the power of the test. For 5% level of the significance zα = 1.96 and zβ = 0.84 for 80% power of the test.

Patients were allocated into groups in a randomization method by ‘opening a sealed envelope’:

a) Group A (tramadol, n=75)
b) Group B (tapentadol, n=75)

An informed,written consent was taken from patients during pre-anesthetic evaluation a day prior to surgery.

Ninety minutes prior to surgery, Group received oral formulation Tramadol 50mg and Group B received oral formulation Tapentadol 50mg with sips of water.

INCLUSION CRITERIA:

- ASA status-I, II
- Age:50-80 years
- Patients undergoing TURP under Subarachnoid Block

EXCLUSION CRITERIA:

- Obesity (BMI>=30)
- Presence of febrile illness
- Patients with known allergies to either drug
- Neuro-behavioral Disorders
- Severe diabetic/autonomic neuropathy
- Patients on vasodilator medications

Anaesthesia assisstants who were not involved in the study were assigned to handle trial preparations and record the group randomizations. Both patients and treating anaesthesiologists were unaware of the specific preparations administered to ensure unbiased results.

Under sterile precautions, a subarachnoid-block was administered to achieve a sensory block up to the T10 level using 2-3 ml of 0.5% hyperbaric levobupivacaine. All surgical procedures were conducted in single operating room, which maintained consistent humidity and ambient temperature. The operating room did provide laminar flow capabilities.No means of active rewarming was allowed unless deemed essential for rescue measures. Intravenous and irrigating fluids prewarmed up to body temperature were used.

Throughout the perioperative period, vital indicators such as blood pressure, heart rate, respiratory rate, and arterial oxygen saturation were monitored.Skin temperature was monitored on the forehead using the Braun BNT400® thermometer, while core body temperature was assessed using the Braun Thermoscan® device from the tympanic membrane. Measurements were taken every 5 minutes interval from the base values, which started 5 minutes before the subarachnoid block, continuing for 60 minutes, and subsequently every 10 minutes for the remainder of study period. The attending anesthesiologist evaluated shivering at time intervals of 0-, 1-, 5-, 10-, 15-, 30-, 45-, 60- and 90- minutes from base values.

An assessment tool created by Wrench and colleagues was used to gauge shivering:

GRADE	DESCRIPTION
0	Nil shivering
1	Piloerection and peripheral cyanosis without any other cause; no visible muscle activity
2	Visible muscle activity limited to a single muscle group
3	Visible muscle activity involving more than one muscle group
4	Intense muscle activity throughout the entire body

Perioperatively if patients experienced shivering, was managed by reassurance, using a warming blanket, or injection of IV pethidine in both groups depending on the severity of the shivering.

Forced airwarming blankets were used whenever required.

Complications like hypotension & bradycardia were managed with Atropine IV & Mephentermine IV accordingly. The anti-emetic for treatment of nausea and vomiting was IV Ondansetron. Sedative adverse effects of the study drugs were monitored using a 4-point sedation scale. According to the criteria set by Filos et al., the sedation scores are defined as follows:

SCORE	DESCRIPTION
1	The patient is alert and awake.
2	The patient responds to commands but drowsy
3	The patient is drowsy and only arousable with physical stimulus.
4	The patient is unarousable

STATISTICAL ANALYSIS:

Results were analysed using statistical software R version 4.4.0. and Microsoft Excel. Categoricalvariables given in the form of frequency tables. Continuous variables given in Mean ± SD /Median form. Chi square test is used to check the association of categoricalvariables with groups. Normality of variable is checked by Shapiro Wilk test and QQplot. The data were not normally distributed. Hence, non-parametric tests are used for analysis. Mann Whitney U test is used to compare the distribution of variables over groups. Friedman's test is used to compare the distribution of variables over time points. P-value less than or equal to 0.05 indicates statistical significance.

RESULTS

150 male patients, ASA grades 1 or 2, who underwent TURP under subarachnoid block and were between the ages of 50 and 80, were included in this study. The analysis covered 150 individuals who were included in the research.

Measurements from 150 subjects, equally divided into two groups of 75 people each, are included in the dataset.

Patients were assigned into 2 groups,

a) group-A (Tramadol, n=75)
b) group-B (Tapentadol, n=75)

Demographic data

Table 1: Distribution of age

Variable	Sub Category	Group-A	Group-B	Total	p-value
Age (years)	Mean ± SD	68.41 ± 6.98	69.15 ± 5.42	68.78 ± 6.24	0.4115
	Median	68	69	69	

Group-A had a mean age of 68.41 ± 6.98 years, with a median age of 68 years (ranging from 55 to 80 years). In contrast, Group-B exhibited a slightly higher mean age of 69.15 ± 5.42 years, with a median age of 69 years (ranging from 57 to 80 years). However, the differences in age among both groups were statistically insignificant (p-value = 0.4115).

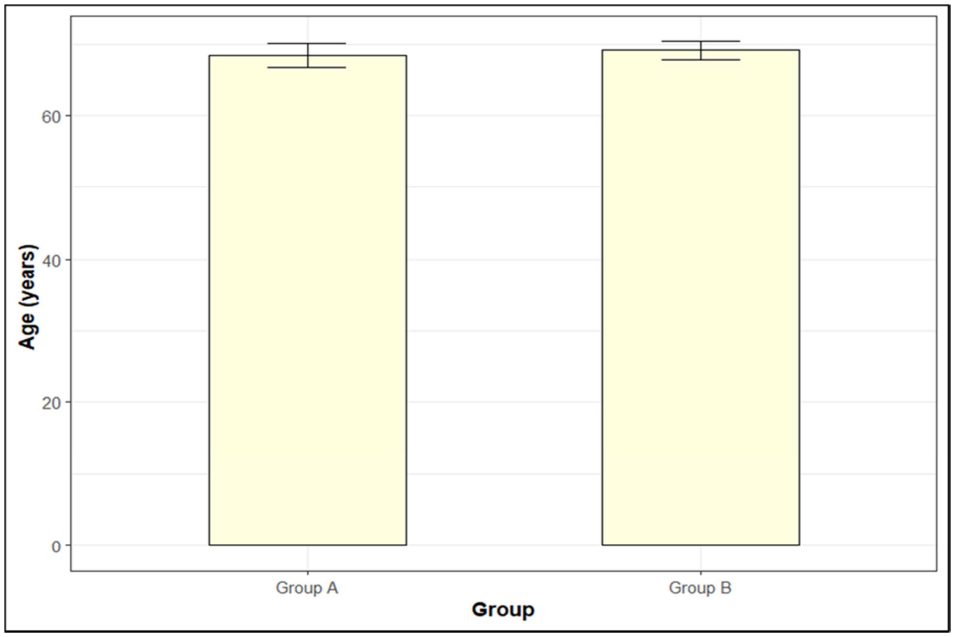


Figure 1: Mean plot of age distribution

Table 2: Comparison of clinical details

Variable	Sub Category	Group -A	Group-B	Total	p-value
ASA grade	I	15 (20%)	10 (13.33%)	25 (16.67%)	0.2733
	II	60 (80%)	65 (86.67%)	125 (83.33%)	
Height (cm)	Mean ± SD Median	172.53 ± 6.44 173	173.85 ± 6.59 176	173.19 ± 6.53 174.5	0.1088
Weight (kg)	Mean ± SD Median	71.97 ± 7.09 72	74.2 ± 7.56 74	73.09 ± 7.39 73	0.0936
BMI	Mean ± SD Median	24.16 ± 1.83 24.3	24.5 ± 1.39 24.6	24.33 ± 1.63 24.55	0.1572

In Group-A, 20% of patients were ASA Grade-I and 80% were to ASA Grade-II. In Group-B, 13.33% were to ASA Grade-I and 86.67% were to ASA Grade-II. However, the distribution of ASA grades among both groups shows no significant variation (p-value = 0.2733).

The difference in the distribution of height, weight, and BMI among groups were not statistically significant.

