A COMPARATIVE STUDY OF THE EFFECT OF CLONIDINE TRAMADOL AND NALBUPHINE ON POSTSPINAL ANAESTHESIA SHIVERING

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CHENNAI,

TAMIL NADU

BONAFIDE CERTIFICATE BY THE GUIDE

This is certify that this dissertation entitled A COMPARATIVE STUDY OF THE EFFECT OF CLONIDINE TRAMADOL AND NALBUPHINE ON POSTSPINAL ANAESTHESIA SHIVERING a bonafide record work done by Dr. J.VASANTHY under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch X – Anaesthesiology

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I hereby declare that this dissertation entitled A COMPARATIVE STUDY OF THE EFFECT OF CLONIDINE TRAMADOL AND NALBUPHINE ON POSTSPINAL ANAESTHESIA SHIVERING is a bonafide and genuine research work carried out by me in the Department of Anaesthesiology, Thanjavur Medical College.

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LIST OF ABBREVIATIONS USED

mg	-	milligrams
µg	-	micrograms
kg	-	Kilograms
ASA	-	American society of anaesthesiology
C max	-	concentration maximum
mts	-	minutes
hrs	-	Hours
i.v	-	intravenous
SBP	-	Systolic blood pressure
DBP	-	Diastolic blood pressure
SPO2	-	Arterial Oxygen Saturation
NS	-	Not Significant
EMG	-	Electromyogram
LSCS	-	Lower Segment Caesarean Section
RCT	-	Randomised Controlled Trial
ATP	-	Adenosine Triphosphate
NA	-	Noradrenaline
5HT	-	Serotonin
MAOI	-	Monoamine oxidase inhibitors
NSAID	-	Non steroidal anti inflammatory drug

ABSTRACT

BACKGROUND OBJECTIVES

To compare the efficacy of Tramadol, Nalbuphine, and Clonidine in the treatment of shivering after spinal anaesthesia in caesarean section .

METHODS:

A prospective randomised comparative study was conducted between 1.8.2013 to 1.9.2014 to compare the efficacy of Tramadol, Nalbuphine, Clonidine in treatment of shivering after spinal anaesthesia in casearean section. Patients included in this study are those who developed shivering after spinal anaesthesia for caesarean section.

Patients were randomly allotted to one of the three groups, namely T group (25) who received Tramadol 0.5mg/kg i.v., N group (25) who received Nalbuphine 0.1mg/kg i.v and C group (25)who received clonidine 0.5µg/kg iv.

Vital parameters of the patient such as H.R. B.P. SPO_2, RR and temperature were monitored at regular intervals as per protocol. Events such as onset of shivering, time taken to stop shivering, recurrence of shivering and side effects like nausea, vomiting bradycardia, hypotension and sedation were also noted.

Statistical tests like chi square test, Anova test were applied to the data collected.

Results:

Among the 75 patients who developed shivering of grades 3 & 4 requiring treatment were randomly allotted to one of the three group.

The mean temperature at which patient developed shivering was 36.4°C, and the mean duration of shivering to occur following spinal anaesthesia was 22.5 mts.

Tramadol 0.5 mg/kg controlled shivering in mean time of 4 minutes, clonidine 0.5 µg/kg, controlled shivering in mean time of 2 minutes and Nalbuphine 0.1 mg/kg controlled shivering in mean time of 4 minutes .

Conclusion :-

Our study concludes that all three drugs namely Tramadol clonidine and nalbuphine were effective in controlling postspinal anesthesia shivering . among them clonidine took lesser time to achieve complete cessation of shivering and also maintained better hemodynamics throughout the study.

Key words:-

Shivering, Spinal anaesthesia, Nalbuphine, Tramadol, clonidine.

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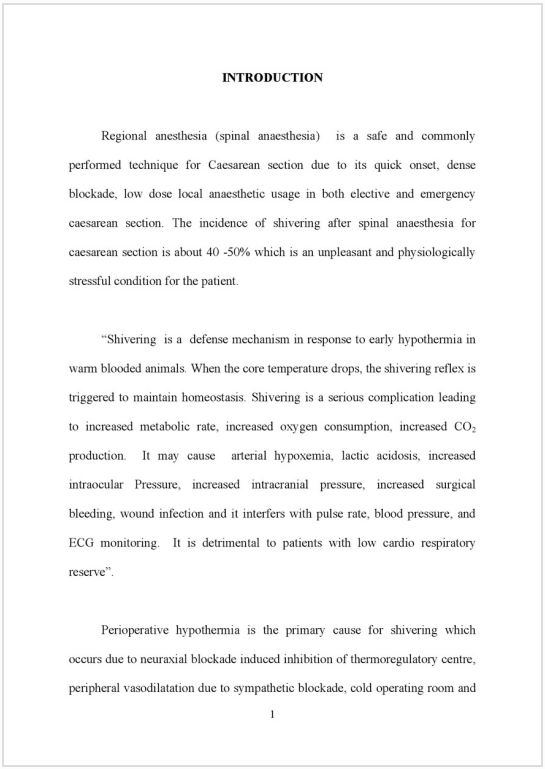

INTRODUCTION

Regional anesthesia (spinal anaesthesia) is a safe and commonly performed technique for Caesarean section due to its quick onset, dense blockade, low dose local anaesthetic usage in both elective and emergency caesarean section. The incidence of shivering after spinal anaesthesia for caesarean section is about 40 -50% which is an unpleasant and physiologically stressful condition for the patient.

"Shivering is a defense mechanism in response to early hypothermia in warm blooded animals. When the core temperature drops, the shivering reflex is triggered to maintain homeostasis. Shivering is a serious complication leading to increased metabolic rate, increased oxygen consumption, increased CO_2 production. It may cause arterial hypoxemia, lactic acidosis, increased intraocular Pressure, increased intracranial pressure, increased surgical bleeding, wound infection and it interfers with pulse rate, blood pressure, and ECG monitoring. It is detrimental to patients with low cardio respiratory reserve".

Perioperative hypothermia is the primary cause for shivering which occurs due to neuraxial blockade induced inhibition of thermoregulatory centre, peripheral vasodilatation due to sympathetic blockade, cold operating room and

1

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Perioperative hypothermia is the primary cause for shivering which occurs due to neuraxial blockade induced inhibition of thermoregulatory centre, peripheral vasodilatation due to sympathetic blockade, cold

operating room and cold iv fluids .Various non pharmacological and pharmacological interventions are used to control post spinal anesthesia shivering. Non pharmacological methods includes convection warming system and radiant heat system which uses specialized equipments to control or prevent shivering which are often expensive and are not practical in all clinical settings. Pharmacological agents used to control shivering include pethidine, clonidine, tramadol, nalbuphine, ondasetron, ketanserin, magnesiumsulphate, propofol, alfentanil, sufentanil, physostigmine, doxapram, methylphenidate, ketamine, etc. Among them pethidine is the commonly used drug to treat shivering, but it has its own limitation.

So we undertook a prospective, randomized clinical study to compare the efficacy of tramadol, clonidine and nalbuphine in the treatment of shivering after spinal anaesthesia in caesarean patients. Tramadol is a synthetic opioid which has lesser respiratory depression and less sedation. clonidine is a alpha2 agonist which has better hemodynamics. Nalbuphine is a opioid agonist antagonist with ceiling effect on respiration. Hence these three drugs are selected for study.

AIM AND OBJECTIVES

The aim of this prospective double blind randomized clinical study was to compare the efficacy, potency, hemodynamic effects, complications and side effects of clonidine, nalbuphine and tramadol for control of shivering after Spinal anesthesia in caesarean section and to determine which of these pharmacological interventions serves the best to achieve benefit with minimal side effect.

REVIEW OF LITERATURE

People's journal of scientific research vol 7, Jan 2014; research article by S Kulshrestha, R.K. Methta, conducted RCT on efficacy of intravenous clonidine and tramadol on postspinal aneasthesia shivering in elective lower segment caesarean section. In this double blind study 90 patients belonging to ASA grade I & II between 18-35 years scheduled for elective LSCS under spinal anaesthesia who developed shivering were allocated into 2 groups, Group C and Group T, given clonidine 50µg and tramadol 50mg iv respectively. The mean interval between the drug injection and complete cessation of shivering was significantly earlier in group C than group T. The side effects were less in clonidine than tramadol group.

Beena yousuf, et al, 2013; evaluated the efficacy of tramadol in preventing post-operative shivering using thiopentone and propofol as induction agent in general anaesthesia. It was a randomized controlled trial, 124 patients under going general anaesthesia for various procedures who received either thiopentone or propofol as induction agent. Each group subdivided to receive either tramadol or saline before wound closure. They observed higher incidence of post operative shivering in Thiopentone

group and lowest in propofol group ($P<0.05$) . They concluded that prophylactic use of tramadol in a dose of 1mg/1kg with propofol as an induction agent, significantly reduced the incidence of post operative shivering in patients recovering from general anaesthesia.

Ushashukla, et al., IJA 2011; conducted a prospective double blind randomized controlled clinical trails, to evaluate the efficacy, potency, side effects of clonidine and tramadol in post spinal anaesthesia shivering. In that study 80 ASA I & II patients scheduled for various surgical procedures under spinal anaesthesia were selected who developed shivering, were selected into two groups. Group C(n=40) and group T(n=40) given clonidine 0.5µg/kg and tramadol 0.5mg/kg iv respectively. Disappearance of shivering was significantly earlier in groupC than in group T ($P= 0.0000001$). Nausea, vomiting, dizziness were found to be higher in group T.

Cari A miller, Harris college, Texas, October 2011 conducted study on drugs to reduce post spinal anaesthesia shivering. In his project, he compared the drugs with anti shivering property, he recommended tramadol is equally effective to meperidine and also recommended, clonidine, nalbuphine and doxapram in the treatment of post-spinal anaesthesia shivering.

Fatemeh Haji Mohammadi, et al., in 2010 conducted a double blind clinical trial on patients suffering from shivering following general anaesthesia and compared the effectiveness of tramadol and meperidine in controlling post anaesthesia shivering. The patients received tramadol 1mg/kg or 0.5mg/kg meperidine i.v, over 30 seconds, with shivering grade 2 or 3. Shivering disappeared in 40% following tramadol and 53.3% after meperidine. They concluded both drugs were effective in reducing shivering and tramadol is as effective as meperidine in tackling postanaesthetic shivering.

Dhimar and colleagues in 2010, compared meperidine and tramadol in the treatment of post Anaesthesia shivering under regional anesthesia. It included 60 patients undergoing various surgeries in both genders with ASA grade I, II or III, this study found tramadol and meperidine equally effective and however tramadol stopped shivering faster than meperidine. Doses were 1mg/kg for both drugs. Tramadol was superior since the disappearance of shivering took 5mts with Tramadol and 20mts in meperidine group.

Trakalthong C, Areejuathawa J, et al; in 2009: reviewed studies relating the effectiveness of drugs in controlling shivering, included 9 RCTS for meperidine, 3 for Tramadol, ketanserin, Doxapram and clonidine and 2 for nalbuphine; Evidence was sufficient and statistically significant for these six drugs.

Fatemeh, et al, in 2009; conducted a randomized double blind study on 90 ASA I & II candidates for caesarean section. They randomly allocated two groups (study and control). All patients undergone spinal anaesthesia . At the end of surgery ,1mg/kg tramadol in 20ml normal saline given to study group and 20ml normal saline given to control group intravenously. Patients evaluated for hemodynamics, arterial O_2 saturation, oral temperature, presence and intensity of shivering and nausea and vomiting. Thirty nine patients (86.6%) in control group and (8.8%) only four patients in study group developed shivering. In control group, thirty three patients has moderate shivering and six patient has mild shivering. In study group two patients has moderate and two has mild shivering ($P < 0.001$) there were no significant differences with respect to heart rate, systolic and diastolic blood pressure, oxygen saturation, nausea, vomiting and body temperature of the patients. They concluded tramadol was effective in the prevention of post spinal anaesthesia shivering and the drug does not lead into any hemodynamic complications.

Mohta M. Kumari N. et al, in 2009; conducted a study to compare the effects of tramadol with pethidine for prevention of post-anesthetic shivering, to find the dose of tramadol that provide the dual effect of anti shivering and analgesic effect; they included 165 patients allocated to 5 groups of 33 each. Tramadol in doses of 1,2,3 mg/kg and pethidine 0.5mg/kg and normal saline were given at the time of wound closure. All the three doses were effective in preventing post anaesthetic shivering . Tramadol 2mg/kg had the best effect of antishivering and analgesic efficacy, without excessive sedation.

S. Atashkhoyi and S. Negargar in 2008; conducted a double blind study on 70 healthy obstetric patients scheduled for caesarean section under spinal anaesthesia. Immediately after spinal anaesthesia, 35 patients received 1mg/kg tramadol and normal saline for 35 patients, the incidence of shivering was lower in patients who got Tramadol than placebo (28.57%) Vs (65.71%) ($P<0.001$). In placebo group 26 patients (74.28%) had post-operative pain compared to 4 in the study group (11.42% $P(<0.0001)$, there was no difference in side effects between the two groups. The result revealed that tramadol 1mg//1kg was effective in the prevention of shivering in caesarean patients after spinal anaesthesia.

Oranuch Kyokong et al., 2007 conducted a double blind randomised controlled study on two hundred and eighty parturients were divided into 4 groups, group T, group N, group O and , group P were given tramadol 0.5mg/kg, nalbuphine 0.05mg/kg, Ondansetron 0.1mg/kg and normal saline 5ml IV given respectively for controlling post anaesthesia shivering. Evaluated at 15mts after treatment. The success rate in controlling shivering were 88, 81, 61 and 36% respectively in group T,N,O,P with p value of (P<0.001, 0.001, 0.003 and < 0.001 and 0.009) respectively. Recurrence rate of post anaesthesia shivering in groups T, N, O, P were 14% 15% 11% and 28%; p = 0.329. other side effects were few. They concluded that tramadol, nalbuphine, ondansetron were effective after intrathecal morphine in caesarean patients with low recurrence rates of shivering. Tramadol and nalbuphine were superior to ondansetron.

Vander stappen, et al; in april 1999; conducted a large prospective double blind study to evaluate the effect of prophylactic clonidine on post operative shivering. 280 patients of ASA I and II were selected who undergone elective peripheral surgery, were given either placebo or clonidine 2µg/kg iv, over 10 mts after induction of anaesthesia, Clonidine was found to reduce the severity (P=0.005) and duration of post-op shivering (p=0.01) . It did not increase post-operative sedation and concluded clonidine reduces postoperative shivering.

Zahedi in 2004; conducted and published a larger RCT. This study was a double blind trial on patients undergoing cataract surgery under general anaesthesia. The participants were ASA I and II. In 120 patients with shivering who were treated with tramadol 1mg/kg and meperidine 0.5mg/kg, Zahedi reported tramadol was more effective due to faster onset, no recurrence of shivering, shorter duration of recovery and fewer adverse effects.

Kranke P, et al., in 2004 conducted a study to evaluate the anti shivering property of certain drugs like clonidine, meperidine, ketanserin & doxapram and found clonidine was equally potent to meperidine and its role as an anti shivering drug.

Trekova NA et al, in 2004 conducted a double blind study to evaluate the effect of Tramadol in the treatment of post- operative shivering. The study was undertaken in 2 groups, 50 patients each in tramadol and placebo group, tramadol at 1-2 mg/kg completely stopped the shivering post operatively and reduced intensity in 49 patients (98%) They found mild sedation compared to placebo group and concluded tramadol is effective in post anaesthetic shivering.

In a review article by Pradip K.Bhattacharya, Lata Bhattacharaya, et al in 2003;on mechanism of action of tramadol in the treatment of post spinal anaesthesia shivering, concluded that tramadol is an anti-shivering drug with similar mechanism of nefopam which is an analgesic NSAID. It inhibits the reuptake of NA, 5 HT and dopamine and facilitates 5HT release. Cerebral $\propto_2$ adrenoceptors play a role in the attenuation of shivering by tramadol. They concluded that tramadol can be used to treat post-anaesthesia shivering.

Sessler studied "thermoregulation under anaesthesia" and various modes of temperature monitoring in 2000; he observed core temperature is the best single indicator of thermal status in humans, and monitored at the tympanic membrane, pulmonary artery, distal oesophagus and nasopharnyx. Axillary temperature are reasonably accurate but work best. Core temperature should be measured during regional anaesthesia in patients who become hypothermic.

Most ascending thermal information traverses via spinothalamic tracts in the anterior spinal cord but no single spinal tract is critical in conveying information. Central thermoregulatory control is impaired in regional anaesthesia. Cold signals from the skin travel via A delta fibres, whereas warm signals are transduced by unmyelinated c fibres. During

regional anaesthesia, core hypothermia is associated by increase in skin temperature. The paradoxical result is perception of increased warmth accompanied by shivering from automonic thermoregulatory response.

Jan De witte and Sessler DI in a review article written in 2002; stated that tramadol is similar to nefopam in its mechanism of action as an anti-shivering drug. In human volunteers, a high dose of naloxone only partially reverses the anti shivering effect of tramadol, cerebral alpha receptors are thought to play a role in the attenuation of post operative shivering by tramadol.

Bhatnagar et al, in 2001; studied the pharmacological control of shivering using tramadol and pethidine. They conducted a randomized double blind trial with 30 ASA patients of grade 1 or 2 patients and evaluated the efficacy of tramadol and pethidine in the treatment of post anaesthetic shivering. Patients received either tramadol 1mg/1kg or pethidine 0.5mg/kg iv. The grade of shivering pulse rate, blood pressure and respiratory rate were observed every 10mts for 1 hour, shivering was significantly ceased in the tramadol group ($P<0.05$). No patients receiving tramadol had recurrence of shivering, and they concluded that iv tramadol 1mg/kg is more effective than pethidine 0.5mg/kg for the treatment of post- anaesthetic shivering.

Buggy DT and crossly AW, British Journal of anaesthesia 2000 reviewed thermoregulation and post anaesthetic shivering. They observed 120 obstetrics patients, among them 33% of patients had shivering after epidural anaesthesia and concluded that shivering was due to impairment of physiological set points and also concluded that combined general and epidural anesthesia cause more fall in core temperature than epidural anesthesia only.

Delaunayh, SesslerDI et al, 1999 concluded that clonidine decreases the thermoregulatory thresholds for vasoconstriction and shivering in humans.

Wang JJ, et,al, in 1999; conducted a prospective double blind randomized study and evaluated the potency of nalbuphine with meperidine and saline for treating post anaesthesia shivering. 90 patients of ASA I & II patients included in the study, were divided into three groups, 30 each, who received Inj. nalbuphine 0.08mg/kg, and Inj. meperidine 0.4mg/ kg and saline iv. The response rate after 5mts was noted. Both nalbuphine and meperidine provided a rapid and potent anti shivering effect with high success rates of 80% and 83% and 0% ($P<0.01$). The differences between nalbuphine and meperidine were not significant. They concluded

nalbuphine may be an alternative to meperidine for treating post anaesthesia shivering.

Sebastiano mercadante, et al in 1994, studied the effect of clonidine on shivering after epidural analgesia. A randomized controlled double blind study conducted on sixty obstetric patients who developed shivering after receiving epidural analgesia were randomly allocated to treat with clonidine 150µg, and meperidine 50mg iv (n=20) or saline (n-20). After injection of drugs patients were, evaluated at 5mts intervals, clonidine was effective as meperidine in controlling shivering and caused reduction in heart rate. Drowsiness noted in both groups. Thus they concluded that clonidine was effective in controlling shivering at an acceptable level of drowsiness.

Bansal P. Jain G.1999 conducted the study on control of shivering with clonidine, tramadol and butorphanol under spinal anaesthesia to compare the efficacy and side effects. This randomized control prospective study was conducted on 90 patients undergoing various abdominal and orthopedic surgeries. Those patients who developed shivering were randomly allocated to receive tramadol 50mg, butorphanol 1mg and 150µg clonidine in a double blind manner. Control of shivering, time taken for cessation, recurrence, hemodynamic changes, axillary

temperature and side effects were noted; collected data were analysed using statistical tests. They found butorphanol and tramadol were more effective than clonidine. Butorphanol, tramadol and clonidine suppressed shivering in 83%, 73% and 53% of patients ,time taken to terminate shivering was higher with clonidine (3.3±0.9mts) than butorphanol and tramadol (2.1± mts) and 1.8 ± 0.5 mts ($P<0.001$).

Chan and co-workers in 1999 investigated the dosage of tramadol which was effective in controlling shivering under regional anesthesia in obstetric patients in randomized double blinded study on 36 patients, 12 were allocated to 0.5mg/kg tramadol group, 13 were allocated to 0.25 mg/kg tramadol group and 11 were allocated to 0.05 ml/kg normal saline group. Shivering was controlled in 80% patients in 0.5 mg/kg group, 92% patients in 0.25% mg/kg group, and 27% in Normal saline group. They concluded that intravenous tramadol controlled shivering in obstetric patients and no demonstrable difference in response rate or incidence of side effects between the two doses 0.5mg /kg and 0.25mg/kg.

S Sia in 1998, BJA, studied the efficacy of clonidine to prevent post extradural shivering in 100 healthy patients who received extradural block for knee arthroscopy. It was a prospective randomized double blind study. Patients (n=50) were allocated into 2 groups just before

extradural anaesthesia, group I (n=50) received iv clonidine 1µg/kg and group II (N=50) received iv saline bolus. The heart rate, arterial blood pressure, $spo_{2,}$ cutaneous temperature, level of sedation were all recorded at baseline, after 10,20,30,40,50 60 mts, shivering was graded as moderate or severe, 3 patients in group I and 19 patients in group II had shivering ($P<0.0001$) .There is no significant differences in parameters during the study in arterial blood pressure,. Heart rate, $spo_{2,}$ cutaneous temperature and level of sedation. They concluded iv clonidine 1mg/kg provides significant reduction in the incidence of shivering, without any adverse side effect.

Capogna and D cellano in 1993; BJA, studied the efficacy of iv clonidine to suppress post extradural shivering in parturients. 40 parturients who received extradural block for labour (n=20) and casearean section (n=20) and who requiring treatment for shivering after delivery were allocated into 2 groups; group I received iv clonidine 30 µgm and maximum of 90 µgm iv given; and Group II received iv saline 5ml. After 15mts, patients who received clonidine with stopping of shivering within 5 mts were 75%, in contrast to no improvement in saline group. Arterial pressure, heart rate, core and peripheral temperature, spo_2 did not differ significantly between groups. They concluded that a small dose of i.v clonidine is enough to suppress extradural shivering in parturients.

PHYSIOLOGY OF SHIVERING

Normal body temperature is 36.5-37.5^0 C. Core body temperature is maintained near a constant level through thermo regulation. However when exposed to cold environment , the internal mechanism is unable to replenish heat that is lost to the surroundings. Hypothermia is defined as any body temperature below 35^0 C (95^{0}F). It is subdivided as

- Mild (32-35^0 C)
- Moderate (28-32^{0}C)
- Severe (20-28^0 C)
- Profound (less than 20^{0}C)]

Shivering[20] is a bodily defense function in response to early hypothermia in warm blooded animals. When the core temperature drops, The shivering reflex is triggered. Muscle groups begin to shake in small movements in an attempt to create warmth by energy. Increased muscle activity results in heat generation. Shivering is also observed in fever, though their core temperature is elevated already.

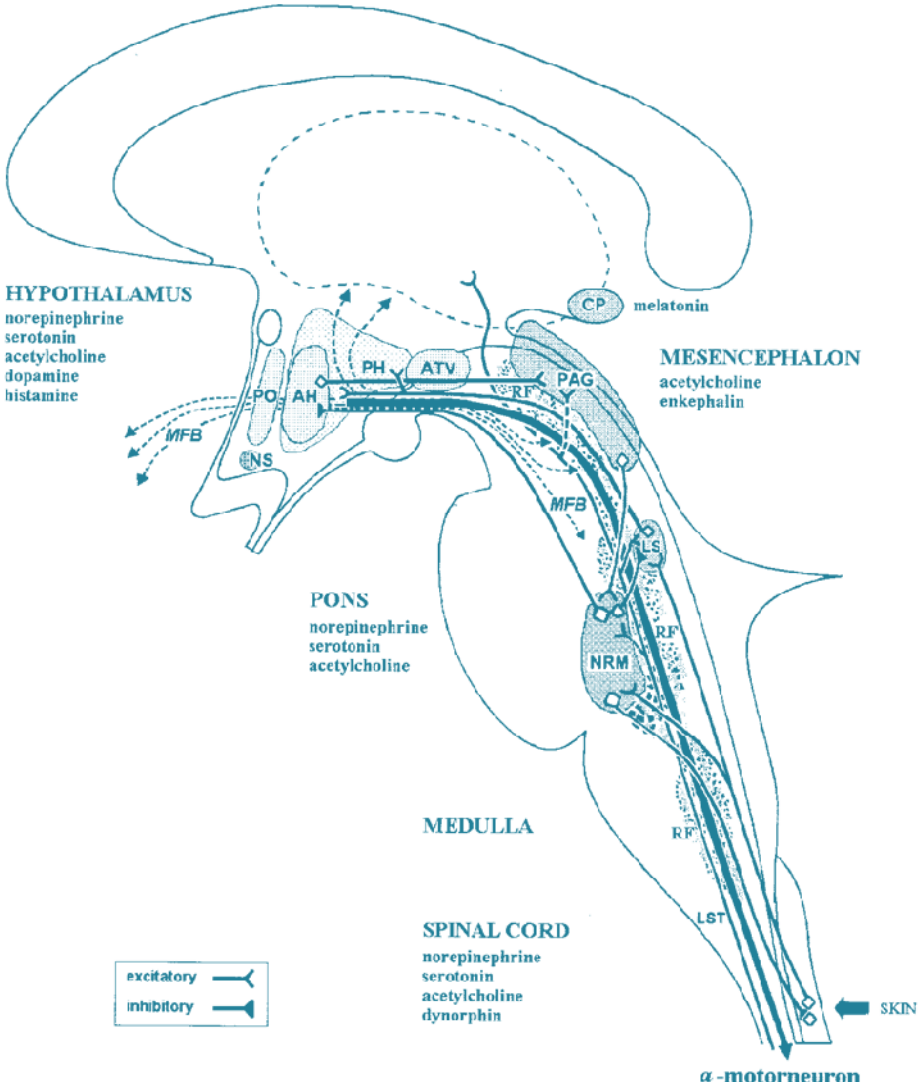


Fig:1 Thermo Regulatory centre

The thermoregulatory system coordinates defenses against cold and heat to maintain internal body temperature to optimise the metabolic function. The organisation of the thermoregulatory system particularly in the post anaesthetic shivering is discussed below:

Neuronal networks controlling thermoregulation

Multiple inputs from various thermo sensitive sites are integrated at numerous levels within the spinal cord and brain to provide networks controlling thermoregulation. Three components of thermoregulation includes thermosensors and afferent neural pathways, integration of thermal inputs , and effector pathways for autonomic and behavioral effects.

I. **Thermosensors and afferent neural pathways** –

A. Spinal cord:

Cold signals from skin travel primarily through Aδ nerve fibres whereas warm signals travel through unmyelinated c fibres, both detect cutaneous temperature. Recently it appears that Transient receptor potential protein receptors in skin and dorsal root ganglia are fundamental temperature sensing element both in skin and dorsal root ganglia, which are highly temperature sensitive. TRPV1- 4 receptors are heat activated and TRP M8 and A delta are activated by cold. All afferent cold sensitive neurons are modulated at spinal cord level which is carried by lateral spinothalamic tract to hypothalamus.

B. Extra hypothalamic Brain stem

Two groups of neurons are involved in thermal response and control of muscle tone and shivering. Nucleus raphe magnus and subcoerules area .In medulla, nucleus raphe magnus has high percentage of serotonergic neurons which responsed to warmth. The locus subcoeruleus is an area in pons, ventromedially which contain noradrenergic neurons, which responsed to cold. These areas behave as relay stations and responsible for modulation of thermal afferent information.

II. Integration of Thermal inputs

The preoptic region of the anterior hypothalamus is the dominant autonomic thermoregulatory controller. Excitatory input from the warm sensitive neurons comes from the hippocampus which links the limbic system to thermoregulatory responses. The warm sensitive neurons not only sense core temperature but also compare the thermal and non thermal synaptic afferents. Thus anterior hypothalamic neurons act as sensors as well as integrators.

III. Effector Responses and Effective mechanisms

Effector Responses

1. Sweating,
2. Peripheral cutaneous Vasoconstriction
3. Brown fat metabolism

Effective mechanisms

1. Shivering (Postural and locomotive muscular activity)
2. Vasomotion (Blood pressure and osmotic control)
3. Behavioural Regulation (powerful effector)

Shivering and Non shivering thermogenesis:

It is an involuntary oscillatory muscular activity augmenting heat production. Vigorous shivering[9] increases heat production upto 600% above baseline. The fundamental tremor frequency on Eletromyogram is near 200Hz in humans. Normal shivering is modulated by a slow 4-8 cycles/mt waxing and waning pattern. Increased muscular activity results in the generation of heat. In shivering the heat is the main product utilized for warmth.