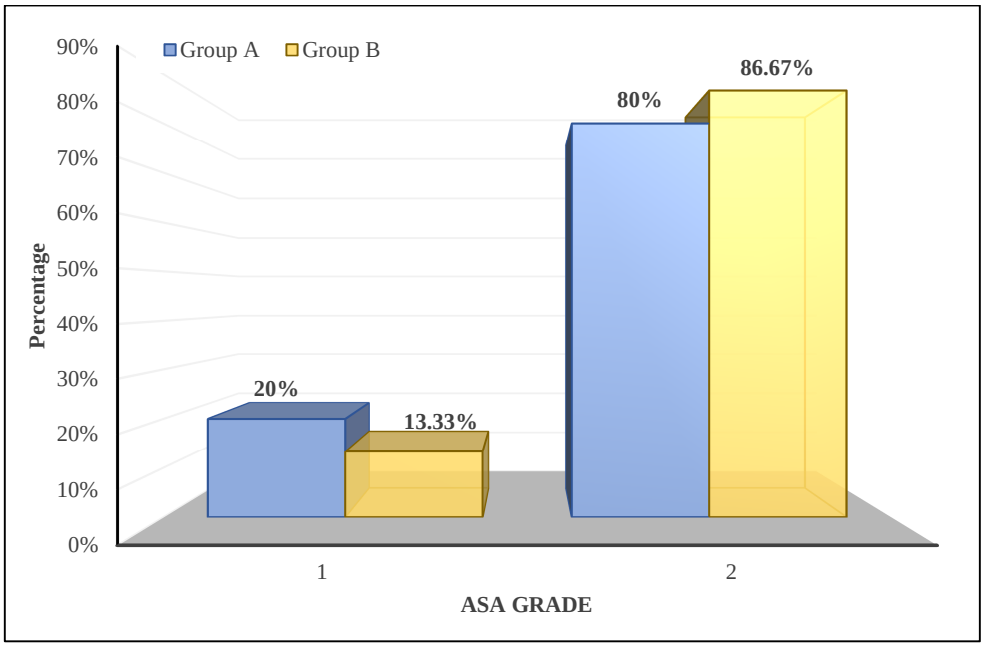


Figure 2: ASA grade distribution

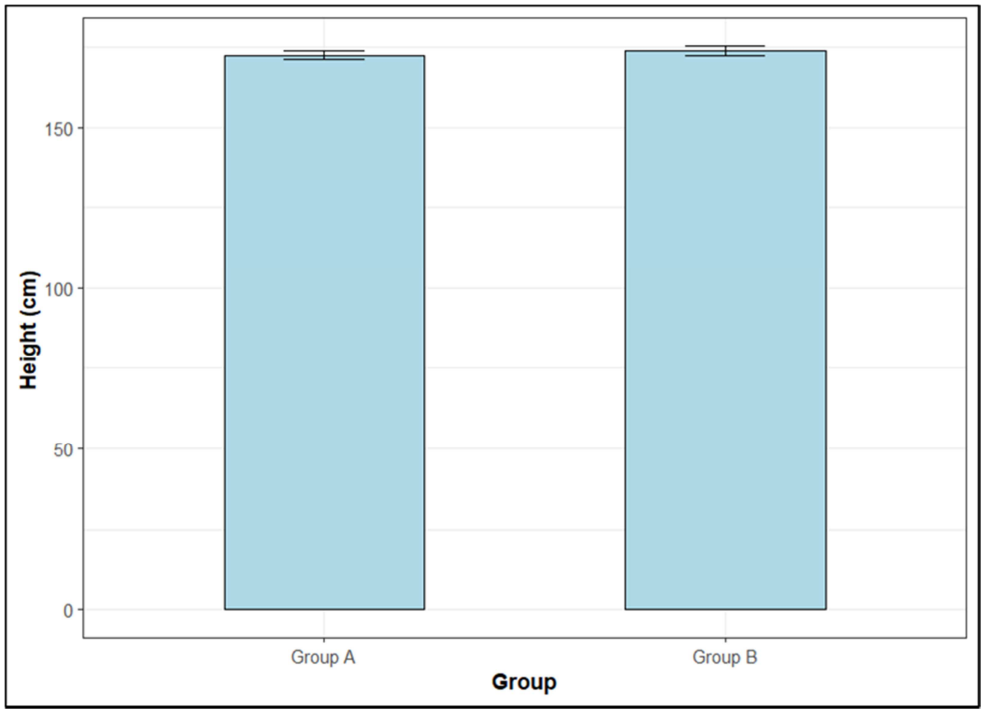


Figure 3: Mean plot of height

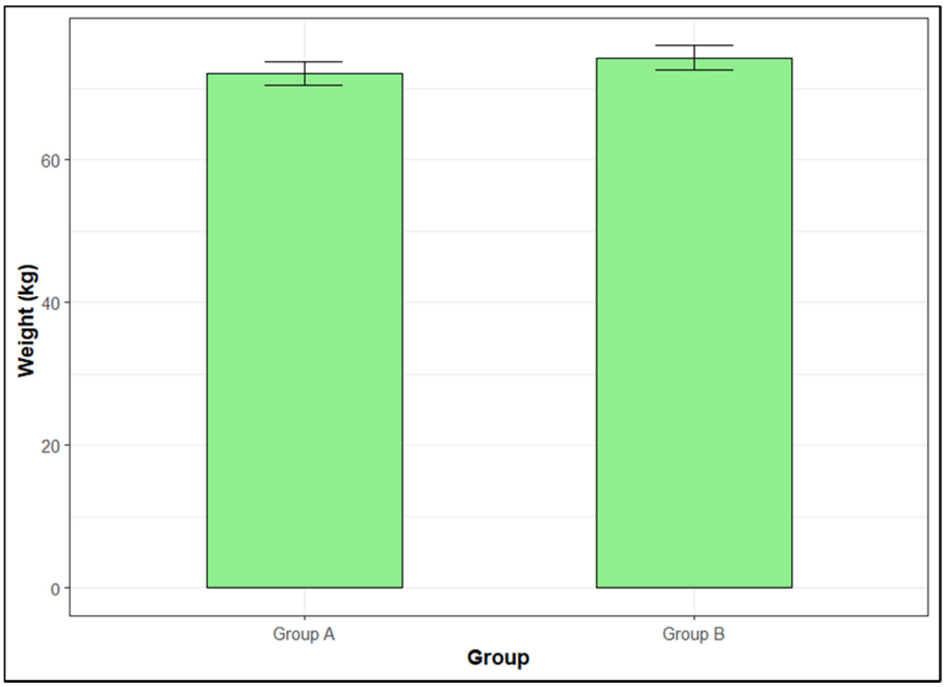


Figure 4: Mean plot of weight distribution

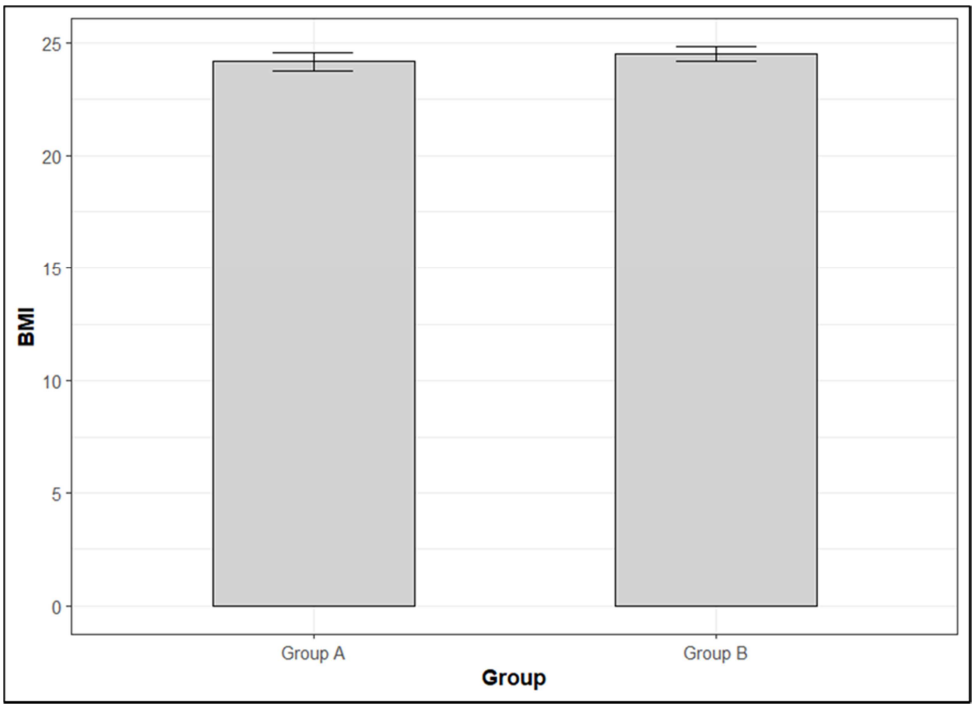


Figure 5: Mean plot of BMI distribution

Table 3: Comparison of duration of surgery

Variables	Sub-Category	Group-A	Group-B	Total	p-value
Duration of surgery in minutes	Mean ± SD Median	61.33 ± 7.9 60	61.73 ± 9.13 60	61.53 ± 8.51 60	0.7265

The mean duration of surgery for Group-A is 61.33 ± 7.9 minutes, and the median duration is 60 minutes, ranging from a minimum of 45 minutes to a maximum of 80 minutes. Group-B has a mean surgery duration of 61.73 ± 9.13 minutes, and the median is also 60 minutes, ranging from 45 to 85 minutes. It was observed that there is no significant difference in the mean duration of surgery between the two groups (p-value = 0.7265).

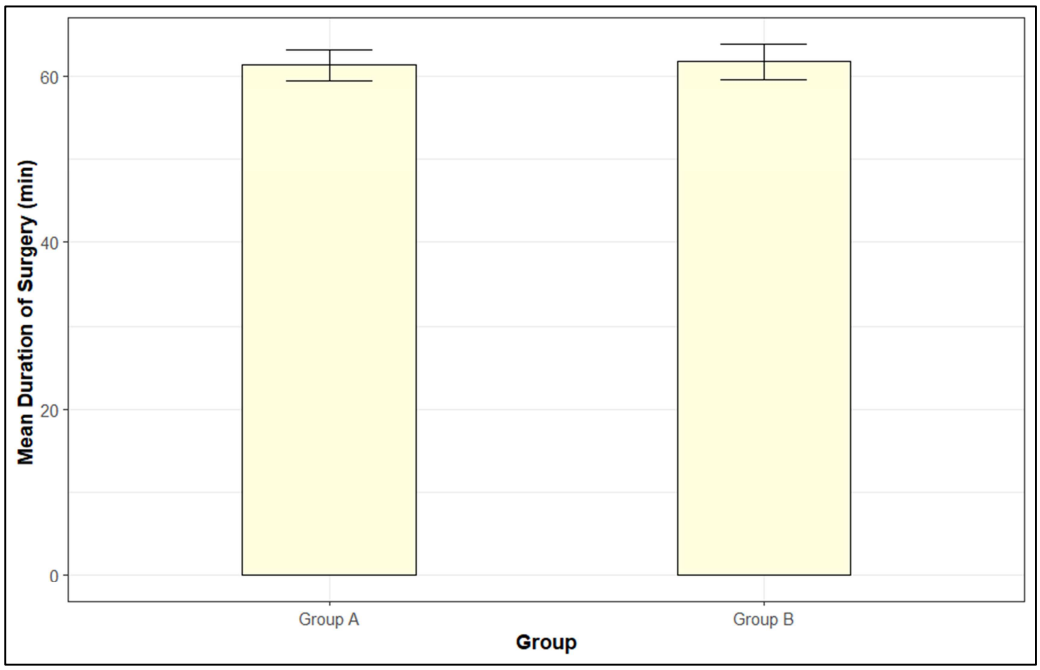


Figure 6: Mean plot of mean duration of surgery

Table 4: Comparision of core body temperature

Time points	Group-A	Group-B	Total	p-value
Baseline	36.73 ± 0.43 36.7	36.72 ± 0.45 36.6	36.73 ± 0.44 36.7	0.7826
1min	36.76 ± 0.42 36.6	36.74 ± 0.43 36.6	36.75 ± 0.42 36.6	0.7949
5 mins	36.74 ± 0.43 36.6	36.72 ± 0.44 36.6	36.73 ± 0.43 36.6	0.8311
10 mins	36.78 ± 0.42 36.7	36.72 ± 0.44 36.6	36.75 ± 0.43 36.6	0.4134
15 mins	36.71 ± 0.42 36.7	36.69 ± 0.44 36.6	36.7 ± 0.43 36.65	0.8232
30 mins	36.74 ± 0.41 36.7	36.72 ± 0.42 36.6	36.73 ± 0.41 36.7	0.7390
45 mins	36.73 ± 0.47 36.7	36.74 ± 0.47 36.7	36.74 ± 0.47 36.7	0.8901
60 mins	36.75 ± 0.44 36.7	36.73 ± 0.45 36.7	36.74 ± 0.44 36.7	0.8960
90 mins	36.75 ± 0.44 36.7	36.73 ± 0.45 36.7	36.74 ± 0.44 36.7	0.8960
p-value	0.2141	0.4402	-	-

There was no statistically significant differences in core body temperature in Group-A and Group-B at any time point of study duration (p-value > 0.05) and no significant differences in core body temperature were noted over time for Group-A (p-value = 0.2141) or Group-B (p-value = 0.4402).

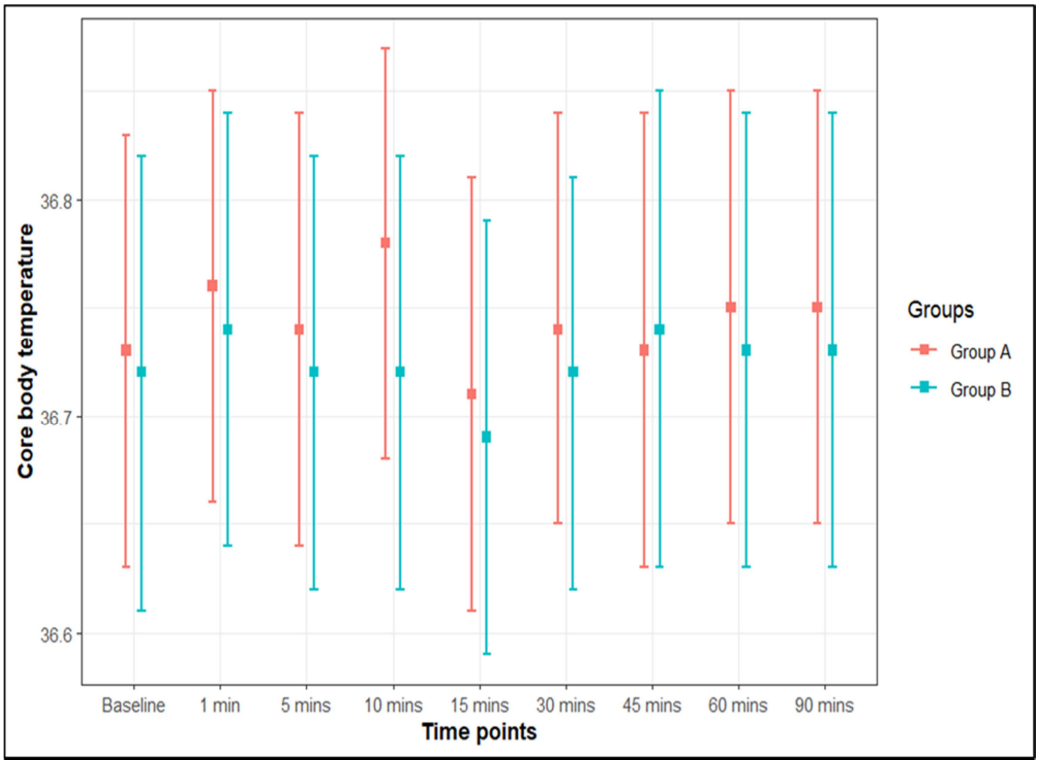


Figure 7: Mean plot of core body temperature

Table 5: Comparison of skin temperature

Time points	Group-A	Group-B	Total	p-value
Baseline	36.78 ± 0.43 36.8	36.76 ± 0.42 36.8	36.77 ± 0.43 36.8	0.8360
1min	36.72 ± 0.41 36.6	36.71 ± 0.43 36.7	36.72 ± 0.42 36.65	0.9909
5 mins	36.74 ± 0.39 36.8	36.75 ± 0.42 36.8	36.75 ± 0.4 36.8	0.9032
10 mins	36.75 ± 0.39 36.8	36.75 ± 0.42 36.8	36.75 ± 0.41 36.8	0.9289
15 mins	36.7 ± 0.38 36.6	36.72 ± 0.38 36.7	36.71 ± 0.38 36.7	0.7738
30 mins	36.71 ± 0.38 36.6	36.73 ± 0.35 36.6	36.72 ± 0.36 36.6	0.9118
45 mins	36.67 ± 0.48 36.7	36.73 ± 0.39 36.7	36.7 ± 0.44 36.7	0.4905
60 mins	36.64 ± 0.51 36.6	36.71 ± 0.42 36.7	36.68 ± 0.47 36.7	0.4215
90 mins	36.64 ± 0.51 36.6	36.71 ± 0.42 36.7	36.68 ± 0.47 36.7	0.4215
p-value	0.0756	0.1559	-	-

It is observed that, there is no statistically significant differences in skin temperature between Group-A and Group-B at any time point (p-value > 0.05 for all time points). There were no significant differences in skin temperature over time for Group-A (p-value = 0.0756) or Group-B (p-value = 0.1559).