New born babies, infants and young children experience greater heat loss than adults because they cannot shiver to maintain heat. They rely on non shivering thermogenesis. Children have an increased amount of brown adipose tissue. When cold stressed , they will release norepinephrine which reacts with lipases in brown fat. The energy is produced in the form of ATP by **Non Shivering Thermogenesis[9].**

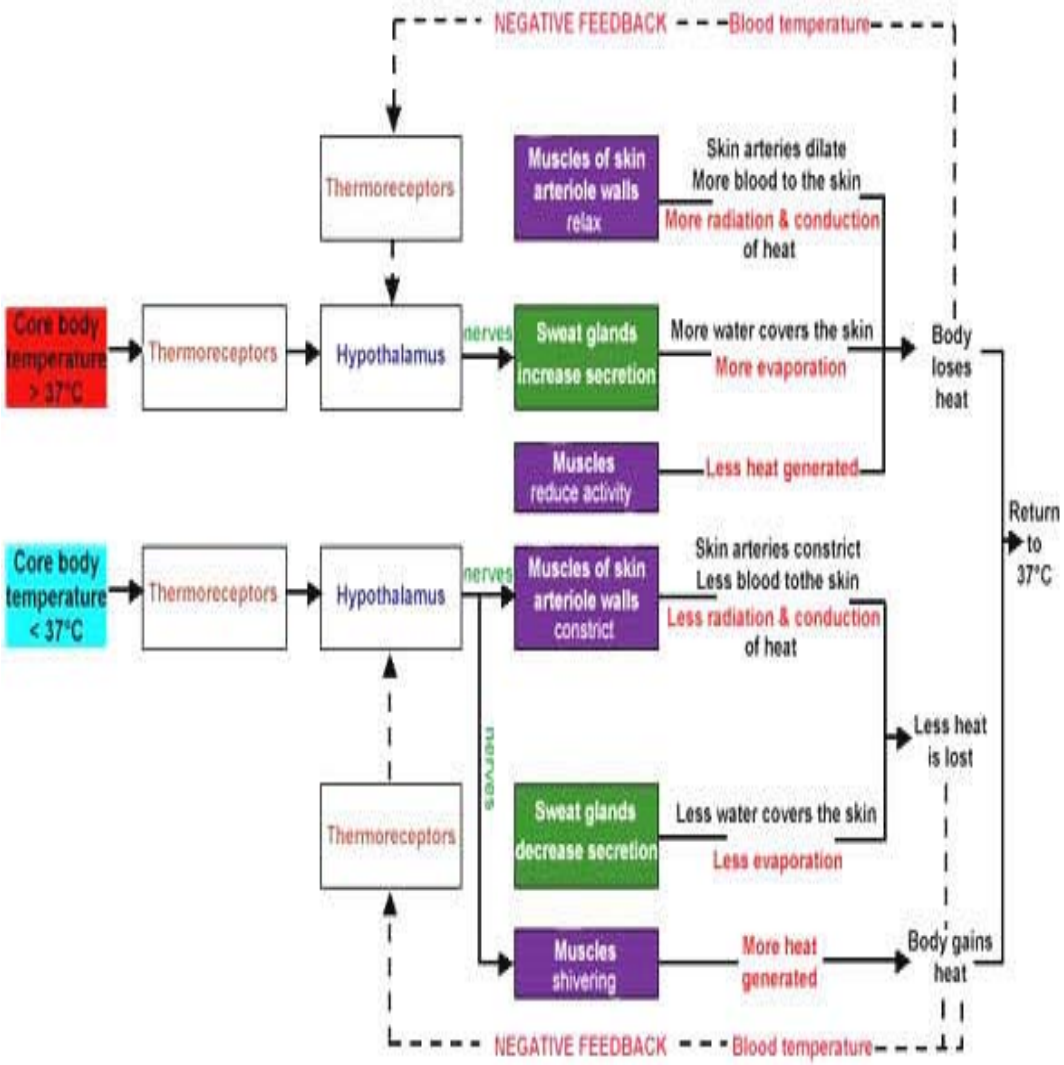


Fig:2 PHYSIOLOGY OF POSTANAESTHETIC SHIVERING

Vasomotion:

Most metabolic heat lost from skin is prevented by vasoconstriction, an autonomic effector mechanisms[9]. Total digital blood flow is divided into nutritional (mostly capillary) and thermo regulatory (mostly arteriovenous shunts) components. Roughly 10% of cardiac output traverses these arteriovenous shunts and consequently increases mean arterial pressure by 15mm Hg.

Heat loss is normally regulated without major responses of sweating or shivering because cutaneous vasodilatation and vasoconstriction is enough to control heat loss. Thermoregulatory vasoconstriction decreases cutaneous heat loss and constrains metabolic heat to the core thermal compartment. This prevents body temperature from decreasing by 1^0C which is required to activate intraoperative shivering. So shivering is a last resort defense.

Shivering[9] is elicited from the preoptic region of the hypothalamus. Efferent signals descend in the medial forebrain bundle. Although pre optic region suppress shivering by inhibition of posterior hypothalamus, evidence is lacking. The neuronal activity in the mesencephalic reticular formation and dorso lateral pontine and medullary

reticular formation exhibit descending influences on the spinal cord which increase muscle tone.

Spinal alpha motor neurons and their axons form the final common path, both co-ordinated movement and shivering, synchronization of motor neurons may be mediated by recurrent inhibition through Renshaw cells, inhibitory neurons identified.

Heat Transfer

Normal mechanism of heat loss[4] includes

I. Conduction

II. Convection

III. Radiation

IV. Evaporation

Conduction[4] heat loss are negligible during surgery. It is heat transfer between two adjacent surfaces. Convection heat loss is the important mechanism by which heat is transferred from patients to the environment. It increases in operating rooms equipped with laminar flow. Sweating increases cutaneous evaporative loss enormously but is rare during anesthesia.

All surfaces with a temperature above absolute zero radiate heat. All surfaces absorb heat radiating from surrounding surfaces. Heat transfer via this mechanism is proportional to the difference of the fourth power of the absolute temperature difference between the surfaces. Radiation is the major type of heat loss in most surgical patients.

Temperature Monitoring

Core temperature monitoring[9] is used to monitor intraoperative hypothermia, prevent over heating and facilitate detection of malignant hyperthermia .Core temperature can be accurately monitored at four sites, the tympanic membrane, pulmonary artery, distal oesophagus and nasopharynx. It can also be reliably estimated from mouth, axilla, and bladder.

Fig:3 Thermometer

Mercury in glass thermometer are slow and cumbersome and spilt mercury is a biohazard. The most common electronic thermometer are thermistors and thermocouples. Thermistors are temperature sensitive semi

conductors whereas thermocouples depend on the tiny current generated when dissimilar metals are joined. Both devices are sufficiently accurate for clinical use and inexpensive.

TEMPERATURE REGULATION

The slope of response intensity[4] versus core temperature define the gain of the thermoregulatory response. When the response intensity, no longer increasing, with further deviation in core temperature identifies the maximum intensity. This system of thresholds and gain is a model for a thermoregulatory system.

The mechanism by which the body determines absolute thresholds of temperatures is unknown. But it appear to be mediated by neurotransmitters like NA, dopamine, 5HT, Acetylcholine, Prostaglandin E_1 and neuropeptides. Control of autonomic responses is 80% determined by thermal inputs from core structures. Temperature is regulated by hypothalamus that compare integrated thermal inputs from skin surface, spinal cord and deeper tissues . In human inter thresholds range is usually 0.2 – 0.4-° C, which is bounded between sweating and vasoconstriction thresholds.

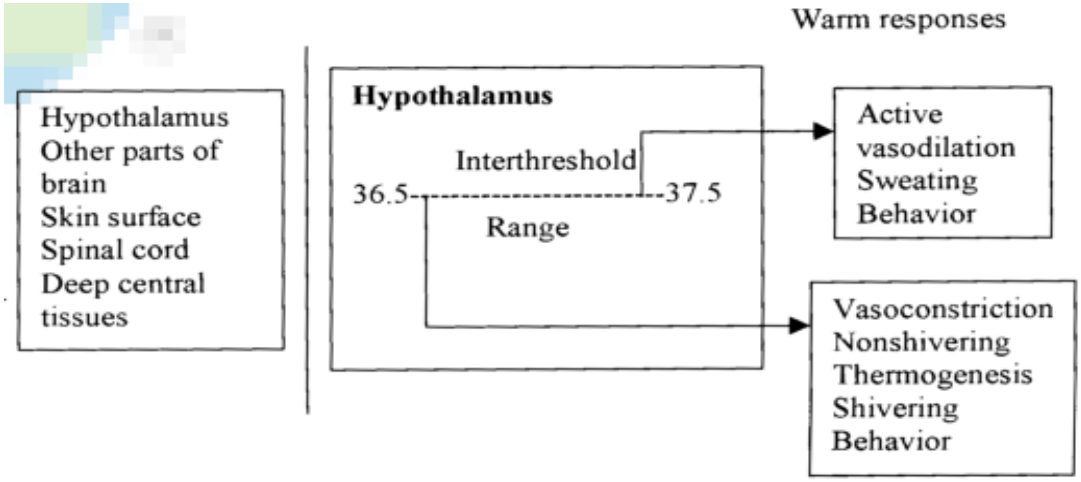


Fig. 4 Temperature Regulation

Thermo regulation during general Anaesthesia

Major disturbances are observed during and after general anaesthesia in thermoregulation. The induction of general anaestheisia impairs the function of neurons in the preoptic nuclei and hypothalamus thereby cause slighty elevated warm response thresholds whereas cold response thresholds are markedly reduced. Behavioural adaptations are not relevant under general anaesthesia when paralysed and unconscious. All general anaesthetics inhibit autonomic thermo regulatory control. It slightly elevates warm response and reduces cold response threshold. The interthreshold is increased from 0.3^0C to approximately 2^0-4^0C . The gain and maximum intensity of sweating are best preserved whereas the thresholds for vasoconstriction and shivering are markedly reduced by general anaesthesia.

Thermoregulation during regional anaesthesia

Spinal anaesthesia[9] and epidural anaesthesia decrease the vasoconstriction and shivering thresholds to a comparable degree by 0.6^0C, but to lesser amount at the level above the upper level of the block. The gain of shivering is reduced and maximum intensity of shivering is reduced in regional anaesthesia. This occurs due to shivering above block compensates for the inability of muscles below the block to response in shivering. The core temperature decreases by $0.6\text{-}1.5^0$C during the epidural anaesthesia in the first hour is due to core to peripheral redistribution of heat and epidural vasodilatation. However with prolonged epidural anaesthesia, the degree of core hypothermia is less than that of general anesthesia. This is explained that vasoconstriction above the block compensates for heat losses in epidural Anaesthesia.

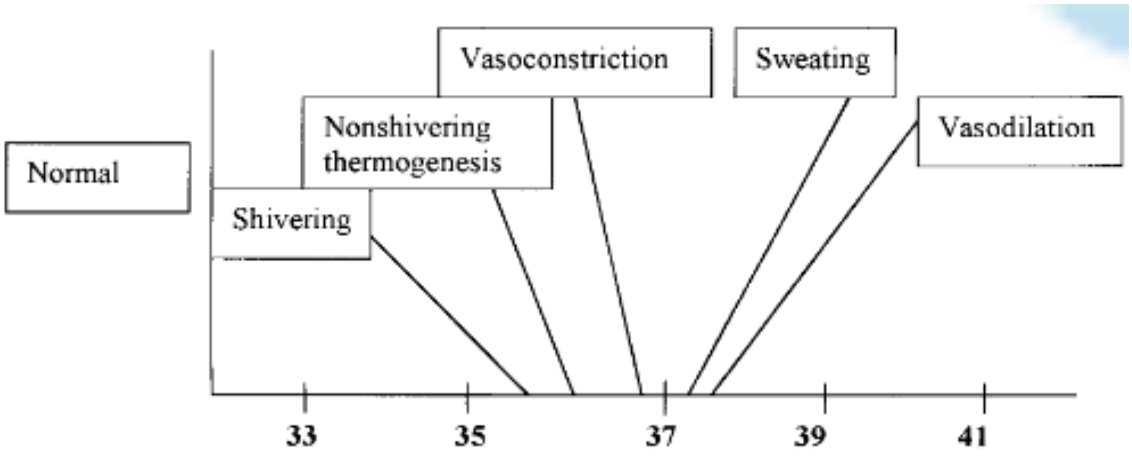


Fig:5 Thermoregulatory threshold in Normal humans

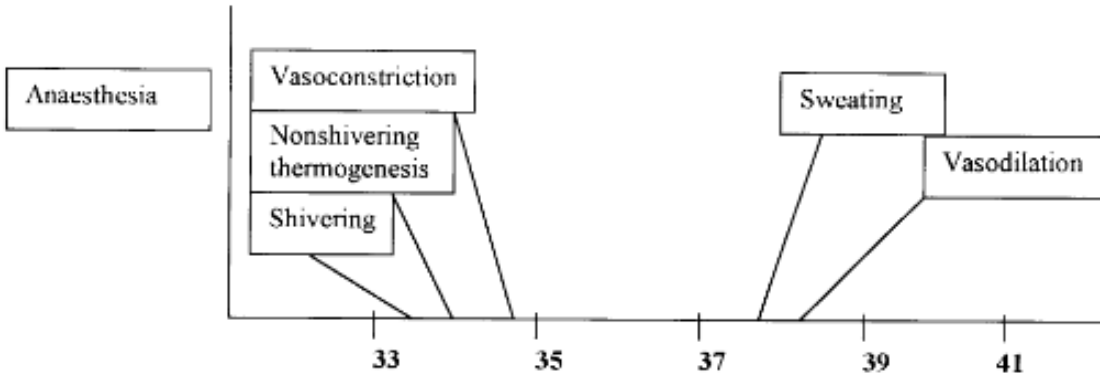


Fig:6 Thermoregulatory threshold in Anaesthetised humans

Shivering[9] during regional anaesthesia like that of general anesthesia preceded by core hypothermia. It has same electro myography characteristics as that of general anaesthesia.

Interestingly core hypothermia may not trigger a sensation of cold during regional anaesthesia this may reflect the fact that subjective cold perception depends on afferents and cutaneous vasodilatation**,** leading to sensation of warmth although accompanied by thermoregulatory shivering. Awareness of core hypothermia is impaired by epidural anaesthesia.

After the core to peripheral redistribution of body heat with induction of regional anesthesia, subsequent hypothermia depends on balance of cutaneous heat loss and metabolic heat production.. The vasoconstriction

and shivering threshold are reduced by regional anaesthesia which is further reduced by adjuvant drugs and advanced age.

Shivering Patterns in intraoperative hypothermia

Has four potential patterns:

1. Normal thermoregulatory shivering in response to core Hypothermia.
2. Normal shivering in Normothermic patients.
3. Stimulation of cold receptors by local anesthetic drug.
4. Non thermoregulatory muscular activity resembles shivering.

Electromyographic studies indicates tremor has 4-8 cycles/mt waxing and waning pattern in normal shivering.

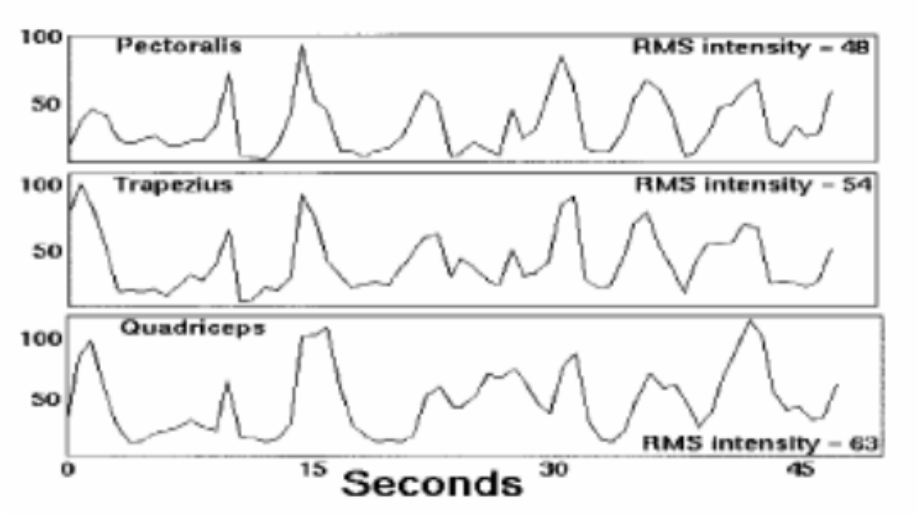


Fig:7 Shivering patterns

Skin temperature contributes to 20% of thermoregulatory responses. Hence shivering is treated by warming the skin surface, which contributes to 20% of thermoregulatory control.