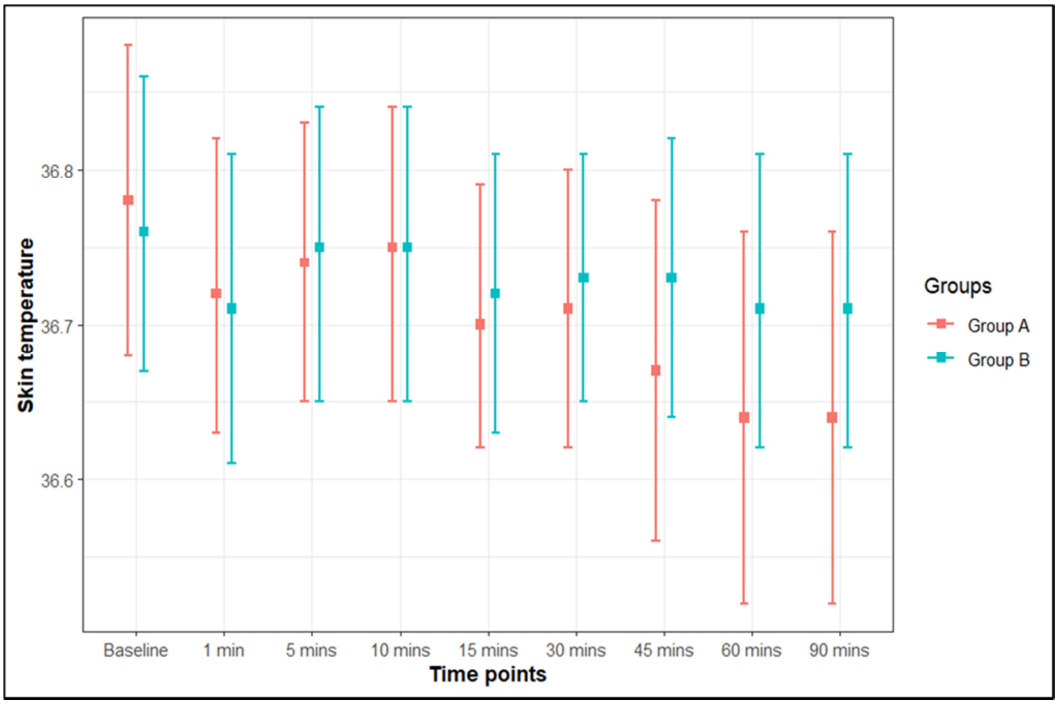


Figure 8: Mean plot of skin temperature

Table 6: Comparison of shivering grades

Time points	Group-A				Group-B				p-value
	0	**1**	**2**	**3**	**0**	**1**	**2**	**3**	
Baseline	75 (100%)	0	0	0	75 (100%)	0	0	0	1
1 min	72 (96%)	2 (2.67%)	1 (1.33%)	0	71 (94.67%)	3 (4%)	1 (1.33%)	0	0.9999
5 mins	47 (62.67%)	24 (32%)	4 (5.33%)	0	44 (58.67%)	25 (33.33%)	6 (8%)	0	0.7713
10 mins	47 (62.67%)	23 (30.67%)	5 (6.67%)	0	43 (57.33%)	23 (30.67%)	9 (12%)	0	0.5167
15 mins	35 (46.67%)	25 (33.33%)	14 (18.67%)	0	34 (45.33%)	23 (30.67%)	18 (24%)	0	0.7441
30 mins	40 (53.33%)	24 (32%)	10 (13.33%)	1 (1.33%)	44 (58.67%)	18 (24%)	13 (17.33%)	0	0.4993
45 mins	64 (85.33%)	8 (10.67%)	2 (2.67%)	0	70 (93.33%)	3 (4%)	2 (2.67%)	0	0.3718
60 mins	73 (97.33%)	1 (1.33%)	1 (1.33%)	0	73 (97.33%)	1 (1.33%)	1 (1.33%)	0	0.9999
90 mins	73 (97.33%)	1 (1.33%)	1 (1.33%)	0	73 (97.33%)	1 (1.33%)	1 (1.33%)	0	0.9999

At baseline, all participants had a shivering grade of 0. Over time, the majority maintained a shivering grade of 0, with no significant differences between Group A and Group B. At 30 minutes, 53.33% of Group A and 58.67% of Group B had grade 0. At 45 minutes, 85.33% of Group A and 93.33% of Group B had grade 0. By 60 minutes, 97.33% of both groups had grade 0. No significant differences in shivering grades were observed between the groups at any time point.

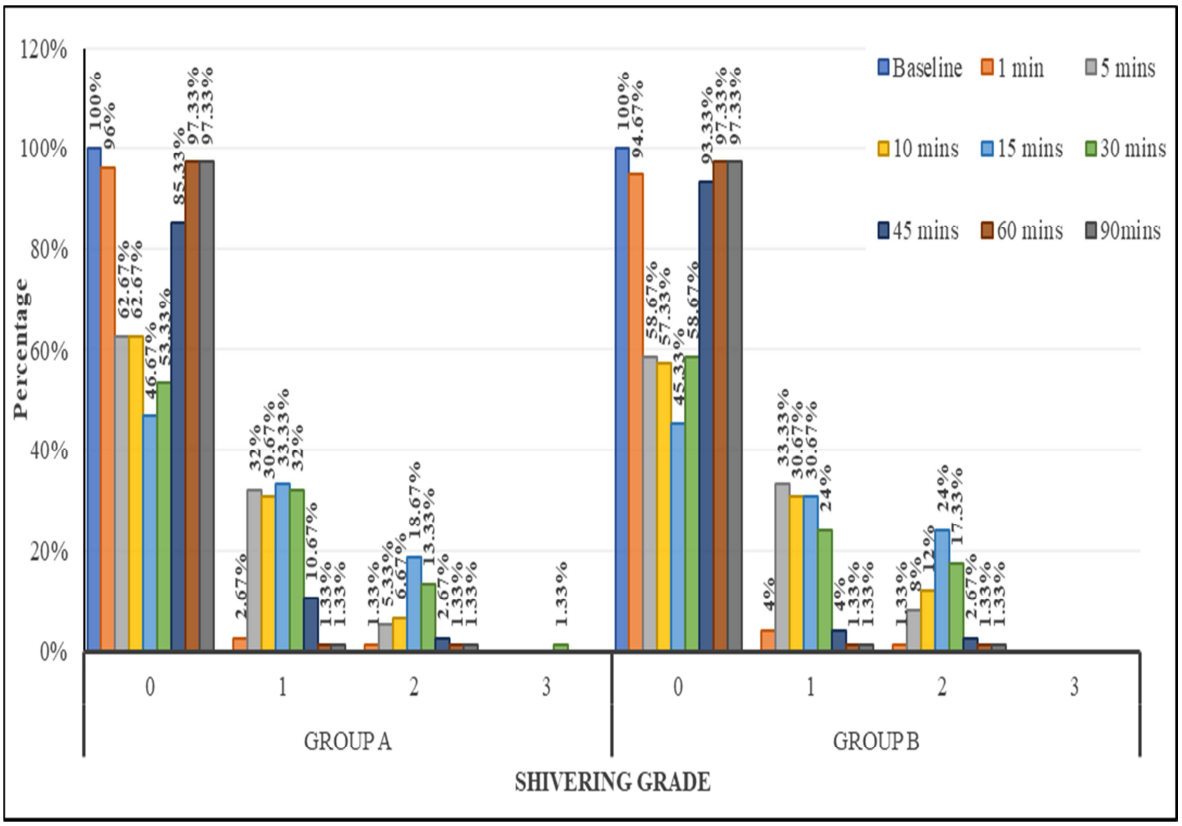


Figure 9:Distribution of shivering grade over time and groups

Table 7: Comparison of sedation score

Time points	Group-A				Group-B				p-value
	0	**1**	**2**	**3**	**0**	**1**	**2**	**3**	
Baseline	75 (100%)	0	0	0	75 (100%)	0	0	0	1
1 min	71 (94.67%)	3 (4%)	1 (1.33%)	0	71 (94.67%)	3 (4%)	1 (1.33%)	0	1
5 mins	61 (81.33%)	9 (12%)	4 (5.33%)	1 (1.33%)	60 (80%)	9 (12%)	5 (6.67%)	1 (1.33%)	0.9999
10 mins	61 (81.33%)	9 (12%)	4 (5.33%)	1 (1.33%)	60 (80%)	9 (12%)	5 (6.67%)	1 (1.33%)	0.9999
15 mins	56 (74.67%)	10 (13.33%)	8 (10.67%)	1 (1.33%)	55 (73.33%)	10 (13.33%)	9 (12%)	1 (1.33%)	0.9999
30 mins	58 (77.33%)	6 (8%)	7 (9.33%)	4 (5.33%)	57 (76%)	6 (8%)	8 (10.67%)	4 (5.33%)	0.9999
45 mins	58 (77.33%)	7 (9.33%)	6 (8%)	4 (5.33%)	57 (76%)	7 (9.33%)	7 (9.33%)	4 (5.33%)	0.9999
60 mins	60 (80%)	2 (2.67%)	10 (13.33%)	3 (4%)	60 (80%)	2 (2.67%)	9 (12%)	4 (5.33%)	1
90 mins	60 (80%)	2 (2.67%)	10 (13.33%)	3 (4%)	60 (80%)	2 (2.67%)	9 (12%)	4 (5.33%)	1

At baseline, all participants had a sedation score of 0. At 1 minute, 94.67% still had a score of 0, with 4% scoring 1 and 1.33% scoring 2. This trend continued at 5 and 10 minutes with around 80% in both groups having a score of 0. By 15, 30, and 45 minutes, roughly 75% of both groups had a score of 0, and by 60 minutes, 62.67% had a score of 0. There were no statistically significant differences in sedation scores between the groups at any time point.

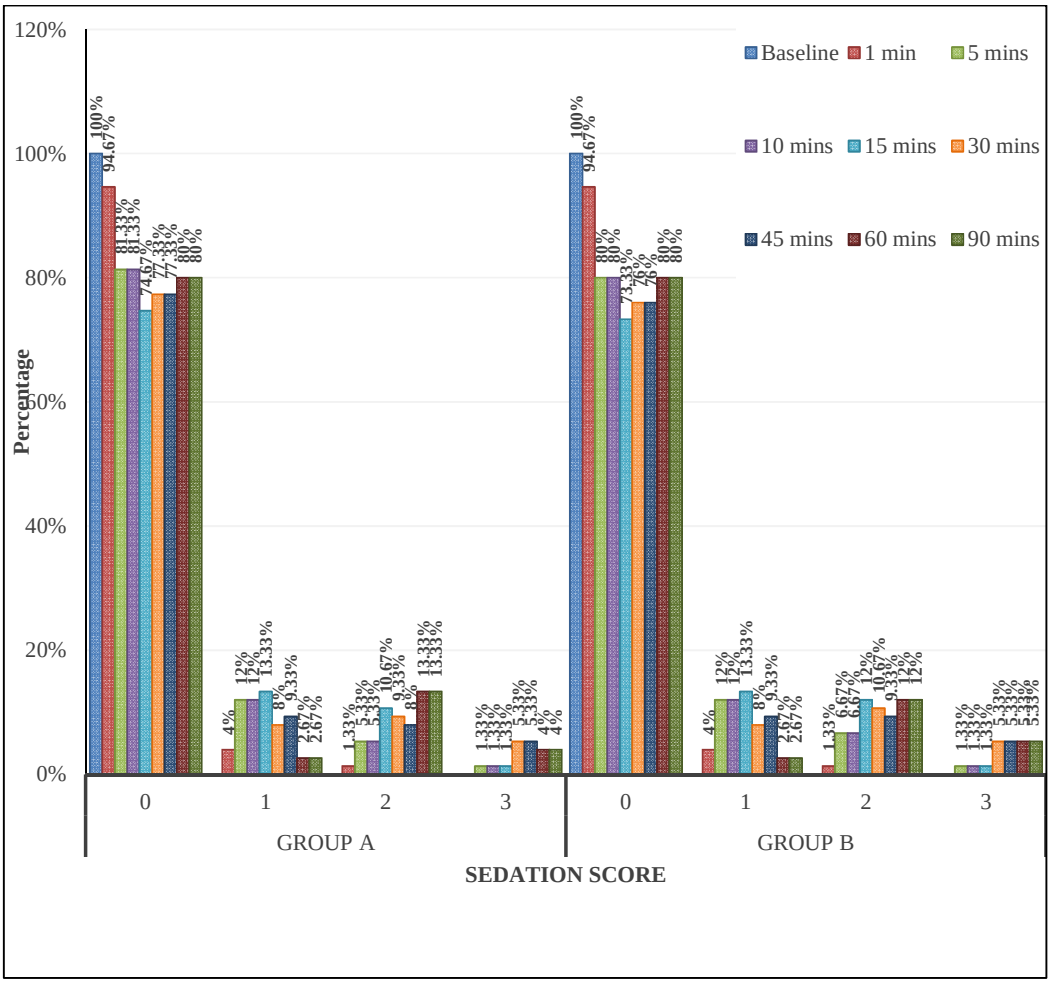


Figure 10: Mean plot of sedation score

Table 8: Comparison of the need for additional measures and side effects

Variables	Sub Category	Group-A	Group-B	Total	p-value
Need for additional measures	No	74 (98.67%)	74 (98.67%)	148 (98.67%)	1
	Yes	1 (1.33%)	1 (1.33%)	2 (1.33%)	
Side effects	Nil	75 (100%)	75 (100%)	150 (100%)	1

The vast majority of participants in both groups did not require any additional interventions, with 98.67% of participants in each group reporting no need for additional measures. Only a very small proportion of participants in each group (1.33%) required additional measures. Similarly, regarding side effects, all participants in both Group-A and Group-B reported experiencing no side effects. However it is observed that, there is no significant difference in the distribution of need for additional measures and side effects over groups.

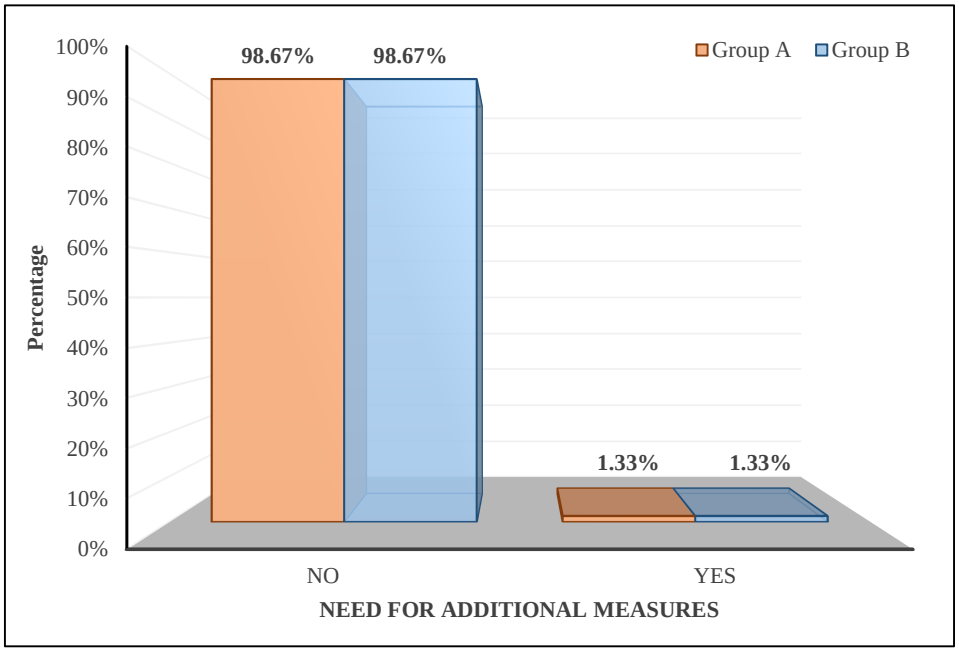


Figure 11: Distribution of need for additional measures

DISCUSSION

The core body temperature of human beings ranges between 36.5˚ C and 37.5˚ C. The autonomic nervous system maintains this core temperature with behavioral and physiological responses. Subarchanoid block impairs thermoregulation by abolishing tonic vasoconstriction below the blocked segments and also causes the redistribution of body heat from the center to periphery leading to intraoperative hypothermia and shivering. [32,33]

Shivering is incredibly uncomfortable, according to many patients, who even find that the cold feeling that follows is worse than the pain from the surgery. Shivering often raises oxygen demand for metabolism and interferes with monitoring methods. [9-13]

There many treatment modalities for shivering. Unfortunately the established guidelines for treatment options are rarely found in the available literature data. Among all pharmacological and non-pharmacological methods, ASA recommendations on use of forced air warming and pethidine have been considered as reliable and acceptable strategies.[34]

Apart from Pethidine, various other opioid medications have been studied and suggested for management of shivering, but certain side effects like sedation, nausea, vomiting, hypotension and respiratory depression.[4,6,9,13] Many reports suggesting use of lower dose of intravenous Tramadol administered immediately after establishment of subarchanoid block for prevention and treatment of shivering have proven its efficacy with fewer side -effect profiles.[14, 16, 35] Oral Tramadol is a simple, cost effective and readily available preparation, being considered for clinical trials as an

prophylactic measure against intraoperative shivering following subarchanoid block.[3,23]

Tramadol is a synthetic opioid displaying dual action of being a mu receptor agonist and weak inhibitor of norepinephrine and 5-hydroxytryptamine(5-HT) neuronal uptake. After oral administration, the bioavailability of Tramadol in adults is 68% and it is 20% protein bound. There are numerous well established reviews narrating role of 5-hydroxytryptamine receptors in the thermoregulation mechanisms in humans. The preoptic nucleus of hypothalamus releases 5-HT3 to activate heat production thereby increasing body temperature. 5-HT antagonists like Tramadol might prevent perioperative shivering by inhibiting reuptake of -HT in the preoptic areas of brain.[4,5,9,36] Tramadol also reportedly inhibits NMDA receptors at clinically useful concentrations.[4] Hereby we assume that tramadol also has effects in decreasing core to peripheral heat distribution.

The newer opioid analogue Tapentadol available exclusively in oral form has its mechanism of action similar to tramadol on noradrenaline reuptake and approximately five times less potent as tramadol on 5-HT reuptake. In vitro studes suggests that dual actions of Tramadol contribute to its analgesic properties and whereas noradrenergic activity of Tapentadol likely to be more important than serotonergic activity. However, in vivo studies in humans suggest Tapentadol is said to be as potent as Tramadol with greater gastrointestinal tolerability.[31,37]

The incidence of shivering among both Tramadol and Tapentadol groups were similar in our study and were statistically insignificant. All patients in both the groups patients experienced only either grade 1 or 2 of shivering with onset at 15 minutes following subarchanoid block. More than 98% of study population didn't require

additional rescue measures for treatment of intraoperative shivering. Most episodes of shivering occurred within first 30 minutes of subarchanoid block and shivering lasted for next 15 to 30 minutes. Maximal redistribution of heat from center to periphery takes place within first 1 hour following subarchanoid block.[38]

This results in intraoperative hypothermia and shivering thermogenesis. The study drugs used do not have any thermogenic properties. So, their antishivering effects may be related to lowering the threshold of shivering. The study results suggests both Tramadol and Tapentadol can be considered for prophylactic therapy against perioperative shivering following subarchanoid block.

Tramadol, like other opioid analgesics is frequently associated with nausea and vomiting, our study did not report any significant adverse effects following oral administration of Tramadol. Similarly, incidence of nausea and vomiting was significantly lower with Tapentadol. None of the patients in either group experienced respiratory depression. Both medications demonstrated better tolerability than traditional strong opioids. Although the results on the efficacy and safety of Tramadol and Tapentadol in the study population is reassuring, there is still insufficient evidence to support their use in vulnerable geriatric patients.

Many research studies have evaluated the role of Tapentadol as a potent analgesic drug for prevention of chronic pain and early postoperative pain.[17-19, 27,28] The current study is the first attempt to investigate its efficacy as an antishivering agent in perioperative settings as Tapentadol shares similar mechanism of action in the central nervous system.

LIMITATIONS

Although advanced age and extent of subarchanoid block are critical factors for prediction of hypothermia, several other factors like ambient temperature, body composition, amount of blood loss, duration of surgery and volume of irrigation fluids are significant for determining the magnitude of hypothermia. A fixed dose of study drugs was used as premedication for whole study population. However, this might not have confounded the results considering the statistically comparable BMI among both the groups. In addition, the study period was limited to duration of surgery. Incidence of hypothermia following neuraxial anaesthesia increases significantly in the postoperative period ranging 60% to 90%.

CONCLUSION

Both oral Tramadol and oral Tapentadol are equally effective in prevention of perioperative shivering in patients undergoing TURP under subarachnoid block.

SUMMARY

In this study, we compare the effectiveness of oral Tramadol and oral Tapentadol as premedications in preventing peri-operative shivering among patients undergoing Transurethral Resection of the Prostate under spinal anesthesia.

The study was carried out in male patients belonging to ASA grade 1,2 undergoing Transurethral resection of the Prostate under subarachnoid Block. The patients were allocated in a randomized manner by opening a "sealed envelope method" into two groups, group A (Tramadol, n=75) and group B (Tapentadol, n=75). The demographic data were comparable in both groups.

Under strict aseptic precautions, subarachnoid block with a sensory blockade up to T9-10 level is achieved using hyperbaric levobupivacaine (0.5%) 2-3ml.

Heart rate, non-invasive blood pressure, respiratory rate, arterial oxygen saturation, forehead skin temperature (measured with the Braun BNT400® thermometer), and core temperature (assessed via tympanic membrane temperature using the Braun Thermoscan®) were recorded at 5-minute intervals beginning 5 minutes prior to the subarachnoid block and continued for 1 hour. Subsequently, measurements were taken every 10 minutes for the duration of the observation period.

Shivering is recorded by the same attending anaesthesiologist at a period of 0, 1, 5, 10, 15, 30, 45, 60 and 90minutes from the baseline.

The sedative side effects of study drugs were assessed with a four-point sedation score.

Both oral Tramadol and oral Tapentadol demonstrated comparable efficacy in preventing perioperative shivering in patients undergoing TURP under subarachnoid block. Neither drug was superior in terms of reducing shivering, and both exhibited a similar safety profile with no significant adverse effects.

BIBLIOGRAPHY

1. O'Donnell AM, Irwin TH. Anaesthesia for transurethral resection of the prostate. Contin Educ Anaesth Crit Care Pain. 2009;9(3):92-6.
2. Reeves MD, Myles PS. Does anaesthetic technique affect the outcome after transurethral resection of the prostate? BJU Int. 1999;84:982-6.
3. Tewari A, Dhawan I, Garg S. Use of oral tramadol to prevent perianesthetic shivering in patients undergoing transurethral resection of prostate under subarchanoid blockade. Saudi J Anaesth. 2014;8(1):11-6.
4. Lopez MB. Postanaesthetic shivering—From pathophysiology to prevention. Rom J Anaesth Intensive Care. 2018;25:73–81.
5. De Witte J, Sessler DI. Perioperative shivering: Physiology and pharmacology. Anesthesiology. 2002;96:467–84.
6. Tsai YC, Chu KS. A comparison of tramadol, amitriptyline, and meperidine for postepidural anesthetic shivering in parturients. Anesth Analg. 2001;93:1288-92.
7. Abdelrahman RS. Prevention of shivering during regional anaesthesia: comparison of midazolam, midazolam plus ketamine, tramadol, and tramadol plus ketamine. Life Sci J. 2012;9(2):132-9.
8. 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-blinded placebo controlled trial. Br J Anaesth. 2008;101(4):557-62.
9. Witte JD, Sessler DI. Perioperative shivering: physiology and pharmacology. Anesthesiology. 2002;96:467-84.