To summarise, General anaesthetics and opioids have less influence on sweating but the gain and maximum intensity of sweating slightly increased. Whereas the thresholds for vasoconstriction and shivering are markedly reduced. In regional anaesthesia, central thermoregulatory control is slightly impaired.The vasoconstriction and shivering thresholds are comparably decreased. The gain and maximum response intensity of shivering are reduced. Finally behavioral thermoregulation is impaired.

Origins of postanaesthesia shivering

Several hypothesis[9] raised to explain the origins of post anaesthetic shivering which include perioperative hypothermia, the direct effect of anesthetics, post operative pain, hypercapnia, respiratory alkalosis, hypoxia, existence of pyrogens, early recovery of spinal reflex activity and sympathetic over activity. For more than 10 years, different studies provided clearer insight into the origins of anaesthesia induced shivering. One hypothesis, explain the clonic movements corresponds to spinal reflex hyperactivity, resulting from inhibition of descending cortical control by

residual anaesthetics. These EMG signals[9] are compatible with the clinical description of abnormal reflexes during the early recovery phase.

Another existence of a link is between post-operative pain and incidence of shivering; which was confirmed by a study comparing the frequency of shivering after intra-articular li**d**ocaine who underwent knee arthroscopy. Those patients with severe pain who did not receive local anaesthesia was accompanied by higher incidence of post anaesthetic shivering.

Most frequently tested and proposed hypothesis is anesthesia induced hypothermia and resulting thermo regulatory shivering. EMG analysis of shivering patterns are similar during anesthesia and hypothermia in normal population. Of all the different hypothesis, to explain the incidence of post anaesthetic shivering, only peri operative hypothermia and pain have been clearly explained.

Consequences of Post aneasthetic shivering

The first consequence of post anesthetic shivering is discomfort and stressful sensation. Another consequence is increased pain caused by muscular contractions on the operated site, and tension of suture

line. Following ophthamological surgery, shivering increases intra ocular pressure and may worsen the morbitidity.

Shivering is perceived as unpleasant experience by the parturient under regional Anaesthesia. Ostherimer and Datta noted that "Of all the side effects associated with anesthesia and birth, shivering alone was the only symptom as a disconcerting and unacceptable". The main effect of post anaesthetic shivering is the increase in oxygen consumption Vo_2 approximately 40-120% by affecting several muscle groups; shivering triggers increase in metabolic demand combined with increased minute ventilation. Sometimes the metabolic demand can exceed the capacity to deliver oxygen and it is quite rare, to result in anaerobic metabolism.

Prospective randomised data suggested that the high risk patients with reduction in Core temperature by 1.3°C were three times more likely to experience adverse myocardial outcomes due to marked increase in plasma catecholamines. Mild hypothermia doubles the incidence of morbid cardiac events in patients with coronary disease and hence strategies to prevent perioperative shivering is mandatory for the comfort and safety of the patients.

Measures to combat shivering

(1) Passive insulators[9]

Cotton blankets, surgical drapes, disposable plastic draps, plastic bags are passive insulators which reduce heat loss to environment. Heat conservation is directly proportional to area covered. A single layer covering material decreases approximately 30% heat loss. Unfortunately adding layers do not increase the benefit.

(2) Active warming system

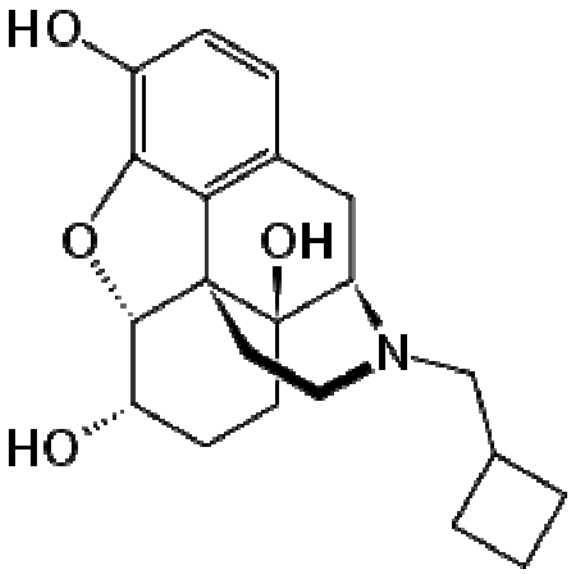
In Convection warming system, when warmed air is forced through a quilt like porous blanket covering the body. It replaces air envelope of normal body with a warm air envelope. This is the most effective system for conservation of body heat (Bair Hugger unit). Radiant heat system like infrared light, thermal ceiling lights are used for warming. Other measures like warming inspired air, warming intravenous fluids, blood and blood components before infusion. Maintaining post operative environment at 24^0C are useful in preserving body temperature and reducing shivering

3) Pharmacotherapy[20]

Potent anti shivering properties have been attributed to many drugs. These include biogenic monoamines, cholinomimetis, cations, endogenous peptides and NMDA receptor antagonists. All these drugs appear to modulate the central thermoregulatory control mechanisms.

NALBUPHINE – PHARMACOLOGY

Nalbuphine is a semi-synthetic opioid agoinst antagonist analgesic which belongs to phenanthrene series. It is chemically similar to opioid antagonist, naloxone and naltrexone and oxymorphone.



(–)-17-(cyclobutylmethyl)- 4,5α-epoxymorphinan- 3,6α,14-triol hydrochloride

Fig:8 Chemical Structure of Nalbuphine

Preparations

It is available in two formulations. 10mg/ml and 20mg/ml of Nalbuphine hydrochloride. Both strengths comprise of 0.94% sodium citrate hydrous, 1.20% citric acid anhydrous, 0.1% sodium metabisulfite and 0.2% of 9:1 mixture of methyl paraben and propyl paraben as

preservatives where as 10mg/ml contain 0.1% sodium chloride. It is soluble in water and ethanol, available as an injectable solution.

Pharmaco kineties

Nalbuphine is a potent analgesic, its potency equivalent to that of morphine on a milligram basis. Its oral administration is three times more potent than codeine.

- Onset of action occurs within 5-10mts after intravenous administration.
- Its plasma half life is 5 hrs
- Duration of analgesic activity has been in the range from 3-6 hrs.

The opioid antagonist activity of nalbuphine is one fourth as potent as nalorphine and 10 times that of pentazocine.

MECHANISM OF ACTION

The exact mechanism of action is unknown. But it interacts with μ opioid receptors and delta opioid receptors by competitive inhibition. It acts as agonist at kappa opioid receptor and its interaction with kappa opioid receptors is responsible for its analgesic and anti shivering property. Activation of supraspinal and spinal k receptors results in less respiratory depression, sedation and limited analgesia.

ADVANTAGE OF NALBUPHINE

An important difference between nalbuphine and pure opioid analgesia is the ceiling effect on respiration. The ceiling effect is that increase in dose >30mg do not produce further respiratory depression in absence of other drugs affecting respiration. Nalbuphine has limited ability to depress respiratory function[4]. When administered with concurrent μ-agonist analgesics eg.morphine, fentanyl, it may partially reverse or block opioid induce respiratory depression. Nalbuphine[4] 10 mg/ml caused no significant changes in systemic, pulmonary ,arterial and pulmonary capillary wedge pressure.

Clinical uses

1) It is used for the relief of moderate to severe pain
2) Used as a supplement to balanced anaesthesia for pre-op and postop analgesia
3) For obstetrical analgesia during labor and delivery
4) In addition to relief of pain,
5) It is used as a treatment for morphine induced pruritis.

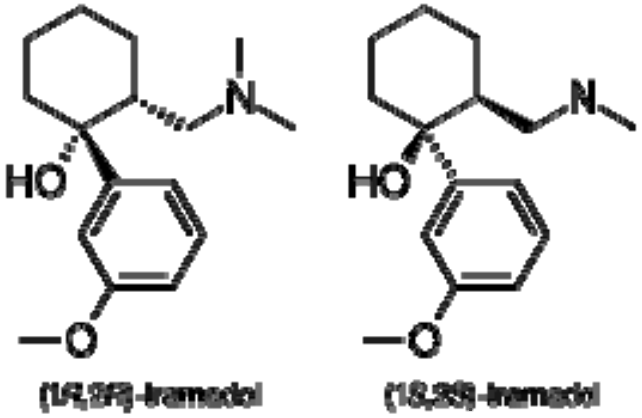
Overdose and side effects:

In case of overdose, the specific antidote is Naloxone. Tolerance to side effects of nausea, sedation and cognitive symptoms are seen. Nalbuphine has less ability to depress respiratory function than other pure μ-opiod analgesic drugs.

Other side effect is sedation and less frequent side effects are nausea, vomiting , dizziness, vertigo, dry mouth and headache. Other rare side effects (include <1%) are CNS side effects like restlessness, euphoria hallucinations and CVS side effects like hypotension, bradycardia, pulmonary edema and GI cramps, dyspepsia.

PHARMACOLOGY OF TRAMADOL

Tramadol is a synthetic, centrally acting analgesic agent which is structurally related to codeine and morphine. It is a racemic mixture of 2 enantiomers, which enhance analgesic actions. It was first synthesised by Grunenthal in 1962.



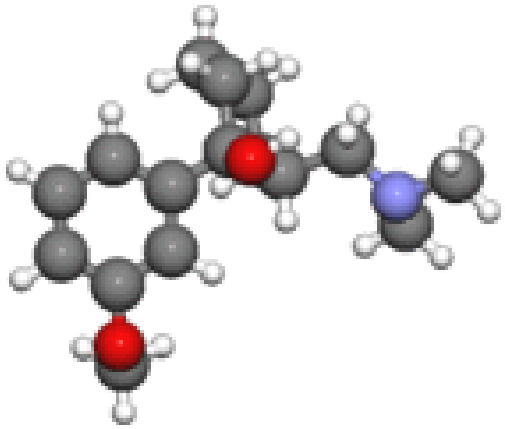


Fig:9 Chemical Structure of Tramadol

Mechanism of action

Tramadol act synergistically on descending inhibitory pathway in the CNS, resulting in the modulation of second order neurons in the spinal cord. These inhibitory pathways mediated by the raphe nuclei, periaqueductal grey, locus coeruleus and reticulospinal projections involve both opioid and monoamine neurotransmitters. In healthy volunteers, it decreased sweating, shivering thresholds, and vasoconstriction and these effects were partially reversed by naloxone.

Tramadol unique dual mechanism of action like weak opioid agoinst,it stimulates μ receptor and weak NA and 5-HT reuptake inhibitor synergistic actions enhance its analgesic effects. It activates spinal inhibition of pain by decreasing the reuptake of NA and serotonin Tramadol is one fifth to one tenth as potent as morphine.

Pharmaco kinectis

It is available in various forms

1) Solutions for IV, IM, SC administration
2) Formulations for oral like capsules, tablets or drops. Sustained release formulations are also available.
3) Suppositories for per rectal administration
4) Preservative free forms are used in epidural blocks and neuromuscular blocks.

Absorption

Tramadol is rapidly absorbed after intramuscular injection. C max of 166µg/L is reached in 0.75 hrs after 50mg intramuscular injection. Intravenous and intramuscular infusion are bioequivalent in respect to systemic bio-availability. Cmax values of 355-369 µg/L reached in 0.9 hrs and 1.1 hrs after intra muscular injection of 100mg of tramadol.

Distribution

It is rapidly distributed with a half-life of 6 minutes in the initial phase followed by a slower distribution phase of 1.7 hrs. The total volume distribution of 306L after oral & 203 L after parentral administration indicates high tissue affinity, its plasma binding is 20% brain peak concentration of tramadol occurs after 10mts of oral administration and those of its major active metabolite o–desmethyl tramadol(M_1) 20-60 mts after oral administration. Tramadol crosses the placental barrier with 80% maternal concentration in umbilical venous various plasma. Very small 0.1% excreted in breast milk.

Metabolism and Elimination

Tramadol undergoes extensive first pass metabolism in the liver via two main metabolic pathways CYP3A and CYP2 D6, only one metabolite is active. About 10-30% eliminated in urine as unmetabolised form. It is excreted via kidneys 90% and 10% via feces.

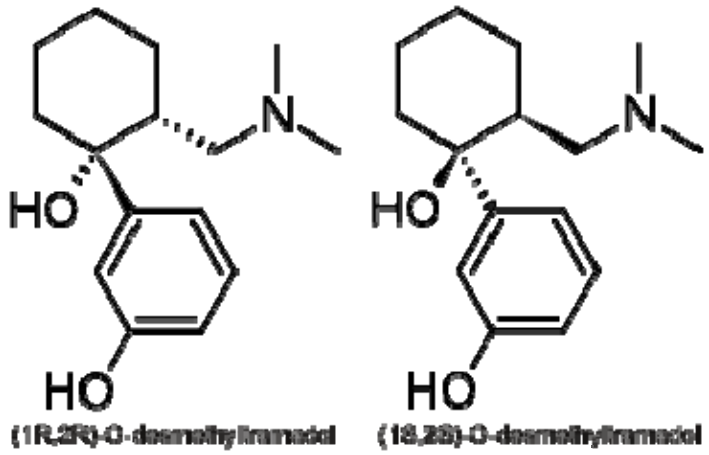


Fig 10: Tramadol metabolites

Age

The pharmaco kinetis is not age dependent; according to available studies there is no pharmacokinetic difference between adults and children. However elimination is prolonged in elderly peoples.

Renal & Hepatic Diseases

Since tramadol is eliminated renally, its elimination is relatively prolonged in hepatic and renal disorders. In patients with advanced cirrhosis its elimination half life is extended to a mean of 13 hrs to 22 hrs.

Drug Interaction

Tramadol is metabolized by CYP3A and CYP2D6 enzymes, Drugs acting on these enzymes, should be used with utmost care. It includes, cimetidine, quinidine, fluoxetine, carbamazepine, amitriptyline etc. MAOI inhibitiors and other drugs that lower seizure thresholds are used cautiously with tramadol.

Pharmaco dynamics

Respiratory system

Opioids analgesics produce dose dependent respiratory depression, this is mediated by a decrease in the sensitivity of respiratory centre to CO_2 which results in decreased respiratory rate and tidal volume; clinically significant respiratory depression is not noted at the recommended dose of tramadol unlike other opioids commonly used.

Cardiovascular system

It does not have effects on heart rate or blood pressure. No major side effects noticed in 57 cardiac risk patients posted for major surgery. No effects on mean pulmonary artery pressure[4], pulmonary capillary wedge pressure, strokevolume index and total peripheral resistance were observed. Tramadol 1mg/kg administered intravenously produced no significant change in heart rate and blood pressure in patients with unstable angina and myocardial infarction.

Gastrointestinal system

It causes minimal effect on gastro intestinal function when compared to other opiods. It causes minimal increase in gastric emptying and colonic transit time. Side effects noted are nausea, vomiting and altered appetite. Incidence of constipation is very less compared to other opioids.

Central nervous system

Tramadol produces sedation headache dizziness, euphoria dysphoria and seizures. Incidence of seizures is less than 1% . Hence cautiously used in epileptic, alcohol and drug withdrawal patients and those on anti depressant therapy. It is known to have anti-convulsant property mediated by kappa receptors. Antidepressant effect is observed based on its monoaminergic uptake inhibition.

Analgesic effects

The analgesic effect is due to synergistic activity of its racemate with metabolite O-desmethyl Tramadol, , The peak effect occurs 1 to 4 hrs after oral administration. Duration persists for 3 to 6 hrs after onset. Intravenous tramadol 2mg/kg provides similar effects on pain and tolerance

thresholds compared to pethidine 1mg/kg. Recent evidence suggests that hepatic demethylation by liver enzyme sparteine oxygenase and CYP450/CYP 2D6 play a major role in mediating analgesic effect.

Overdose

It can produce significant neurotoxicity like seizures, coma, respiratory failure, tachycardia and hypertension on over dosage. The most common overdose symptoms are lethargy(30%), Nausea(14%) agitation (10%) ,seizures(8%), coma (5%), Hypertension (5%), Respiratory depression 2%. No serious cardiotoxicity noted on overdose. The risk of abuse with Tramadol is low.

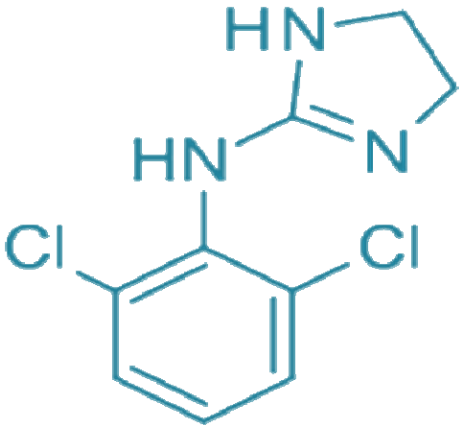
Uses

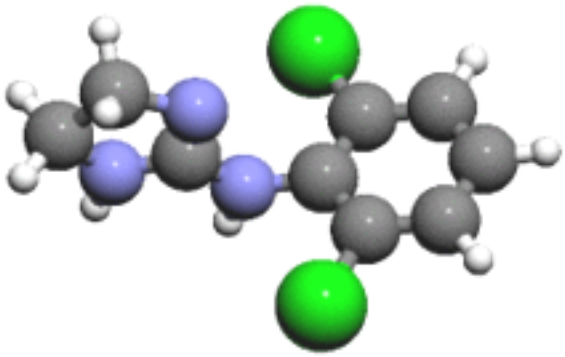
1. Tramadol is used in the treatment of acute pain;
2. Tramadol is used in patients with low pulmonary reserve like elderly, obese and preexisting cardiopulmonary diseases.
3. Pain relief for surgical procedures of thorax and upper abdomen
4. In patient control analgesia in surgical procedures including abdominal, orthopedic and cardiac surgery.

5. In day care patients
6. Used in acute orthopaedic trauma and sports injuries.
7. Used in patients with colicky abdominal pain and acute appendicitis
8. It is found to be effective in obstetric analgesia.
9. Tramadol improve gastro intestinal recovery from abdominal surgery.
10. It is beneficial in whom NSAIDS are contra-indicated like patients with peptic ulcers.
11. It is cautiously used in patients with impaired renal, hepatic or cardiac function.
12. Recently it has shown positive effects on immune system function.

PHARMACOLOGY OF CLONIDINE

Clonidine is centrally acting sympatholytic α_2 adrenergic agoinst and imidazole receptor agoinst. It activates α_2 adrenoreceptors and release acetycholine , noradrenaline, dynorphine. The depressor effects of these transmitters modulate thermal inputs.Clonidine also reduces the thresholds for vasoconstriction and shivering.





***N*-(2,6-dichlorophenyl)-4,5-dihydro-1*H*-imidazol-2-amine**

Fig:11 Chemical Structure of Clonidine

Pharmaco kinetics:

The oral bio availability of clonidine is 75 -95%. Its protein binding is about 20- 40% .Clonidine is metabolized in liver to inactive metabolites and 72% is excreted in urine. Its plasma half life is 8hrs , average of 5-13hrs for single dose and 41hrs for repeated dosing. It can be dministered through oral, epidural, intra venous routes and transdermal and topical applicators are available.

Mechanism of action.

Clonidine has high specificity towards the presynaptic α_2 receptors in the vasomotor center located in brain stem.By acting on α_2 receptor clonidine decreases presynaptic calcium level and subsequent nor epinephrine release with resulting fall in sympathetic tone and blood pressure. It has also been proposed that the anti hypertensive effect of clonidine is due to agonism on I_1 receptor (Imidazoline receptor) which mediates sympathominhibitory action of Imidazoline receptor to lower blood pressure. Its mechanism in the treatment of attention deficit hyperactivity disorder is to increase the nor-adrenergic tone in pre frontal cortex and also from the locus coeruleus.

Synthesis :

It is a 2-imidazoline derivative (2,6 dichloro phenylamino imidazoline) synthesized from 2,6 dichloroaniline the reaction of which with ammoniumthiocyanate gives N-(2,6-dichlorophenyl) thiourea. Methylation of thiourea and subsequent reaction with ethylene diamine gives clonidine.

Withdrawal

Sudden discontinuation cause rebound hypertension due to rebound sympathetic outflow. It should be tapered slowly to avoid rebound effects. Reintroduction of clonidine in mild cases and both alpha and Beta blockers for more urgent conditions. Beta blockers should never be used alone to treat clonidine withdrawal as alpha vasoconstriction continues.

Clinical uses

1. Clonidine is commonly used as anti-hypertensive agent.
2. Used for Attention deficit hyperactivity disorder**.**
3. And used in the treatment of tourette syndrome
4. It is used for the withdrawal symptoms produced by long term Narcortics, alcohol and nicotine.

5. Used to treat psychiatric disorders including stress, sleep disorders, borderline personality disorder and anxiety disorders.
6. It produces mild sedation can be used as premedication.
7. It is used in Epidural analgesia extensively.

Other Uses

It is used in restless leg syndrome, to treat facial flushing, redness with rosacea. It is topically used in diabetic neuropathy, Clonidine used for migraine headaches and hot flushes of menopause.

Adverse effects

Principal adverse effects are dizziness, dry mouth, drowsiness and hypotension; dose dependent sedation, headache, fatigue and drowsiness noticed.

Other side effects are anxiety, constipation, rashes, weight gain, erectile dysfunction. Uncommon,side effects are paresthesia, delusional perception, night mare,sinus bradycardia, raynaud's phenomenon, itchiness & hives. Rare complications are atrio-ventricular block, alopecia, high blood sugar, nasal dryness and gynaecomastia.

MATERIALS AND METHODS

STUDY TYPE :

Observational

STUDY DESIGN :

Prospective

Randomised

Clinical trial, double blinded

STUDY POPULATION

The study is under taken at **Raja Mirasudhar Hospital,Thanjavur** during the period of September 2013 to September 2014. Institutional ethical committee approval was obtained. Informed written consent was also obtained from participating patients.

CASE DEFINITION

Total of 75 patients from obstetrics aged between 20-30 years of ASA grade I or II undergoing elective and emergency caesarean section under spinal anaesthesia who subsequently developed shivering were included in this study.

Groups

The Patients were randomly divided into 3 groups.

1. Group T – 25 Patients who received 0.5 mg /kg tramadol intravenously.
2. Group C – 25 Patients who received 0.5 µgm/kg of clonidine intravenously.
3. Group N – 25 patients who received 0.1 mg/ kg of nalbuphine intravenously.

Outcome Measure

Primary Measure

(i) To evaluate the efficacy of tramadol, clonidine and nalbuphine in controlling Post anaesthesia shivering after caesarean secction.

Secondary measure

I. Time of onset of shivering after spinal Anaesthesia

II. Time interval of disappearance of shivering after the drug given iv.

III. Side effects.

Inclusion Criteria

1. Patients from obstetrics group aged between 20 – 32 years of ASA grade I and II undergoing elective or emergency casearean section who developed shivering after spinal anaesthesia
2. Patients who gave a valid informed written consent.

Exclusion Criteria

1. Patients with significant systemic diseases like cardiovascular, renal, hepatic, respiratory or neurological diseases.
2. Patients with thyroid disease, eclampsia, GHT, GDM and obesity
3. Patients with known hypersensitivity to Tramadol clonidine and nalbuphine.
4. Patients on long term Phenothiazines and MAO Inhibitors
5. Patients who did not give valid informed consent.

Procedure

After getting informed written consent from all participating patients, this randomized double blind clinical study was conducted in our institution. Ambient temperature was noted, baseline vital parameters were recorded. iv fluid started with iv access of 18 G cannula. The volume of the local anaesthetic, use of vasopressors, volume of fluid is determined by the

attending anaesthesiologist and was not affected by inclusion in the study. Baseline preoperative axillary temperature was noted in all the patients. A standard double layered blanket was used to cover the chest and upper limb of the patient. All the preloading fluid and drugs were given at room temperature. Oxygen at rate of 5L / mt was administered through facemask to all parturients. Monitoring of NIBP, pulse oximetry, ECG was done throughout the procedure. Central neuraxial blockade was given with Inj. bupivacaine(0.5%) 2ml for all casearean section as per protocol. Patients who developed Shivering after neuaxial blockade were included in the study. A total of 75 cases filling the above criteria were selected for study were randomly divided into one of the three groups.

Group T - 25 Patients receiving 0.5 mg /kg Tramadol IV

Group C - 25 Patients receiving 0.5 µgm /kg clonidine IV

Group N - 25 Patients receiving 0.1 mg /kg nalbuphine IV

Shivering was graded as follows as per **Wrench** which is as follows

Grade 0 - No shivering

Grade 1 - One or more of the following, piloerection, peripheral vasoconstriction, peripheral cyanosis or without visible muscle activity.

Grade 2 - Visible muscle activity confined to one muscle group.

Grade 3 - Visible muscle activity in more than one muscle group.

Grade 4 - Gross muscle activity involving the whole body.

All the patients who developed shivering of grade 3 or 4 of shivering were included in the study randomly divided in one of the three groups. Group T received tramadol 0.5 mg/kg, Group 'C' received clonidine 0.5 μg/kg and group 'N' received nalbuphine 0.1 mg/kg.

Data Collection

The drug was administered by another personnel who is blinded to whether the drug contains clonidine, tramadol or nalbuphine. The same person assessed the effect of the drug administration based on the format provided. All the patients were assessed for grade of shivering, its disappearance, hemodynamic status and side effects if any.

Patients were observed at intervals of 1mt till 5 mts and thereafter 10,20,30,45,60 mts. Baseline pulse rate, BP, SPO_2, Respiratory rate and temperature were noted, during shivering and after the drug

administration at regular intervals. Recurrence of shivering and requirement of additional dose were also noted.

Sedation characteristics were noted and graded according to **"Filos Sedation Score"** as follows:

1. Awake and alert
2. Drowsy, responsive to verbal stimuli.
3. Drowsy, arousable to physical stimuli.
4. Unarousable

Statistical methods

Descriptive statistical analysis, was carried out in the present study. Results on continuous measurements are presented on mean ± 5D(min-Max) and results on categorical measurements are presented at 5% level of significance. One way ANOVA test has been used to find the significance of study parameter between the three groups of patients. Chi square test has been used to find the significance of study parameters on categories scale between two or more groups.

Significant figures

- ❖ Suggestive significance (p value $0.05 < p < 0.10$)
- ❖ Moderately significance (p value $0.01 < p \leq 0.05$)
- ❖ Strongly significance (p value $p \leq 0.01$)

OBSERVATION AND RESULTS

75 Patients of Antenatal mothers aged between 20-32 years of ASA grade I or II under going caesarean section under spinal anaesthesia who developed shivering were included in the study.

The patients were randomly allocated into three groups.

Group – T	25 patients received 0.5mg /kg of tramadol intravenously.
Group – C	25 patients received 0.5 µgm/kg of clonidine intravenously.
Group – N	25- patients received 0.1mg/kg of Nalbuphine intravenously.

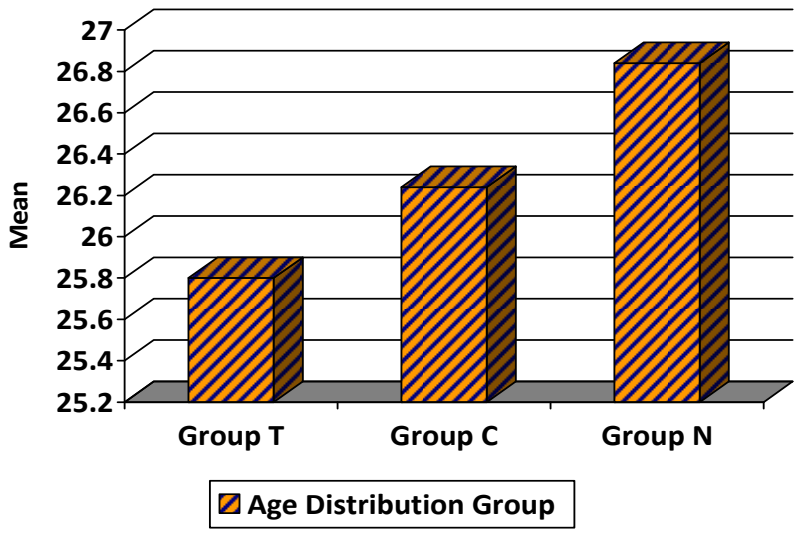
Table-1

Demographic Data :

Age Distribution among groups

Study Group	Mean	SD	P Value	Significant
Group T	25.80	2.739	0.375	Not
Group C	26.24	2.773	.> 0.05	Significant
Group N	26.84	2.322		

The minimum age of the patient was 20 years and the maximum age was 31 years. The mean age of the patients in group T is 25.80+2.739 in group C is 26.24+2.739 , and group N=26.84 years. The statistical analysis is not significant for age (p=0.375) between groups.