10. Kurz A, Sessler DI, Narzt E, Bekar A, Lenhardt R, et al. Postoperative hemodynamic and thermoregulatory consequences of intraoperative core hypothermia. J Clin Anesth. 1995;7:359-66.
11. Morris RH, Wilkey BR. The effects of ambient temperature on patient temperature during surgery not involving body cavities. Anesthesiology. 1970;32:102-7.
12. Lopez MB. Postanaesthetic shivering – from pathophysiology to prevention. Rom J Anaesth Intensive Care. 2018;25(1):73-81.
13. Alfonsi P. Postanaesthetic shivering. Epidemiology, pathophysiology and approaches to prevention and management. Minerva Anestesiol. 2003;69:438-42.
14. Bilotta F, Pietropaoli P, Sanita R, Liberatori G, Rosa G. Nefopam and tramadol for the prevention of shivering during neuraxial anesthesia. Reg Anesth Pain Med. 2002;27:380-4.
15. Adinehmehr L, Salimi S, Majedi MA, Alizadeh A, Sane S. Comparison the effects of oral tizanidine and tramadol on intra and postoperative shivering in patients underwent spinal anesthesia. Adv Biomed Res. 2018;7:140.
16. Lakhe G, Adhikari KM, Khatri K, Maharjan A, Bajracharya A, et al. Prevention of shivering during spinal anesthesia: comparison between tramadol, ketamine and ondansetron. J Nepal Med Assoc. 2017;56(208):395-400.
17. Singh DR, Nag K, Krishnaveni N. Tapentadol: A novel analgesic. Saudi J Anaesth. 2013;7(3):322-6.

18. Iyer SK, Mohan G, Ramakrishnan S, Theodore S. Comparison of tapentadol with tramadol for analgesia after cardiac surgery. Ann Card Anaesth. 2015;18:352-60.
19. Guillen-Astete CA, Cardona-Carballo C, Casa-Resino CD. Tapentadol versus tramadol in the management of low back pain in the emergency department. Medicine (Baltimore). 2017;96:45.
20. Sato H. Raphe-spinal and subcoeruleospinal modulation of temperature signal transmission in rats. J Therm Biol. 1993;18:211-21.
21. Bamigbade TA, Davidson C, Langford RM, Stamford JA. Actions of tramadol, its enantiomers and principal metabolite, odesmethyltramadol, on serotonin (5-HT) efflux and uptake in the rat dorsal raphe nucleus. Br J Anaesth. 1997;79:352-6.
22. Mathews S, Mulla AA, Varghese PK, Radim K, Mumtaz S. Postanaesthetic shivering – a new look at tramadol. Anaesthesia. 2002;57(4):387-403.
23. Nain P, Kundra S, Singh T, Singh MR, Kapoor R, et al. Comparative evaluation of oral tramadol and gabapentin for prophylaxis for post-spinal shivering. Indian J Anaesth. 2021;65(1):5-11.
24. Javaherforoosh F, Akhondzadeh R, Aein KB, Olapour A, Samimi M. Effects of Tramadol on shivering post spinal anesthesia in elective cesarean section. Pak J Med Sci. 2009;25(1):12-7.
25. Tzschentke TM, Christoph T, Schroder W, Englberger W, Jahnel JD, et al. Tapentadol: with two mechanisms of action in one molecule effective against nociceptive and neuropathic pain. Preclinical overview. Schmerz. 2011;25(1):19-25.

26. Pergolizzi JV, Taylor R, Bisney J. Tapentadol extended release in the treatment of severe chronic low back pain and osteoarthritis pain. Pain Ther. 2018;7(1):37-57.
27. Sanchez Del Aguila MJ, Schenk M, Kern KU, Drost T, Steigerwald I. Practical considerations for the use of tapentadol prolonged release for the management of severe chronic pain. Clin Ther. 2014;37(1):94-113.
28. Gedela V, Gururaj S. A prospective double blind randomized comparative study of safety and efficacy of tapentadol versus tramadol in postoperative orthopaedic patients. Int J Basic Clin Pharmacol. 2017;6:2727-32.
29. Saini RK, Raw BK, Yadav DK, Singh V, Mishra LS. A randomized controlled double-blind study to evaluate the efficacy of prophylactic dose of oral clonidine vs oral tapentadol for perioperative shivering and post-operative analgesia in elective surgeries under spinal anaesthesia. Int J Sci Res. 2018;7(12):11-4.
30. Bindal K, Kumar N, Oberoi D, Biswas M. Comparison between pre-emptive oral tramadol and tapentadol for attenuation of catheter-related bladder discomfort and surgical stress response in patients undergoing transurethral resection of prostate: A prospective, randomised, double-blind trial. Indian J Anaesth. 2021;65(4):156-62.
31. Roulet L, Rollason V, Desmeules J, Piguet V. Tapentadol versus tramadol: A narrative and comparative review of their pharmacological, efficacy and safety profiles in adult patients. Drugs. 2021;81(11):1257-72.32. Crowley LJ, Buggy DJ. Shivering and neuraxial anesthesia. Reg Anesth Pain Med. 2008;33:241-52.

32. Crowley LJ, Buggy DJ. Shivering and neuraxial anesthesia. Reg Anesth Pain Med. 2008;33:241-52.
33. Lee C, Choi DH, Chae SU. Circadian effects of neural blockade of intrathecal hyperbaric bupivacaine. Korean J Pain. 2010;23:186-9.
34. Choi KE, Park B, Moheet AM, Rosen A, Lahiri S, et al. Systematic quality assessment of published antishivering protocols. Anesth Analg. 2017;124:1539-46.
35. Tobi KU, Edomwonyi NP, Imarengiaye CO. Tramadol effects on perioperative shivering in lower limb orthopaedic surgeries under spinal anaesthesia. J West Afr Coll Surg, 2012;2(2):46-62.
36. Voronova IP. 5-HT receptors and temperature homeostasis. Biomolecules. 2021;11(12):1914.
37. Raffa RB, Buschmann H, Christoph T, Eichenbaum G, Englberger W, et al. Mechanistic and functional differentiation of tapentadol and tramadol. Expert Opin Pharmacother. 2012;13(10):1437-49.
38. Frank SM, El-Rahmany HK, Cattaneo CG, Barnes RA. Predictors of hypothermia9during spinal anesthesia. Anesthesiology 2000;92:1330-34.
39. Temperature Monitoring. OpenAnesthesia [Internet]. 2024 [cited 2024 Jun 28]. Available from: https://openanesthesia.org/temperature-monitoring
40. Rauch S, Miller C, Bräuer A, Wallner B, Bock M, Paal P. Perioperative hypothermia: a narrative review. Int J Environ Res Public Health. 2021 Aug 19;18(16):8749.
41. Díaz-Redondo A, Soler-Queralt A, Pallarés-Carratalá V. Perioperative thermoregulation and heat balance in anesthesia. Br J Anaesth Educ. 2018;18(7):213-9.

ANNEXURE-I

INFORMED CONSENT FORM

KAHERs JNMC BELAGAVI

"A COMPARISON OF ORAL TRAMADOL AND ORAL TAPENTADOL FOR PREVENTION OF PERIOPERATIVE SHIVERING DURING SUBARACHNOID BLOCK IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF PROSTATE-A RANDOMIZED CONTROL TRIAL"

Name of Student/Principal Investigator:

Name of Guide/Co Investigators:

Objective: To compare oral Tramadol and oral Tapentadol as a premedicant to prevent perioperative shivering following subarachnoid block in patients undergoing Transurethral Resection of Prostate.

Introduction: Mr./Mrs._____ we are requesting you to enroll yourself in the study titled"**A COMPARISON OF ORAL TRAMADOL AND ORAL TAPENTADOL FOR PREVENTION OF PERIOPERATIVE SHIVERING DURING SUBARACHNOID BLOCK IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF PROSTATE-A RANDOMIZED CONTROL TRIAL."** conducted by Dr._____Post Graduate in M.D. Anaesthesiology under the guidance of Dr. _____ M.D,Associate Professor, Department of Anaesthesiology, J.N. Medical College, Belagavi under KLE University, Belagavi.

Explanation of procedure: If you agree to enroll in my study, I will ask you the present and past medical history. Then you will be clinically examined in detail. On the

day of surgery, a sealed envelope will be handed over to you by the anaesthesia technician containing either of the drug which has to be consumed with sips of water 90mins prior to the surgery.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: "Name of student/PI, mobile number, email ID" If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "**A COMPARISON OF ORAL TRAMADOL AND ORAL TAPENTADOL FOR PREVENTION OF PERIOPERATIVE SHIVERING DURING SUBARACHNOID BLOCK IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF PROSTATE-A RANDOMIZED CONTROL TRIAL**". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE-II

PROFORMA

Project Title: "A COMPARISON OF ORAL TRAMADOL AND ORAL TAPENTADOL FOR PREVENTION OF PERIOPERATIVE SHIVERING DURING SUBARACHNOID BLOCK IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF PROSTATE-A RANDOMIZED CONTROL TRIAL"

Patient's Name : I.P No. :

Age : Date of Examination :

Gender : Anaesthesiologist :

Address :

Pre-anesthetic evaluation:

Chief complaints:

HOPI:

Past History:

- H/o co-morbidities and drug intake :
- H/o previous surgery/(s) where difficult airway was encountered :
- Previous anaesthetic experience :

Family History:

General physical examination:

Height (cm) : Weight (Kg): BMI :

Pallor : Icterus :

Cyanosis : Clubbing :

PR : RR : SpO2 :

Systemic examination:

RS:

CVS:

CNS:

GIT:

Airway Assessment:

Teeth:

Jaw movements:

Local examination:

Investigations:

Hb(gm/dl): TLC: Platelet count:

Serum Creatinine: FBS: PT/INR:

Chest x-ray: ECG:

Preoperative physical status: ASA Grade I II

Diagnosis:

Proposed surgery:TURP

Inclusion Criteria:

- ASA Status 1,2
- Age between 50-80 years
- Patients undergoing Transurethral Resection of Prostate under Subarachnoid Block

Exclusion Criteria:

- Patient refusal or who are unable to give consent.
- Obesity (BMI>=30)
- Presence of febrile illness
- Patients with known allergy to either drug
- Neuro-behavioral Disorders
- Severe diabetic/autonomic neuropathy
- Patients on vasodilator medications

METHODOLOGY

After obtaining institutional ethical committee, this prospective, randomized, double blinded study is carried out on 150 patients (American Society of Anaesthesiologists [ASA] physical status I, II) undergoing transurethral resection of prostate under subarachnoid block during one year study period between July 2022 to June 2023.

Patients are allocated in a randomized manner by ‘opening a sealed envelope’ method into two groups,

a) group A (Tramadol, n=75)

b) group B (Tapentadol, n=75)

An informed, written consent is obtained from patients during preanaesthetic check up one day prior to surgery.

Group 1 received oral Tramadol 50mg, while group 2 received oral Tapentadol 50mg with sips of water 90minutes prior to surgery.

Anaesthesia technicians who were not involved in the study prepared trial preparations and recorded the group randomization. Patients and treating anaesthesiologists are unaware of the preparations administered.

Under strict aseptic precautions, subarachnoid block with a sensory blockade up to T9-10 level is achieved using hyperbaric levobupivacaine (0.5%) 2-3ml.

All surgeries are performed in the same operation theatre, which is maintained at a constant humidity and ambient temperature. The operating room is not equipped to provide laminar flow. No means of active rewarming is used unless deemed essential for rescue measures. Pre-warmed (up to the body temperature) intravenous and irrigating fluids are used.

Heart rate, non-invasive blood pressure, respiratory rate, arterial oxygen saturation, skin temperature (forehead, using the Braun BNT400® thermometer) and core temperature (tympanic membrane temperature using the Braun Thermoscan®) are recorded every 5min from the baseline (5minutes prior to subarachnoid block) for 1h and thereafter every 10min for the rest of the observation period.

Shivering is recorded by the same attending anaesthesiologist at a period of 0, 1, 5, 10, 15, 30, 45, 60 and 90minutes from the baseline as per grades given by Wrench et al.Grading of shivering as per Wrench et al.

Grade 0: No shivering observed

Grade 1: One or more of piloerection; peripheral cyanosis without other cause, but without visible muscular activity

Grade 2: Visible muscle activity confined to one muscle group

Grade 3: Visible muscle activity in more than one muscle groups

Grade 4: Gross muscular activity involving the entire body

Perioperatively if shivering occurred, it is treated in the same manner in both groups with reassurance, warming blanket or IV Pethidine depending on the intensity of shivering. Forced air warming blankets are made available when necessary.