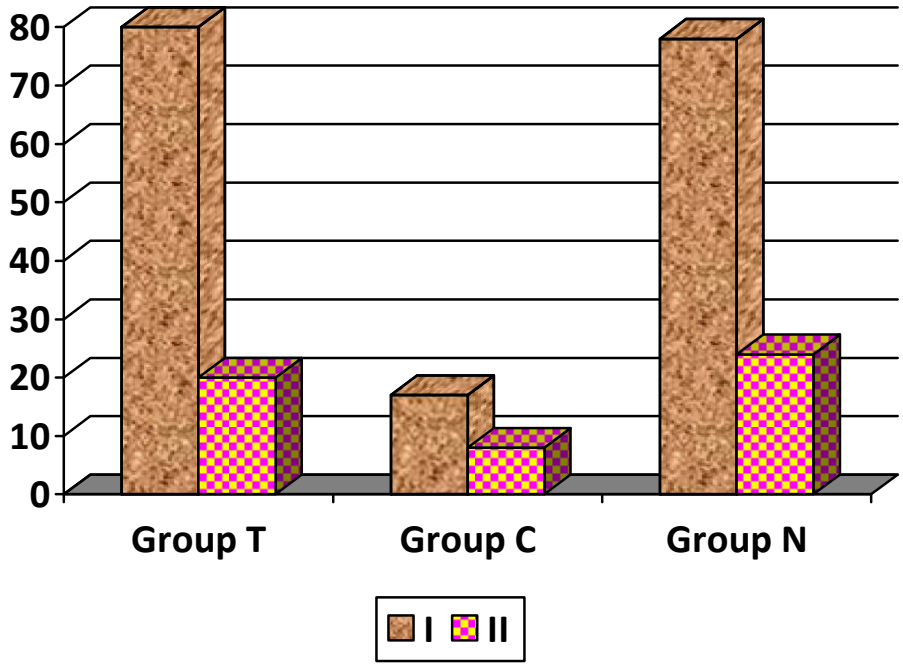
Graph .1 Age Distribution Group

Table 2

ASA GRADING

	GROUP T	GROUP C	GROUP N	TOTAL	STATISTICAL INFERENCE
I	20 (80%)	17 (68%)	19 (78%)	56 (74.7%)	X^2 = 098 P= 0.611>0.05 Not Significant
II	5 (20%)	8 (32%)	6 (24%)	19 (15.2%)	

In the study , Group T has 80% ASA I patients and 20 % ASA II patients, Group C has 68% ASA I patientsand 32 % ASA –II patients and in group N, it is 78% and 24% for ASA I & II. The statistical analysis is not significant for ASA grading (p=0.611) between groups.



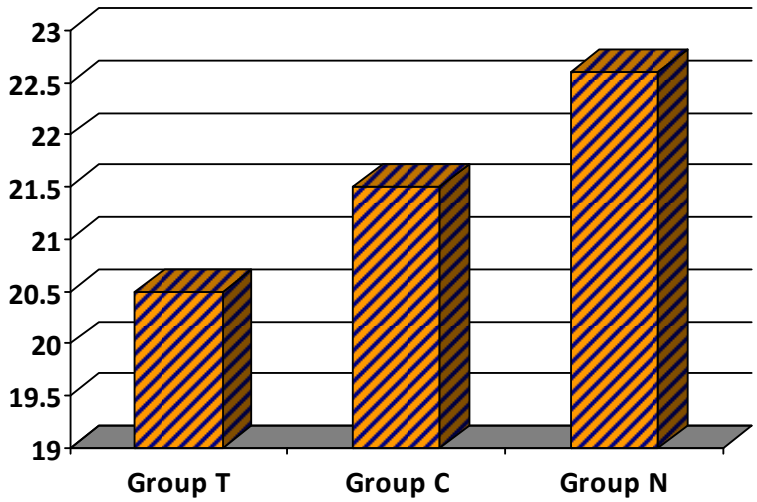
Graph.2 ASA Grading

Table 3

TIME FOR ONSET OF SHIVERING

Study group	Onset time	Mean difference	P value	Significant
Group T Group C Group N	20.5 mts 21.5 mts 22.6 mts	21.53%	0.068>0.05	Not significant

The mean time for onset of shivering in group T was 20.5mts, and in the Group C was 21.5 mts and in group N was 22.6 mts . The statistical analysis showed the time of onset of shivering is not significant(p=0.68) between groups.



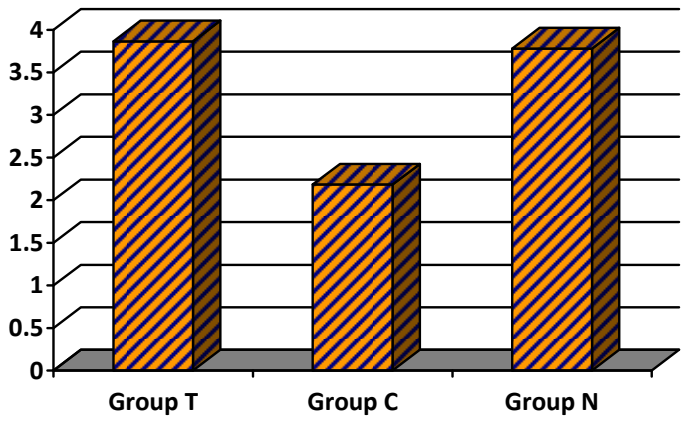
Graph .3 Onset of Shivering

Table 4

TIME INTERVAL FOR DISAPPEARANCE OF SHIVERING

Group	Mean (mts)	SD	P Value	Significant
Group T Group C Group N	3.864 2.184 3.780	0.25 0.188 0.410	0.00< 0.05	Highly significant

In this study the time interval for disappearance of shivering was noted, among groups. In Group T the mean time interval for disappearance was 3.864 +0.25mts, in Group C it is 2.184 + 0.188mts and in Group 'N' the mean time intervals is 3.78+0.410 mts. The 'P' value here is <0.00 <0.05 which is highly signficant suggesting that clonidine group achieved lesser time for complete cessation of shivering when compared to tramadol and naulbuphine group.



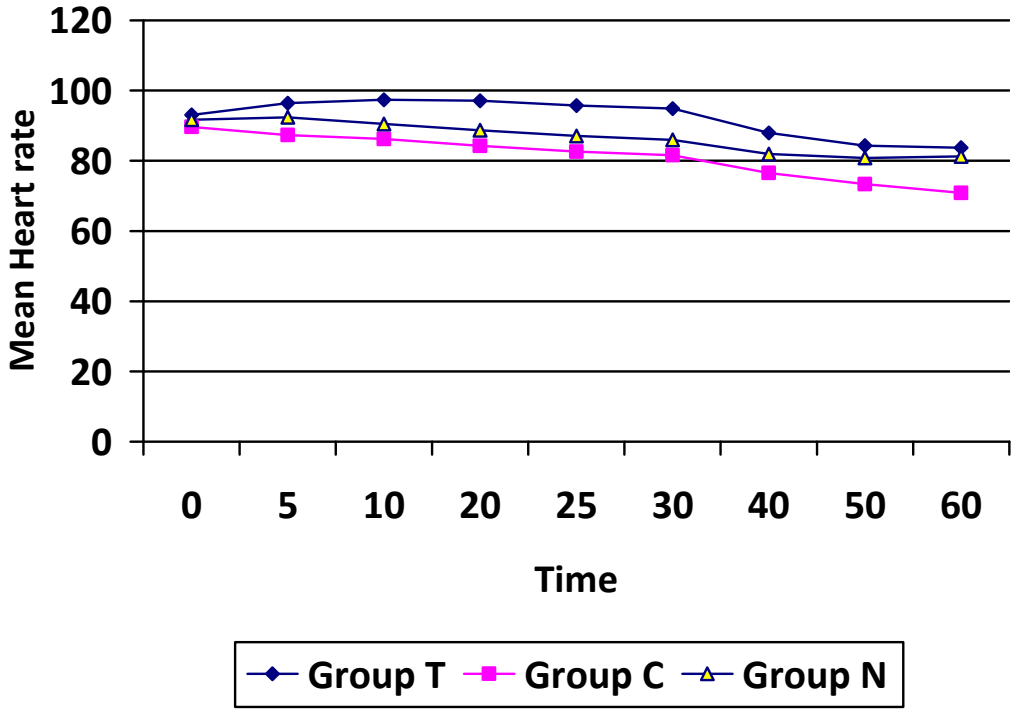
Graph.4 Time Interval for Disappearance of Shivering

Table 5

COMPARISON OF HEART RATE

Time mts	Group T		Group C		Group N		Statistical Inference	
	Mean /Mt	SD	Mean	SD	Mean	SD	P	Significant
0	93.04	9.667	89.62	9.031	91.72	9.46	0.214>0.05	Not significant
5	96.40	9.587	87.28	8.905	92.40	10.67	0.206>0.05	Not significant
10	97.36	8.920	86.24	8.950	90.48	8.70	0.202 >0.05	Not significant
20	97.12	9.558	84.24	8.293	88.72	9.217	0.218 >0.05	Not significant
25	95.76	11.823	82.56	7.924	87.04	9.185	0.200 >0.05	Not significant
30	94.88	10.741	81.60	7.483	85.92	8.878	0.210>0.05	Not Significant
40	87.88	8.565	76.48	7.355	81.92	8.23	0.206>0.05	Not Significant
50	84.32	8.219	73.36	6.897	80.80	9.32	0.208> 0.05	Not significant
60	83.68	7.952	70.88	7.855	81.20	9.539	0.218> 0.05	Not significant

In the present study the heart rate variation was within 15% of basal value, among groups and there is no statistical significance between groups.



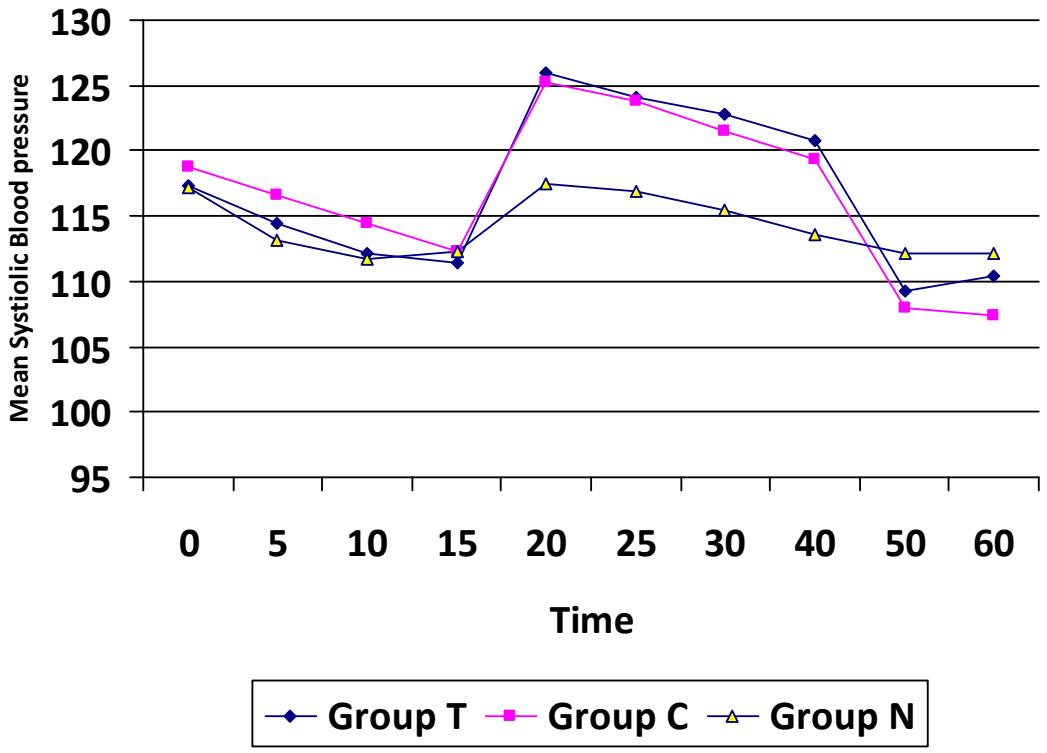
Graph.5 Trend of Heart rate

Table – 6

COMPARISON OF SYSTOLIC BLOOD PRESSURE

Time mts	Group T		Group C		Group N		Statistical Inference	
	Mean/ Mt	SD	Mean	SD	Mean	SD	P	Significant
0 mts	117.28	7.185	118.08	5.901	117.12	7.178	0.457> 0.05	Not significant
5	114.40	6.218	116.56	5.701	113.12	6.030	0.129> 0.05	Not significant
10	112.16	5.998	114.40	6.658	111.76	5.754	0.269> 0.05	Not significant
15	111.4	5.987	112.32	6.625	112.32	5.935	0.845> 0.05	Not significant
20	125.92	4.183	125.28	4.542	117.44	6.259	0.457> 0.05	Not significant
25	117.28	7.185	118.08	5.901	117.12	7.178	0.129> 0.05	Not significant
30	114.40	6.218	116.56	5.701	113.12	6.030	0.269> 0.05	Not significant
40	112.16	5.998	114.40	6.658	111.76	5.754	0.845> 0.05	Not significant
50	111.4	5.987	112.32	6.625	112.32	5.935	0.457> 0.05	Not significant
60	125.92	4.183	125.28	4.542	117.44	6.259	0.129> 0.05	Not significant

In the present study, the systolic blood pressure between groups were recorded at 5 minutes interval and was within 15% basal values. There is no statistical significance between the groups.



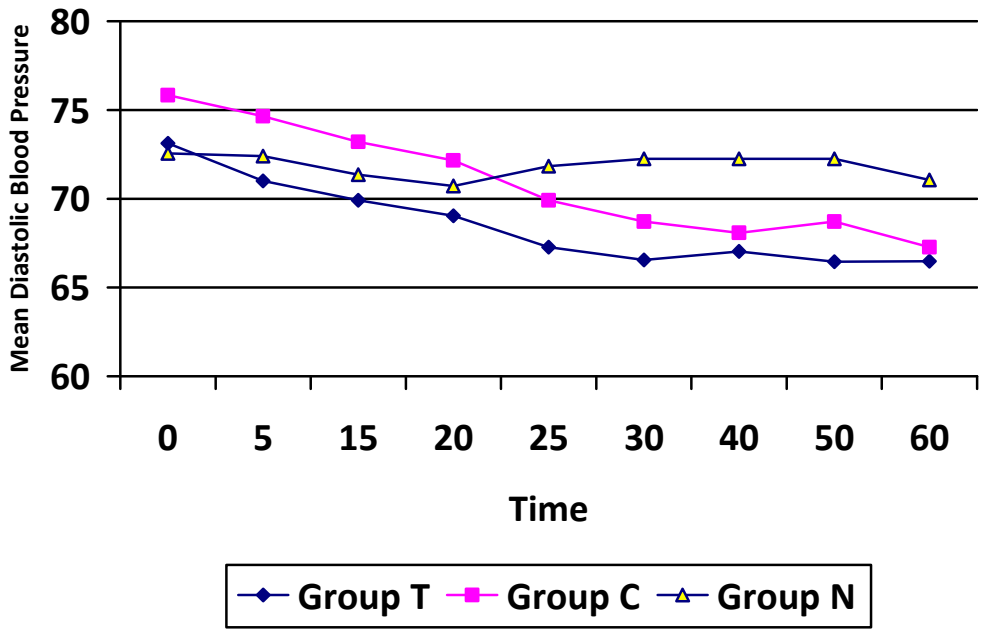
Graph .6 Trend of mean systolic blood pressure

Table - 7

COMPARISON OF DIASTOLIC BLOOD PRESSURE

Time mts	Group T		Group C		Group N		Statistical Inference	Significant
	Mean/ Mt	SD	Mean	SD	Mean	SD	P	Significant
0 mts	73.12	4.798	75.84	4.317	72.56	6.014	0.058 > 0.05	Not significant
5	71.0	3.786	74.64	3.451	72.40	5.859	0.052 > 0.05	Not Significant
15	69.92	4.142	73.20	3.559	71.36	6.264	0.060> 0.05	Not significant
20	73.12	4.798	75.84	4.317	72.56	6.014	0.058 > 0.05	Not significant
25	71.0	3.786	74.64	3.451	72.40	5.859	0.052 > 0.05	Not Significant
30	69.92	4.142	73.20	3.559	71.36	6.264	0.060> 0.05	Not significant
40	73.12	4.798	75.84	4.317	72.56	6.014	0.058 > 0.05	Not significant
50	71.0	3.786	74.64	3.451	72.40	5.859	0.052 > 0.05	Not Significant
60	69.92	4.142	73.20	3.559	71.36	6.264	0.060> 0.05	Not significant

In the present study, the comparison of diastolic blood pressure between groups was within 10-15% of basal value , The statistical analysis reveals no significance between groups.



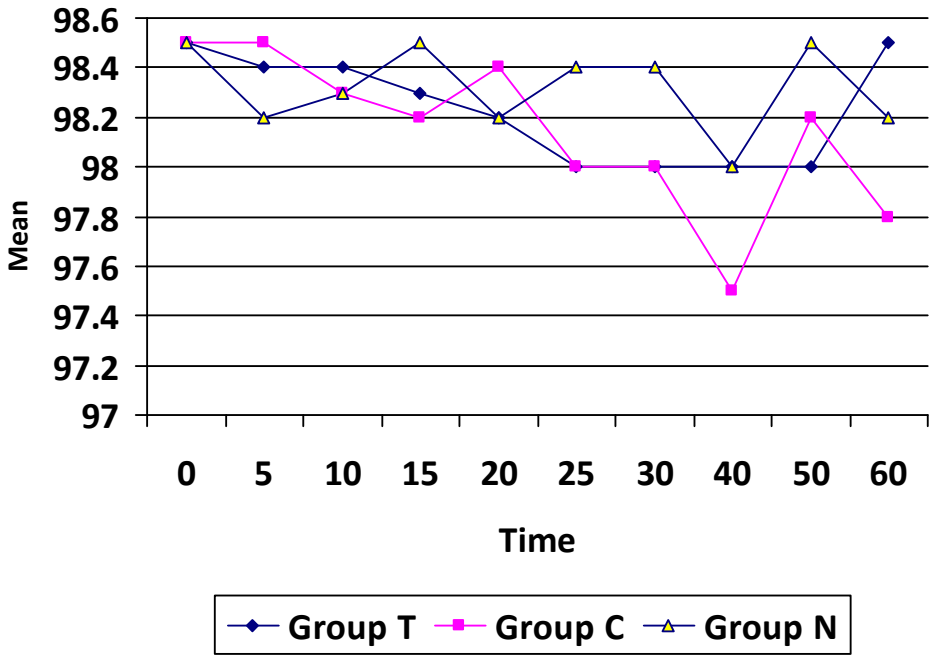
Graph .7 Trend of mean Diastolic blood pressure

Table 8

COMPARISON OF MEAN SPO2

Time mts	Group T		Group C		Group N		Statistical Inference	
	Mean%	SD	Mean	SD	Mean	SD	P	Significant
0 mts	98.5	0.507	98.5	0.504	98.5	0.507	0.799 > 0.05	Not significant
5	98.4	0.502	98.5	0.501	98.2	0.450	0.769 >0.05	not significant
10	98.4	0.500	98.3	0.502	98.3	0.479	0.748 >0.05	Not significant
15	98.3	0.479	98.2	0.479	98.5	0.506	0.434> 0.05	NOT significant
20	98.2	0.450	98.4	0.502	98.2	0.450	0.581 > 0.05	Not significant
25	98	0.365	98	0.450	98.4	0.502	0.302 > 0.05	Not significant
30	98	0.183	98	0.365	98.4	0.500	0.650 > 0.05	Not significant
40	98	0.101	97.5	0.183	98	0.265	0.321 > 0.05	Not significant
50	98	0.263	98.2	0.479	98.5	0.506	0.570 > 0.05	Not significant
60	98.5	0.507	97.8	0.346	98.2	0.456	0.477> 0.05	Not significant

The Comparison of Mean SPO_2 between groups showed a mean value of 98- 98.5%. The statistical analysis is not significant between groups.



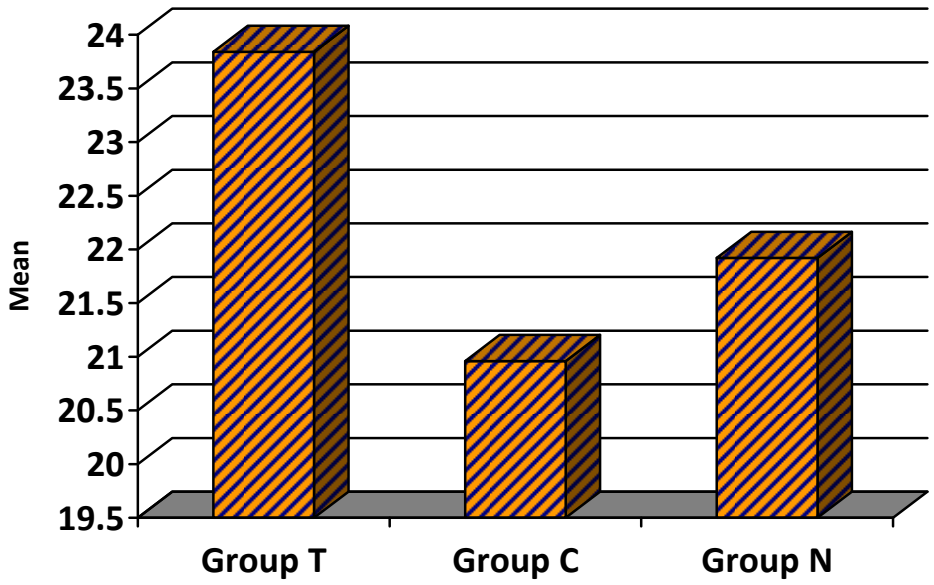
Graph .8 Trend of mean $Spo2$

Table: 9

COMPARISON OF MEAN RESPIRATORY RATE

Groups	Mean Respiratory rate	SD	Statistical inference
Group T (n=25)	23.84	0.473	P value =0.06 >0.05 Not significant
Group C (n=25)	20.96	0.200	
Group N (n=25)	21.92	0.277	

In this study, mean respiratory rate was compared, and there is no statistical significance between groups



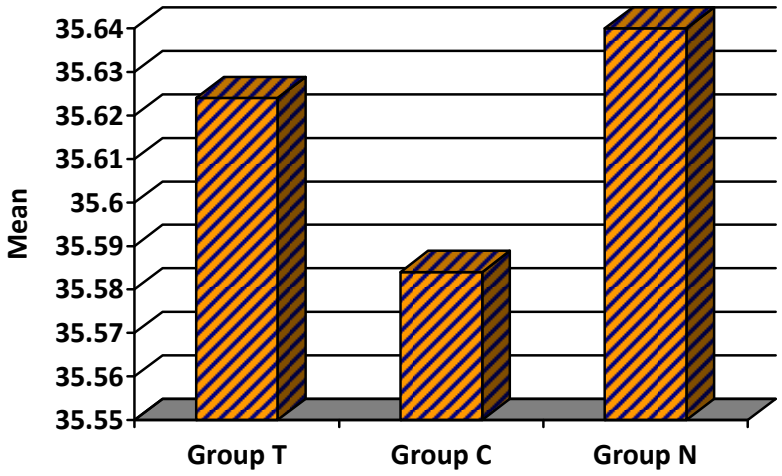
Graph .9 Comparison of mean Respiratory rate

Table –10

COMPARISON OF MEAN BODY TEMPERATURE

Group	Mean	SD	F	P	Significant
Group T (n=25)	35.6240	0.14514	1.012	0.368 > 0.05	N.S
Group C (n=25)	35.5840	0.14629			
Group N (n=25)	35.6400	0.13844			

The comparison of mean body temperature between groups showed a mean value of 35.58 and the p value is not significant between groups.



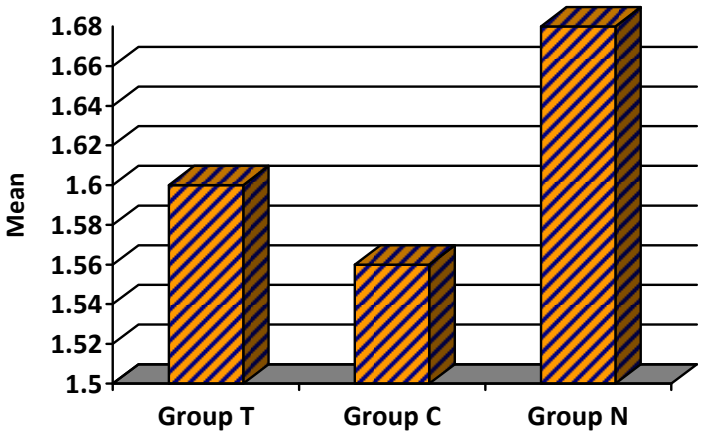
Graph.10 Comparison of mean body Temperature

Table -11

COMPARISON OF SEDATION SCORE

Group	Mean	SD	F	P	Significant
Group T (n=25)	1.60	0.500	0.382	0.684>0.05	Not Significant
Group C (n=25)	1.56	0.507			
Group N (n=25)	1.68	0.476			

The comparison of sedations score between groups in our study showed a sedation's score of 1.6 ± 0.5 which was statistically not significant.



Graph .11 Comparison of Sedation Score

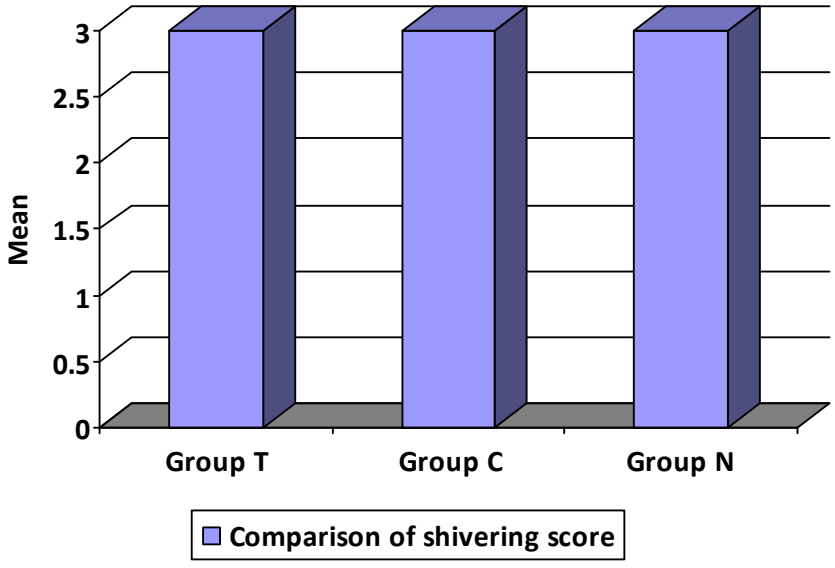
Table -12

COMPARISON OF SHIVERING SCORE

Group	Mean	P	Significant
Group –T	3	NA	NS
Group –C	3	NA	NS
Group –N	3	NA	NS

Grades of Shivering

In our present study, the shivering grade of three was noticed in all the 3 groups. There is no statistical significance between the groups.



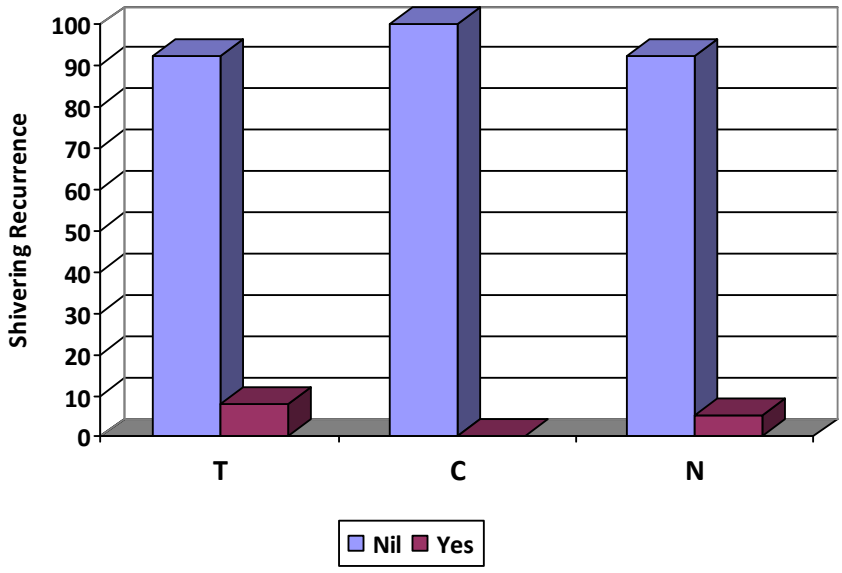
Graph .12 Comparison of Shivering Score

Table :13

RECURRENCE OF SHIVERING

Shivering Recurrence				Groups		
	T (n=25)	C (n=25)	N (n=25)	Total n= 75	Statistical Inference	Significance
Nil	23 (92%)	25(100%)	23 (92%)	71(94.7%)	$X^2 = 2.113$	Not significant
Yes	2(8%)	0	2(8%)	4 (5.3%	P = 0.348 >0.05	

In our study there is no recurrence of shivering in group C, in Group T there were two patient with recurrence of shivering and in Group N there were 4 patients with recurrence of shivering. The statistical analysis revealed there is no significance between groups.



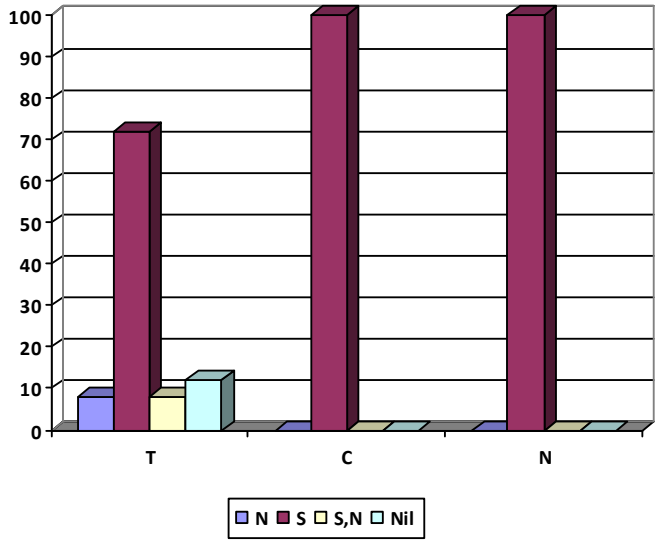
Graph .13 Recurrence of Shivering

Table :14

COMPARISON OF SIDE EFFECTS

Comparison				Group		
	T= n=25	C (n=25)	N (n=25)	Total (n=75)	Statistical inference	Significant
N	2 (8%)	0	0	2 (2.7%)	X^2 = 15.441 Df =6	
S	18(72%)	25 (100%)	25 (100%)	68(90.7%)		
S,N	2 (8%)	0	0	2(2.7%)		
Nil	3 (12%)	0	0	3(4%)	P= 0.17 < 0.05	N.S

Comparison of side effects between study group showed two patients with nausea and sedations, two patients with nausea alone in Group T. In Group C and N all patients were sedated, statistical analysis showed no significance between groups.



Graph.14 Comparison of side effects

DISCUSSION

In Homeothermic species, a thermoregulatory system coordinates defenses against environmental temperature to maintain internal body temperature within a narrow range, thus optimizing normal body function.