Complications such as nausea, vomiting, bradycardia and hypotension are appropriately treated with IV Atropine and Mephentermine respectively in titrated doses when required. Nausea and vomiting is treated with IV Ondansetron.

The sedative side-effects of study drugs are assessed with a four-point sedation score as per Filos et al.

Sedation score as per Filos et al.

Score 1: Awake and alert

Score 2: Drowsy, responsive to verbal stimuli

Score 3: Drowsy, arousable to physical stimuli

Score 4: Unarousable

OBSERVATION

GROUP OF DRUG:

TIME	**CORE BODY TEMPERATURE (DEG CELCIUS)**	**SKIN TEMPERATURE (DEG CELCIUS)**	**SHIVERING GRADE**	**SEDATION SCORE**
BASELINE				
1 MIN				
5 MINS				
15 MINS				
30 MINS				
45 MINS				
60 MINS				
90 MINS				

Need for any additional measures-

Side Effects of the drug if any-

ANNEXURE-III

PHOTOGRAPHS

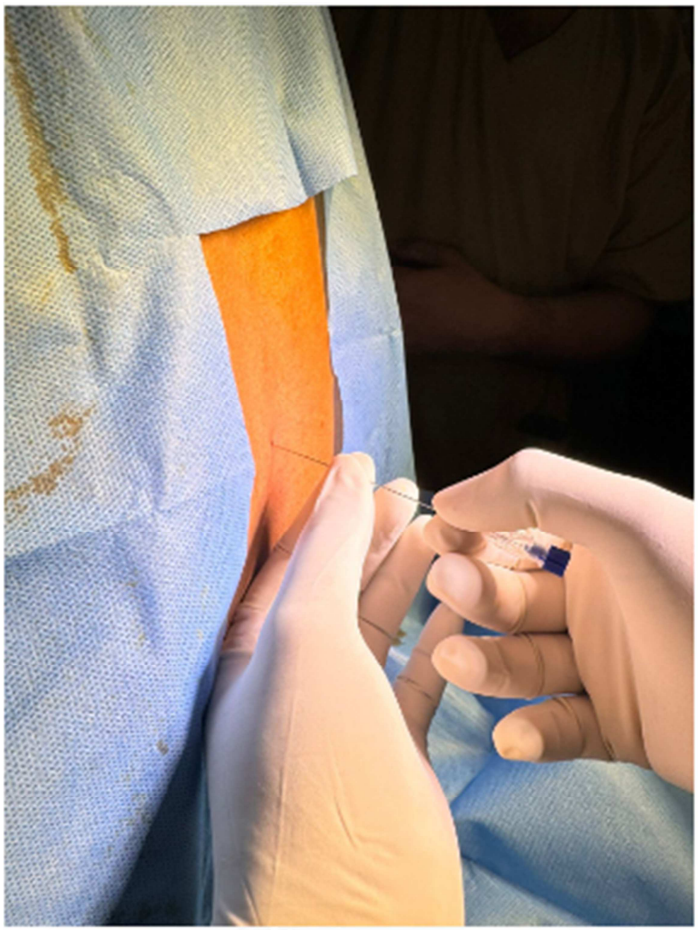
PHOTOGRAPH 1- TABLET TRAMADOL 50 mg

PHOTOGRAPH 2- TABLET TAPENTADOL 50 mg

PHOTOGRAPH 3– BRAUN TYMPANIC MEMBRANE THERMOMETER

PHOTOGRAPH 4– BRAUN FOREHEAD THERMOMETER

PHOTOGRAPH 5-ADMINISTRATION OF SPINAL ANAESTHESIA



ANNEXURE IV- MASTER CHARTS

TABLE - A

s.no	Age(years)	Age	Gender	ASAGrade	Height	Weight	BMI	MeanDurationofSurgery	CBTBaseline	CBT1min	CBT5min	CBT10min	CBT15min	CBT30min	CBT45min	CBT60min	CBT90min	STBaseline	ST1min	ST5min	ST10min	ST15min	ST30min	ST45min	ST60min	ST90min	SGBaseline	SG1min	SG5min	SG10min	SG15min	SG30min	SG45min	SG60min	SG90min	SSBaseline	SS1min	SS5min	SS10min	SS15min	SS30min	SS45min	SS60min	SS90min	NeedForAdditionalMeasure	AdditionalMeasure	Sideeffect	Group
1	56years	56	Male	1	173	76	25.4	45	37.4	37.4	38.4	38.4	38.4	38.2	38.2	38.2	38.2	37.4	37.4	37.4	37.4	37.4	37.4	37.2	37.2	37.2	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
2	74years	74	Male	2	170	70	24.2	60	37.8	37.8	37.6	37.6	37.6	37.6	37.4	37.4	37.4	37.4	37.4	37.6	37.6	37.6	37.6	37.6	37.6	37.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
3	70years	70	Male	2	180	82	25.3	65	36.8	36.8	36.7	36.7	36.7	36.7	36.7	36.7	36.7	36.6	36.6	36.6	36.6	36.6	36.6	36.7	36.7	36.7	0	1	1	1	0	0	0	0	0	0	1	1	1	1	0	0	0	nil		Nil	Group A
4	74years	74	Male	2	168	75	26.6	60	37	37.3	37.3	37.3	37	37	37	37	37	36.2	36.2	36.4	36.4	36.4	36.4	36.3	35.3	35.3	0	0	1	1	1	0	0	0	0	0	0	0	0	1	1	1	2	2	nil		Nil	Group A
5	65years	65	Male	1	178	85	26.8	60	36.9	36.9	36.9	36.8	36.6	36.6	36.5	36.5	36.5	36.6	36.6	36.6	36.6	36.6	36.6	36.7	36.7	36.7	0	0	0	0	1	1	0	0	0	0	0	1	1	1	2	2	2	2	nil		Nil	Group A
6	61years	61	Male	1	188	85	24	60	36.5	37	36.5	36.5	36.5	36.5	36.5	36.6	36.6	36.6	36.5	36.5	36.5	36.6	36.5	36.6	36.5	36.5	0	0	0	0	0	0	0	0	0	0	0	1	1	2	2	2	2	nil		Nil	Group A
7	80years	80	Male	2	175	75	24.5	70	36.5	36.5	36.8	36.8	36.8	36.7	36.7	36.6	36.6	36.6	36.6	36.7	36.7	36.7	36.7	36.6	36.6	36.6	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
8	55years	55	Male	1	168	70	24.8	60	36.6	36.5	36.5	36.7	36.7	36.7	37.7	36.7	36.7	36.7	36.6	36.6	36.6	36.7	36.7	36.7	36.7	36.7	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
9	56years	56	Male	2	165	68	25	60	36.5	36.6	36.6	36.6	36.6	36.6	36.6	36.6	36.6	36.4	36.4	36.4	36.4	36.4	36.4	36.4	36.5	36.5	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
10	67yeras	67	Male	1	183	87	26	60	35.7	35.9	35.8	35.8	35.7	35.7	35.7	35.6	35.6	35.6	35.6	35.6	35.6	35.6	35.6	35.8	35.8	35.6	0	0	0	0	1	1	0	0	0	0	0	1	1	1	1	0	0	nil		Nil	Group A
11	72years	72	Male	2	176	74	23.9	75	36.3	36.2	36.2	36.2	36.1	36.3	36.5	36.2	36.2	36.4	36.4	36.5	36.5	36.6	36.6	36.6	36.6	36.6	0	0	0	0	1	2	0	0	0	0	0	1	1	1	1	0	0	nil		Nil	Group A
12	70years	70	Male	2	182	71	21.4	60	36.6	36.6	36.6	36.6	36.5	36.6	36.5	36.5	36.5	35.5	35.5	35.6	35.6	36.6	36.6	36.6	36.5	36.5	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
13	68years	68	Male	1	157	64	26	80	36.4	36.5	36.6	36.6	36.2	36.5	36.2	36.2	36.2	36.5	36.5	36.3	36.3	36.2	36.2	36.2	36.2	36.2	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
14	66years	66	Male	2	177	77	24.6	45	35.8	35.8	36.4	36.4	36.4	35.8	36.2	36.2	36.2	36.3	36.2	36.2	36.2	36.2	36.5	36.5	36.5	36.5	0	0	0	0	0	0	0	0	0	0	0	2	2	2	3	3	2	2	nil		Nil	Group A
15	72years	72	male	2	178	80	25.2	60	36.5	36.4	36.4	36.7	36.7	36.6	36.5	36.5	36.5	36.6	36.4	36.5	36.5	36.2	36.2	36.4	36.4	36.4	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	2	nil		Nil	Group A
16	64years	64	Male	2	168	69	24.4	70	37.2	37.2	37.1	37.1	37.1	37.4	37.4	37.4	37.4	37.3	37.3	37.2	37.2	37.4	37.4	37.3	37.3	37.3	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
17	63 years	63	Male	2	174	80	26.4	60	37	37.2	37.2	37.4	37.4	37.8	37.6	37.6	37.6	37.6	36.7	36.7	36.7	36.6	36.6	36.7	36.8	36.8	0	0	1	1	1	2	2	1	1	0	0	0	0	0	0	1	1	1	nil		Nil	Group A
18	65years	65	Male	1	178	71	22.4	80	36.4	36.5	36.5	36.6	36.6	36.6	36.6	36.5	36.5	36.5	36.4	36.4	36.4	36.3	36.4	36.4	36.6	36.6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
19	61years	61	Male	1	182	70	21.1	60	36.5	36.5	36.4	36.4	36.4	36.4	36.3	36.5	36.5	36.5	35.6	35.6	35.6	35.6	36.4	36.4	36.4	36.4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
20	70years	70	Male	2	176	72	23.2	60	37	37	37.2	36.8	36.8	36.6	37.8	37.7	37.7	37	37	37	37	37	37	37.2	37.2	36.6	36.6	0	1	1	1	2	3	1	0	0	0	0	0	0	0	0	0	0	yes	Warmer,I.V Pethidine	Nil	Group A
21	79 years	79	Male	2	163	85	32	45	36.4	36.4	36.3	36.4	36.4	36.4	36.8	36.8	36.8	36.8	36.8	36.4	36.4	36.4	36.8	36.4	36.4	36.4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
22	78years	78	Male	2	170	74	25.6	60	36.9	36.5	36.5	36.5	36.4	36.4	36.4	36.5	36.5	36.4	36.6	36.8	36.8	36.2	36.6	36.5	36.4	36.4	0	0	2	2	2	1	1	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
23	74years	74	Male	2	173	67	22.4	70	36.6	36.6	36.6	36.4	36.4	36.4	36.5	36.5	36.5	36.2	36.4	36.4	36.4	36.2	35.6	35.4	35.4	35.4	0	0	0	1	1	2	1	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
24	64 years	64	Male	2	166	56	20.3	60	37	37	37	37	36.6	36.6	36.4	36.4	36.4	37	37.2	37.2	37.2	36.6	36.6	36.6	35.6	35.6	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	1	nil		Nil	Group A
25	59years	59	Male	2	176	72	23.2	60	36.2	36.6	36.7	36.7	36.7	36.3	36.2	36.2	36.2	36.6	36.4	36.4	36.4	36.4	36.4	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
26	66years	66	Male	1	182	78	23.5	60	36.7	36.7	36.6	37.7	36.7	36.6	36.4	36.7	36.7	36.6	36.4	36.4	36.4	36.6	36.6	36.2	36.2	36.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
27	68years	68	Male	2	178	70	22.1	45	35.3	35.3	35.3	35.8	35.8	35.8	36.8	36.8	36.8	36.2	36.2	36.8	36.8	36.8	36.8	36.4	36.4	36.4	0	0	1	1	1	0	0	0	0	0	0	2	2	2	3	3	3	3	nil		Nil	Group A
28	64years	64	Male	2	162	58	22.1	65	36.5	36.4	36.6	37	37	37.4	35.4	35.4	35.4	35.6	36.4	36.8	36.8	36.8	36.5	36.6	36.6	36.6	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
29	78years	78	Male	2	171	69	23.6	45	36.5	36.6	36.7	36.8	36.8	36.8	36.5	36.5	36.5	36.4	36.5	36.6	36.6	36.8	36.8	34.6	34.6	34.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
30	61years	61	Male	1	176	74	23.9	60	36.8	36.6	36.6	36.8	36.8	36.8	35.8	36.6	36.6	36.6	36.4	36.6	36.6	36.6	36.2	36.7	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
31	80years	80	Male	2	170	66	22.8	60	36	36.7	37	37	37	36.8	37	36.6	36.6	36.8	37.2	37	37	36.6	36.6	36.7	36.7	36.7	0	0	1	1	2	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
32	64 years	64	Male	2	174	76	25.1	60	37.6	37.6	37.4	37.6	37.6	37.4	37.4	37.4	37.4	37.6	37.4	37.2	37.2	37.2	37.4	37.6	37.2	37.2	0	2	2	2	1	0	0	0	0	0	1	1	1	1	0	0	0	nil		Nil	Group A
33	70 years	70	Male	2	179	80	25	60	36.8	36.8	37	37	37	36.9	37	36.6	36.6	36.8	36.6	36.8	36.8	36.6	36.6	36.8	36.8	36.8	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
34	79 years	79	Male	2	175	67	21.9	55	36.4	36.4	36.3	36.3	36.3	36.5	36.5	36.5	36.5	36.8	36.6	36.8	36.8	36.6	36.4	36.4	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
35	68years	68	Male	2	165	73	26.8	60	36.4	36.4	36.6	36.6	36.2	36.8	36.6	36.6	36.6	36.6	36.4	36.2	36.2	36.2	36.6	36.4	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
36	67years	67	Male	2	182	89	26.9	60	36.7	36.6	36.6	36.6	36.4	36.6	36.8	36.6	36.6	36.4	36.4	36.6	36.6	36.6	36.4	36.6	36.4	36.4	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
37	70years	70	Male	2	172	68	23	60	36.6	36.6	36.4	36.4	36.4	36.8	36.8	37	37	36.8	36.6	36.6	36.6	36.4	36.6	36.6	36.4	36.4	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
38	70years	70	Male	2	182	77	23.2	75	36.4	36.6	36.6	36.8	36.8	37	37	37	37	36.8	36.6	36.8	36.8	36.6	36.6	36.6	36.4	36.4	0	0	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
39	57years	57	Male	2	170	69	23.9	60	36.4	36.6	36.6	36.6	36.4	36.4	36.7	36.7	36.7	36.8	36.6	36.8	36.8	36.8	36.6	36.5	36.5	36.5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
40	59years	59	Male	2	180	75	23.1	60	36.4	36.4	36.2	36.2	36.2	36.8	36.6	36.8	36.8	36.6	36.6	36.6	36.6	36.4	36.8	36.7	36.7	36.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
41	70years	70	Male	2	174	70	23.1	60	36.8	36.8	36.8	36.8	36.8	36.7	36.7	36.7	36.7	37	36.8	36.8	36.8	36.8	36.8	36.7	36.7	36.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
42	80years	80	Male	2	168	65	23	65	36.5	36.6	36.7	36.7	36.5	36.5	36.6	36.8	36.8	37.2	37	36.8	36.8	36.8	36.6	36.8	36.8	36.8	0	0	2	2	2	2	0	0	0	0	0	2	2	2	2	2	2	nil		Nil	Group A
43	77years	77	Male	2	165	68	25	60	36.7	36.7	36.8	36.8	36.8	36.8	36.6	36.6	36.6	37.2	37	37.1	37.1	36.9	36.8	37.2	37	37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
44	55years	55	Male	1	170	70	24.2	70	36.8	36.8	36.8	36.6	36.6	36.6	36.8	36.8	36.8	37.2	37.2	37	37	36.8	36.8	36.6	36.6	36.6	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
45	70years	70	Male	2	165	67	24.6	60	36.6	36.6	36.4	36.4	36.4	36.8	37	37	37	36.8	36.6	36.6	36.6	36.4	36.6	36.6	36.6	36.6	0	0	1	1	2	2	0	0	0	0	0	0	0	2	2	2	2	2	nil		Nil	Group A
46	68years	68	Male	2	172	72	24.3	75	36.4	36.4	36.6	36.6	36.2	36.8	36.8	36.6	36.6	36.6	36.4	36.2	36.2	36.6	36.6	36.4	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
47	66years	66	Male	1	180	82	25.3	60	36.7	36.6	36.6	36.6	36.7	36.6	36.4	36.7	36.7	36.6	36.8	36.8	36.8	36.6	36.6	36.8	37	37	0	0	0	0	0	0	1	2	2	0	0	0	0	0	0	0	0	nil		Nil	Group A
48	65years	65	Male	2	168	69	24.4	60	36.7	36.7	36.6	36.6	36.6	36.6	36.4	36.7	36.7	36.6	37	37	37	36.6	36.6	36.2	36.2	36.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
49	80years	80	Male	2	178	74	23.4	60	36.6	36.6	36.4	36.4	36.4	36.4	36.5	36.8	36.8	37	36.8	36.4	36.4	36.4	35.6	35.4	35.6	35.6	0	0	1	1	2	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
50	70years	70	Male	2	182	75	22.6	50	37.2	37.2	37.2	37.2	37	37	37	37	37	36.2	36.2	36.5	36.5	36.5	36.5	36.3	36.4	36.4	0	0	1	1	1	1	0	0	0	0	0	0	0	1	1	1	2	2	nil		Nil	Group A
51	59years	59	Male	2	170	73	25.3	60	36.6	36.5	36.5	36.5	36.5	36.4	36.6	36.4	36.4	37	36.8	36.7	36.7	36.7	36.6	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
52	65years	65	Male	1	163	65	24.5	60	37	37	36.8	36.8	36.8	36.8	36.6	36.6	36.6	37	37	36.8	36.8	36.8	37	36.6	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
53	70years	70	Male	2	173	74	24.7	60	37.2	37.2	37	37	36.6	36.6	36.6	36.5	36.5	37	37	37	37	36.6	36.6	36.6	36.6	36.6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
54	80years	80	Male	2	174	65	21.5	45	37.2	37.2	37	37	36.8	36.8	36.6	36.6	36.6	36.6	36.6	36.7	36.7	36.7	36.8	36.8	36.8	36.8	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
55	68years	68	Male	2	160	60	23.4	60	36.8	36.8	36.6	36.6	36.6	37	37	37	37	37.4	37.4	37.4	37.4	37.4	37.2	37.2	37.4	37.4	0	0	1	1	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
56	60years	60	Male	2	175	67	21.9	60	36.8	36.8	36.6	36.6	36.6	36.6	36.8	37	37	37.2	37	37.2	37.2	37.2	37.2	37.2	37.2	37.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A
57	61years	61	Male	2	168	59	20.9	75	36.6	36.6	36.5	36.5	36.5	36.7	36.7	36.7	36.7	37	37	37	37.2	37.2	37	37	37	37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group A

| | | |

TABLE - B

s.no	Age(yesrs)	Gender	ASAGrade	Height	Weight	BMI	MeanDurationofSurgery	CBTBaseline	CBT1min	CBT5min	CBT10min	CBT15min	CBT30min	CBT45min	CBT60min	CBT90min	STBaseline	ST1min	ST5min	ST10min	ST15min	ST30min	ST45min	ST60min	ST90min	SGBaseline	SG1min	SG5min	SG10min	SG15min	SG30min	SG45min	SG60min	SG90min	SBBaseline	SS1min	SS5min	SS10min	SS15min	SS30min	SS45min	SS60min	SS90min	NeedforAdditionalMeasures	AdditionalMeasure	SideEffect	Group
1	66years	Male	2	177	77	24.6	80	37.4	37.4	38.4	38.4	38.4	38.2	38.2	38.2	38.2	37.4	37.4	37.4	37.4	37.4	37.4	37.2	37.2	37.2	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
2	72years	Male	2	164	59	21.9	60	37.8	37.8	37.6	37.6	37.6	37.6	37.4	37.4	37.4	37.4	37.4	37.6	37.6	37.6	37.6	37.6	37.6	37.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
3	70years	Male	2	180	82	25.3	65	36.8	36.8	36.7	36.7	36.7	36.7	36.7	36.7	36.7	36.6	36.6	36.6	36.6	36.6	36.6	36.7	36.7	36.7	0	1	1	1	0	0	0	0	0	0	1	1	1	1	0	0	0	0	nil		Nil	Group B
4	68years	Male	1	157	64	26	60	37	37.3	37.3	37.3	37	37	37	37	37	36.2	36.2	36.5	36.5	36.5	36.5	36.3	35.3	35.3	0	0	1	1	1	1	0	0	0	0	0	0	1	1	1	2	2	0	nil		Nil	Group B
5	70years	Male	2	160	60	23.4	75	36.9	36.9	36.9	36.9	36.6	36.6	36.5	36.5	36.5	36.8	36.6	36.6	36.6	36.6	36.7	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	2	2	nil		Nil	Group B
6	65years	Male	1	165	68	25	60	36.5	37	36.5	36.5	36.5	36.5	36.5	36.6	36.6	36.6	36.5	36.5	36.5	36.5	36.5	36.6	36.5	36.5	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	2	2	2	nil		Nil	Group B
7	67years	Male	2	182	89	26.9	60	36.5	36.5	36.8	36.8	36.8	36.7	36.7	36.6	36.6	36.6	36.6	36.7	36.7	36.7	36.7	36.7	36.7	36.7	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
8	66years	male	2	177	77	24.6	70	36.6	36.5	36.5	36.5	36.5	36.7	37.7	36.7	36.7	36.7	36.5	35.6	35.6	35.6	36.7	36.7	36.7	36.7	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
9	70years	Male	2	172	68	23	60	36.5	36.6	36.6	36.6	36.6	36.6	36.6	36.6	36.6	36.3	36.4	36.4	36.4	36.4	36.4	36.4	36.4	36.4	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
10	58years	Male	1	175	76	24.8	65	35.7	35.9	35.8	35.8	35.7	35.7	35.7	35.6	35.6	35.6	35.6	35.6	35.6	35.6	35.6	35.8	35.8	35.6	0	0	0	0	1	1	0	0	0	0	0	1	1	1	1	1	0	0	nil		Nil	Group B
11	62years	Male	2	178	78	24.6	60	36.3	36.2	36.2	36.2	36.1	36.3	36.5	36.2	36.2	36.4	36.5	36.5	36.5	36.6	36.4	36.4	36.6	36.6	0	0	0	1	2	2	0	0	0	0	0	1	1	1	1	0	0	0	nil		Nil	Group B
12	70years	Male	2	180	82	25.3	75	36.6	36.6	36.6	36.6	36.5	36.6	36.5	36.5	36.5	35.4	35.4	35.6	35.6	35.6	36.6	36.6	36.5	36.5	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
13	59years	Male	2	176	72	23.2	45	36.4	36.5	36.6	36.6	36.2	36.5	36.2	36.2	36.2	36.5	36.3	36.3	36.3	36.2	35.9	35.9	35.9	35.9	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
14	60years	Male	2	175	67	21.9	75	35.8	35.8	36.4	36.4	36.4	35.8	36.2	36.2	36.2	36.3	36.4	36.4	36.4	36.4	36.4	36.5	35.6	35.6	0	0	0	0	0	0	0	0	0	0	0	2	2	2	3	3	3	3	nil		Nil	Group B
15	70years	male	2	172	68	23	60	36.5	36.4	36.4	36.4	36.7	36.6	36.5	36.5	36.5	36.6	36.4	36.5	36.5	36.2	36.2	36.4	36.4	36.4	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	2	2	2	nil		Nil	Group B
16	67years	Male	2	180	62	19.1	70	37.2	37.2	37.1	37.1	37.1	37.4	37.4	37.4	37.4	37.6	37.3	37.2	37.2	37.4	37.4	37.2	37.2	37.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
17	63years	Male	2	170	72	24.9	60	37	37.2	37.2	37.2	37.4	37.5	37.6	37.6	37.6	36.7	36.7	36.7	36.7	36.6	36.6	36.7	36.8	36.8	0	0	1	1	2	2	0	0	0	0	0	0	0	0	1	1	1	0	nil		Nil	Group B
18	65years	Male	1	165	68	25	60	36.4	36.5	36.5	36.5	36.6	36.6	36.6	36.5	36.5	36.5	36.4	36.4	36.4	36.3	36.4	36.4	36.6	36.6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
19	71years	Male	2	180	75	23.1	65	36.5	36.5	36.4	36.4	36.4	36.4	36.3	36.5	36.5	36.5	35.6	35.6	35.6	35.6	36.4	36.4	36.4	36.4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
20	72years	Male	2	176	74	23.9	60	37	37	37.2	37.2	36.8	36.6	37.8	37.7	37.7	37	37	37	37	37	37.2	37.2	36.6	36.6	0	1	1	1	2	2	0	0	0	0	0	0	0	0	0	0	0	0	yes	warmer,i.v.pethidine	Nil	Group B
21	69years	Male	2	165	68	25	45	36.4	36.4	36.3	36.3	36.4	36.4	36.8	36.8	36.8	36.8	36.8	36.8	36.8	36.8	36.8	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
22	59years	Male	2	176	72	23.2	60	36.9	36.5	36.5	36.5	36.4	36.4	36.4	36.5	36.5	36.5	36.5	36.6	36.8	36.8	36.2	36.6	36.5	36.5	0	0	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
23	80years	Male	2	175	75	24.5	45	36.6	36.6	36.4	36.4	36.4	36.4	36.5	36.5	36.5	36.2	36.4	36.4	36.4	36.2	36.2	36.2	36.2	36.2	0	0	1	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
24	72years	Male	2	176	74	23.9	60	37.2	37	36.8	36.8	36.6	36.6	37	36.4	36.4	37	37.2	37.2	37.2	36.8	37	37	37	37	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	1	nil		Nil	Group B
25	58years	Male	2	175	76	24.8	60	36.2	36.6	36.7	36.7	36.7	36.3	36.2	36.2	36.2	36.6	36.6	36.4	36.4	36.4	36.4	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
26	67years	Male	2	170	70	24.2	60	35.8	36.7	36.6	36.6	36.7	36.6	36.4	36.7	36.7	36.6	36.4	36.4	36.4	36.6	36.6	36.2	36.2	36.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
27	69years	Male	2	178	80	25.2	45	35.3	35.3	35.3	35.3	35.8	35.8	36.8	36.8	36.8	36.2	36.2	36.8	36.8	36.8	36.8	36.4	36.4	36.4	0	0	1	1	1	1	0	0	0	0	0	2	2	2	3	3	3	3	nil		Nil	Group B
28	76years	Male	2	172	73	24.7	60	36.5	36.4	36.6	36.6	37	37.4	35.4	35.4	35.4	36.6	36.4	36.8	36.8	36.8	36.5	36.8	36.8	36.8	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
29	72years	Male	2	176	74	23.9	45	36.5	36.6	36.7	36.7	36.8	36.8	36.5	36.5	36.5	36.4	36.5	36.6	36.6	36.8	36.8	36.6	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
30	66years	Male	2	177	77	24.6	80	36.8	36.6	36.6	36.6	36.8	36.8	35.8	36.6	36.6	36.6	36.4	36.6	36.6	36.6	36.2	36.7	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
31	67years	Male	2	182	89	26.9	60	36	36.7	37	37	37	36.8	37	36.6	36.6	36.8	37.2	37	37	36.6	36.6	36.7	36.6	36.6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
32	74years	Male	2	170	70	24.2	60	37.6	37.5	37.4	37.4	37.6	37.4	37.4	37.4	37.4	37.6	37.4	37.2	37.2	37.2	37	37.6	37.2	37.2	0	2	2	2	1	1	0	0	0	0	1	1	1	1	0	0	0	0	nil		Nil	Group B
33	63years	Male	2	170	72	24.9	60	36.8	36.8	37	37	37	36.9	37	36.6	36.6	36.8	36.6	36.8	36.8	36.6	36.6	36.8	36.8	36.8	0	1	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
34	74years	Male	2	170	70	24.2	65	36.4	36.4	36.3	36.3	36.3	36.5	36.5	36.5	36.5	36.8	36.8	36.6	36.8	36.8	36.6	36.4	36.4	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
35	72years	Male	2	178	66	20.8	60	36.4	36.4	36.6	36.6	36.2	36.8	36.6	36.6	36.6	36.6	36.4	36.4	36.4	36.4	36.6	36.4	36.6	36.6	0	0	0	0	2	2	2	2	2	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
36	67years	Male	2	182	89	26.9	65	36.7	35.8	35.8	35.8	36.4	36.6	36.8	36.6	36.6	36.4	36.4	36.8	36.8	36.8	36.6	36.6	36.4	36.4	0	0	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
37	69years	Male	2	179	79	24.7	60	36.6	36.6	36.4	36.4	36.4	36.8	36.8	37	37	36.8	35.6	36.6	36.6	36.4	36.6	36.6	36.6	36.6	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
38	71years	Male	2	180	75	23.1	75	36.4	36.6	36.6	36.6	36.8	37	37	37	37	36.8	36.6	36.8	36.8	36.6	36.6	36.6	36.4	36.4	0	0	2	2	2	2	1	1	1	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
39	67years	Male	1	182	89	26.9	60	36.4	36.6	36.6	36.6	36.4	36.4	36.7	36.7	36.7	36.8	36.6	36.8	36.8	36.8	36.8	36.6	36.5	36.5	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
40	69years	Male	2	179	79	24.7	60	36.4	36.4	36.2	36.2	36.2	36.8	36.6	36.8	36.8	36.6	36.6	36.6	36.6	36.6	36.4	36.8	36.7	36.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
41	74years	Male	2	170	70	24.2	70	36.5	36.8	36.8	36.8	36.8	36.8	36.4	36.7	36.7	36.7	36.8	36.8	36.8	36.8	36.8	36.7	36.7	36.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
42	80years	Male	1	168	65	23	60	36.5	36.6	36.7	36.7	36.5	36.5	36.5	36.8	36.8	37.2	37	36.8	36.8	36.8	36.6	36.8	36.8	36.8	0	0	2	2	2	0	0	0	0	0	0	2	2	2	2	2	2	2	nil		Nil	Group B
43	80years	Male	2	175	75	24.5	60	36.7	36.7	36.6	36.6	36.8	36.8	36.6	36.6	36.6	37.2	37	37.1	37.1	37.1	37.1	37.2	37	37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
44	76years	Male	2	172	73	24.7	45	36.8	36.8	36.8	36.8	36.6	36.6	36.8	36.8	36.8	37.2	37.2	37.5	37.5	36.8	36.8	37.2	37.2	37.2	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
45	67years	Male	2	182	89	26.9	60	36.5	36.6	36.4	36.4	36.4	36.8	37	36.9	36.9	36.8	36.6	36.6	36.6	36.6	36.4	36.6	36.6	36.6	0	0	1	1	1	1	0	0	0	0	0	0	2	2	2	2	2	2	nil		Nil	Group B
46	72years	Male	2	165	66	24.2	60	36.4	36.4	36.6	36.6	36.2	36.8	36.6	36.6	36.6	36.6	36.4	36.2	36.2	36.6	36.6	36.4	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	2	2	2	2	2	0	0	nil		Nil	Group B
47	71years	Male	2	180	75	23.1	75	36.7	36.6	36.6	36.6	36.7	36.6	36.4	36.7	36.7	36.6	36.8	36.8	36.8	36.6	36.6	36.8	37	37	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	nil		Nil	Group B
48	67years	Male	2	182	89	26.9	80	36.7	36.7	36.6	36.6	36.6	36.5	36.4	36.7	36.7	36.6	37	37	37	36.6	36.6	36.6	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
49	68years	Male	1	157	64	26	60	36.6	36.6	36.4	36.4	36.4	36.4	36.5	36.8	36.8	37	36.8	36.4	36.4	36.4	36.4	36.4	36.4	36.4	0	0	1	1	2	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
50	78years	Male	2	168	65	23	60	37.2	37.2	37.2	37.2	37	36.9	37	37	37	36.2	36.5	36.5	36.5	36.5	36.5	36.3	36.4	36.4	0	0	1	1	1	1	0	0	0	0	0	0	1	1	1	1	2	2	nil		Nil	Group B
51	80years	Male	2	172	74	25	85	36.6	36.5	36.5	36.5	36.5	36.4	36.6	36.4	36.4	37	36.8	36.7	36.7	36.7	36.7	36.8	36.6	36.6	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
52	67years	Male	1	182	89	26.9	60	37	37	36.8	36.8	36.8	36.8	36.6	35.8	35.8	37	37	36.8	36.8	36.8	37	36.6	36.6	36.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
53	79years	Male	2	168	65	23	60	37.2	37.2	37	37	36.6	36.6	36.6	36.5	36.5	37	37	37	37	37	36.6	36.4	36.4	36.6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
54	78years	Male	2	171	69	23.6	80	37.2	37.2	37	37	36.8	36.8	36.6	36.6	36.6	36.7	36.7	36.7	36.7	36.7	36.8	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
55	70years	Male	2	180	82	25.3	60	36.8	36.4	36.6	36.6	36.6	37	37	37	37	37.4	37.4	37.4	37.4	37.4	37.4	37.2	37.4	37.4	0	0	1	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
56	64years	Male	2	168	69	24.4	60	36.8	36.8	36.6	36.6	36.6	36.6	36.8	37	37	37.2	37	37.2	37.2	37.2	37.2	37.1	37.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
57	69years	Male	2	179	79	24.7	45	36.6	36.6	36.5	36.5	36.5	36.7	36.7	36.7	36.7	37	36.8	36.8	36.8	37.2	37	37	37	37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
58	69years	Male	2	178	78	24.6	60	36.6	36.6	36.7	36.7	36.7	36.6	36.8	36.8	36.8	37	37	36.8	36.8	36.8	36.8	36.6	36.6	36.6	0	0	1	1	1	0	0	0	0	0	0	0	0	0	2	3	3	3	nil		Nil	Group B
59	57years	Male	1	170	69	23.9	45	36.4	36.4	36.6	36.6	36.4	36.4	36.8	36.8	36.8	36.8	36.8	37	37	37	36.8	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
60	64years	Male	2	168	69	24.4	60	36.5	36.5	36.6	36.6	37	37.4	35.4	35.6	35.6	35.6	36.6	36.8	36.8	36.8	36.6	36.7	36.7	36.7	0	0	1	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
61	75years	Male	2	166	69	25	45	36.8	36.8	36.6	36.6	36.6	36.6	36.6	37	37	37	36.8	36.8	37	37	37.2	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
62	63years	Male	2	170	72	24.9	60	36.8	36.8	36.6	36.6	36.6	36.6	36.7	36.7	36.7	36.8	36.6	36.6	36.6	36.7	36.7	36.8	36.8	36.8	0	0	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0	nil		Nil	Group B
63	69years	Male	2	179	79	24.7	60	36.6	36.6	36.6	36.6	36.4	36.6	36.8	36.8	36.8	37	36.8	36.6	36.6	36.6	36.6	36.7	36.7	36.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
64	68years	Male	1	157	64	26	70	36.7	36.7	36.6	36.6	36.6	36.8	36.6	36.6	36.6	37	37	37	37	36.8	36.8	37	36.8	36.8	0	0	1	1	2	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
65	72years	Male	2	176	74	23.9	60	36.6	36.6	36.4	36.4	36.7	36.7	37	37	37	37	36.8	36.8	36.8	36.6	36.6	36.6	36.6	36.6	0	0	1	1	1	1	0	0	0	0	0	0	0	0	2	2	2	2	nil		Nil	Group B
66	69years	Male	2	178	80	25.2	75	37.2	37.2	37	37	37	36.8	36.8	36.8	36.8	37	36.8	36.8	36.8	36.8	37.2	37.2	37.2	37.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
67	70years	Male	2	180	82	25.3	50	37.4	37.4	37.2	37.2	37.2	37.2	37.4	37.2	37.2	37.2	37.2	37.4	37.4	37	37	37.2	37.6	37.6	0	0	1	1	2	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
68	69years	Male	2	180	78	24.1	60	37.2	37.2	37	37	37	36.8	36.8	37	37	37	37	37.2	37.2	37.2	37	37	37	37	0	0	0	0	0	0	0	0	0	0	0	2	3	3	3	3	3	3	nil		Nil	Group B
69	71years	Male	2	160	62	24.2	70	37	36.8	36.8	36.8	35.6	35.6	36.7	36.7	36.7	36.6	36.6	36.8	36.8	36.8	36.9	36.9	36.8	36.8	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B
70	69years	Male	2	177	81	25.9	60	37	37	36.8	36.8	36.7	36.6	36.6	36.7	36.7	36.6	36.8	36.8	36.8	36.6	36.6	36.8	36.8	36.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	nil		Nil	Group B