Hypothalamus is the seat of thermo regulation. The importance of thermal input form the skin surface was recognized in late 1950's. In Early 1960's physiologists found active thermoregulatory sites other than skin and hypothalamus, including extra hypothalamic portions of brain, deep abdominal tissues and spinal cord. Santario discovered the clinical importance of temperature in 1646, but it took two centuries before body temperature was recognised by wunderlich as a key parameter.

The importance of temperature monitoring was unknown till mid 1960's when the first case of malignant hyperthermia was noticed. The combined effect of anaesthesia induced thermal impairment and exposure to a cool environment makes patients hypothermic in Operation Theatre; As pickering wrote in 1956[11] "The most effective way for cooling a man is to subject him to Anaesthesia".

Spinal Anaesthesia is emerging as safe and popular technique both in elective and emergency surgeries. Incidence of post anaesthesia shivering is high. It occurs both during regional and general anaesthesia. Shivering is an unpleasant experience for the patients receiving spinal anaesthesia. At times, it is a sensation worse than surgical pain. It is physiologically stressful as it increases oxygen consumption, which go up by 100-600%. It interferes with monitoring like ECG, pulse oximeter and NIBP. Shivering causes tension on sutures lines. It is detrimental to patients with low cardio respiratory reserve.

The exact mechanism of development of post anaesthesia shivering is not known; many hypothesis like perioperative heat loss, direct effect of certain anaesthetics, hypoxia, hypercapnia, uninhibited spinal reflex activity may contribute to shivering.

Many non–pharmacological methods like active and passive warming systems, warming of iv fluids, inspired air, blood and its products are tried in many studies. But these methods require use of specialized equipment which is not economically feasible and practical in clinical settings.

Pharmacological methods are cost effective, when compared to non pharmacological methods. There is no gold standard drug for treatment of shivering. Many drugs like pethidine doxapram, ketabserin, propofol, physostigmine nefopam, clonidine, alfentanil, ondansetran, sufentanil are tried, with success rates ranging from 30-95%. Pethidine and clonidine are most commonly studied drugs. Pethidine is associated with nausea, vomitting and respiratory depression, whereas clonidine has lesser side effects and better hemodynamics.

Tramadol is a novel analgesic drug, It is a synthetic drug with opioid effect mediated via the mu-receptor, with minimal effect on kappa and delta receptors anti shivering effects of tramadol is mediated through inhibition of 5- HT_3 and NA reuptake. Tramadol inhibits 5-HT_3 reuptake and promotes its release. It also inhibits synaptosomal noradrenaline reuptake,which contributes to its antishivering effect.

Electrophysiologic, neurophysiological and neuropharmacolo gical experiments in animals established role of noradrenaline and serotonin in the control of body temperature. Activation of nucleus raphe magnus, where serotonin acts as a neurotransmitter has inhibitory effect on shivering. The anti Shivering effect of tramadol is mediated by its effect on these receptors.

Tramadol is likely to have better clinical utility as a anti-shivering drug. With its pharmacodynamic advantage in causing less sedation and less respiratory depression, it has potential use in the control of shivering and convenient and safer than meperidine.Tramadol in a dose of 0.5mg/kg is selected similar to the study conducted by Usha Shukla et al[3].

Nalbuphine is a semi synthetic opioid agonist antagonist opioid analgesic with μ antagonist and kappa agonist activity. Its analgesic potency is equivalent to that of morphine. It has less ability to depress respiratory function, when compared to other opioids[4].Nalbuphine in the dose of 0.1mg/kg is selected for the study similar to the study of O kyokong et al[11.]

Clonidine is a centrally acting selective α2 – agonist. It exerts anti shivering effects at three levels, hypothalamus, spinal cord and locus coeruleus. At the hypothalamic level, it decreases thermoregulatory threshold for shivering and vasoconstriction, since there are high density of α2 receptors in hypothalamus. At locus coeruleus, a pro shivering centre in pons, clonidine reduces the spontaneous firing in locus coeruleus. At the spinal cord level, it activates α2 adreno receptors and release acetylcholine nor-epinephirine and dynorphine. The depressor effects of these transmitters at dorsal horn modulate thermal inputs. Clonidine is highly

lipid soluble and crosses the blood brain barrier and has quick onset. Due to these advantages, interaction of α2 adreno receptors at spinal and supraspinal occurs within the central nervous system . The dose of clonidine is selected as 0.5µg/kg which was similar to the study conducted by Kulshrestha et al[1.]

In our study ,75 antenatal mothers who undergone caesarean section under spinal anaesthesia and developed shivering were included for treatment with study drugs namely nalbuphine, tramadol and clonidine. Group n (n=25) who received inj. nalbuphine, 0.1mg/kg, group c (n=25) who received inj clonidine 0.5µgm/kg and group t(n=25) who received inj tramadol 0.5mg/kg and data were collected as per protocol.

Statistical analysis of collected data showed no statistical significance among demographic datas, age distribution and ASA grading between three groups. The onset of shivering between groups were with a mean difference of 21.53 ± 2 minutes. It showed no statistical significance between groups.

The time interval for disappearance of shivering were noticed and found that Group C with a mean of 2.184 ± 2 mts and p value of 0.000 analysed by one way ANOVA test, Group T with a mean time of 3.864 ±

0.2 mts and Group N with a mean time of 3.780 ± 0.25 mts. These results were similar by the study of **Usha shukla et al** in 2011, where they concluded clonidine was superior in controlling shivering than tramadol with significant side effects of nausea, vomiting and dizziness.

The recurrence of shivering after 15 mts of response time was noticed. In our present study, Group C showed no recurrence of shivering Whereas group – T showed recurrence in 2 patients (8%) and group –N showed recurrence in 2 patients (8%) with p value of 0.348>0.05; which was similar to the study conducted by **oranuch Kyokong et al** in 2007. They conducted a double blind randomnised controlled study of 280 parturient with treatment for shivering after spinal anaesthesia. The recurrence rate of shivering and p value significance were similar to their study. They concluded that tramadol, nalbuphine were superior to ondansetron with low recurrence rates of shivering.

The comparison of heart rate, systolic, diastolic, blood pressure respiratory rate, and mean Spo_2 between groups showed no statistical significance which was similar to studies of **Kranke P et al in 2004;** who evaluated the efficacy of many pharmachological drugs in the treatment of shivering, and concluded there is no significant difference in parameters of heart rate, arterial blood pressure, respiratory rate, spo_2, cutaneous

temperature and level of sedation. Which was similar to study by **S.sia et al;** British Journal of Anaesthesia 1998 conducted a study with clonidine to suppress post extradural shivering in 90 parturients and concluded there is no significant difference in parameters of heart rate, arterial blood pressure, respiratory rate, spo_2.

The core body temperature was measured from axilla, before giving anaethesia and then when patients developed shivering .The mean body temperature was calculated and statistical analysis between three groups was 35.60, with a p value of 0.368 ($P < 0.05$) not significant. **Sessler DI et al** studied the temperature monitoring and thermoregulation under anaesthesia" in 2002. They concluded that core temperature is the best indicator of thermal status of humans. Various sites of monitoring done in tympanic membrane pulmonary artery nasopharynx distal oesophages. and also found that axillary temperature are reasonably accurate and best.

In our study, the sedation score as stated by "Filos" were used for evaluation. During anaesthesia, all patients were awake and alert with a sedation score of 1. And after treatment for shivering, the sedation score was 2. No patients in our study were noticed with a score of 3 or 4. There is no statistical significance between three groups; It was similar to study conducted by **vander stappen et al** in 1996, to evaluate the efficacy of

clonidine on post operative shivering and concluded there is no increase in post operative sedation.

In our study, the comparison of shivering score done between three groups showed grade -3 as per Wrench grades of shivering. All patients in three groups were in the grade-3 shivering; the statistical analysis showed no significance between groups. The comparison of side effects in our study; 2 patients in group T with nausea and sedation: 2 patients with nausea alone and others with sedation noticed: In group C and group N: all the 25 patients had sedation. No other side effects noticed.

SUMMARY

A clinical study was undertaken to compare the effect of drugs in control of shivering. The effect of nalbuphine, clonidine and tramadol in the control of shivering were studied in parturients undergoing caesarean section under spinal Anaesthesia.

The clinical study was conducted in Thanjavur Medical Collage from July 2013 to July 2014. ASA Grade I and II patients subjected to elective or emergency caesarean section under spinal anaesthesia who in due course of anaesthesia developed shivering were included in the study. Total of 75 parturients were studied. They were randomly divided into three groups, group T (n=25) received 0.5mg/kg of tramadol iv, group C (n=25) received 0.5µg/kg of clonidine iv and group N (n= 25) received 0.1mg/kg of nalbuphine iv. The attending anaesthesiologist observed for the cessation of shivering and he/she noted the time elapsed from treatment to the time shivering stopped.

Statistical analysis revealed significant response with 0.5µg/kg iv clonidine when compared with 0.5mg/kg of tramadol and 0.1mg/kg nalbuphine. Also clonidine was found to have better control over hemodynamics especially at 2mts of post anaestheticshivering and also better sedation.

Hence from the above study, it can be concluded that clonidine in a dose of 0.5µg/kg iv is better for control of shivering in parturients undergoing caesarean section under spinal anasthesia.

CONCLUSION

In conclusion all three drugs used in this study namely tramadol (0.5mg/kg), nalbuphine (0.1mg / kg) and clonidine (0.5μg/kg) effectively treated post spinal anaesthesia shivering. Among them clonidine took lesser time to achieve complete cessation of shivering and also maintained better hemodynamics throughout the study. Tramadol and nalbuphine were also equally effective in controlling post spinal anaesthesia shivering and can be used as a safe alternative.

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ANNEXURE IV

Proforma

PROFORMA

Name : I.P. No. :

Age : Hospital :

Sex : Date :

Type of surgery

PRE ANAESTHETIC EVALUATION :

General physical examination :

Pulse rate

B.P.

R.R

Weight

SPO_2

ASA

Systemic examination :

C.V.S :

R.S. :

STUDY DRUGS

GROUP C - Inj Clonidine 0.5 µg/kg iv

GROUP N - Inj Nalbuphine 0.1 mg/kg iv

GROUP T - Inj Tramadol 0.5 mg/kg iv

Time of spinal anaesthesia **:**

Onset of shivering :

Grade of shivering :

Time to disappearance of shivering :

Response rate :

Duration of surgery :

Duration of spinal anaesthesia :

Axillary temperature :

Recurrence of shivering :

Intraop hemodynamics

Parameter	**Onset**	**5mts**	**10mts**	**15mts**	**20mts**	**25mts**	**30mts**	**40mts**	**50 mts**	**60mts**
PR										
BP										
SPO_2										
RR										

SEDATION SCORE

SIDE EFFECTS

Master Chart

S.No	Name	Age	Sex	ASA	Group	Heart Rate (mins)													Systolic Blood pressure (mmHg)												Diastolic Blood pressure (mmHg)												SPo2	Mean body temperature	Sedation score	Shivering score	Shivering stops	Shivering recurs	Complications
						0	5	10	15	20	25	30	35	40	45	50	55	60	0	5	10	15	20	25	30	35	40	45	50	55	60	0	5	10	15	20	25	30	35	40	45	50	55	60							
1	PRIY	26	F	I	T	75	78	102	100	102	98	96	96	88	88	86	86	86	120	122	124	108	102	102	100	110	112	112	120	120	118	80	88	80	76	72	68	66	68	68	66	70	70	72	99	35.8	2	3	3.5	NIL	NO
2	REKH	28	F	I	T	100	102	104	98	96	96	94	92	90	92	88	80	84	130	134	128	122	120	118	108	106	106	100	106	104	110	80	86	82	78	76	74	70	70	68	68	72	72	70	99	35.7	2	3	4	NIL	N
3	AMU	26	F	I	T	98	96	96	112	118	124	104	100	98	92	94	90	92	130	128	126	124	104	106	108	110	112	108	106	106	106	84	82	82	78	76	76	68	68	66	66	64	64	64	98	35.6	2	3	3	NIL	N
4	REVA	27	F	I	T	94	96	96	92	90	92	96	75	76	78	78	74	74	132	130	130	124	120	110	110	116	118	106	106	108	112	74	74	78	78	70	74	74	68	66	64	64	66	68	99	35.7	2	3	4	NIL	NO
5	SAHA	26	F	I	T	98	98	90	90	94	92	92	90	88	86	84	84	86	120	122	124	124	126	106	104	100	104	108	108	108	110	78	76	74	70	70	68	68	66	66	60	66	68	68	98	35.5	2	3	4	NIL	NO
6	MOH	26	F	I	T	94	94	96	96	80	80	82	82	84	84	84	86	88	130	132	130	132	130	110	110	106	108	108	106	106	108	80	76	76	74	74	70	68	62	62	64	64	66	66	98	35.5	2	3	3.5	NIL	S
7	SAHA	29	F	I	T	120	124	124	122	110	112	112	100	98	96	84	86	80	124	120	120	120	118	118	112	112	110	110	108	108	106	80	80	80	78	70	68	68	62	64	66	64	68	60	98	35.8	2	3	4	NIL	S
8	SATH	26	F	I	T	122	120	98	98	96	94	94	92	92	90	90	86	86	120	112	110	112	112	110	108	108	106	106	104	104	106	82	82	84	80	78	78	76	74	70	68	66	68	66	99	35.5	2	3	4	NIL	S
9	SUDH	29	F	II	T	90	94	90	92	94	98	90	90	92	94	98	94	96	124	124	120	120	122	110	112	112	110	108	104	106	108	82	82	80	72	72	74	70	70	68	66	60	60	66	99	35.6	2	3	4	NIL	S
10	SHAM	25	F	I	T	98	98	102	102	100	108	112	100	98	92	88	86	84	122	120	120	118	110	110	108	108	112	110	108	106	106	80	78	76	76	74	70	70	72	68	66	70	72	72	99	35.7	2	3	4	NIL	S
11	SUGU	21	F	I	T	97	87	112	110	122	102	98	98	89	98	80	86	88	120	122	118	118	116	116	114	112	112	110	108	108	106	80	78	78	74	74	60	66	66	68	68	66	68	70	99	35.8	2	3	4	NIL	S
12	FAIR	22	F	I	T	98	99	110	108	104	100	98	96	96	94	94	90	90	130	128	122	122	120	120	118	118	116	110	110	108	110	80	80	76	78	78	74	74	70	70	68	66	64	66	99	35.8	2	3	4	NIL	S
13	PRAT	20	F	II	T	88	88	86	86	84	84	80	80	74	74	70	70	74	128	122	120	112	114	118	112	122	120	124	120	118	118	82	82	82	80	84	78	74	72	72	70	70	68	68	99	35.7	2	3	3.5	NIL	S,N
14	LALIT	26	F	I	T	90	96	96	90	90	88	88	94	94	96	96	112	100	128	124	124	120	122	118	120	122	116	118	118	116	110	84	86	86	84	84	80	80	78	76	74	72	74	70	99	35.7	2	3	4	NIL	S
15	SARA	29	F	I	T	96	96	94	92	90	88	80	78	74	74	78	80	80	130	130	124	124	122	120	120	118	118	116	116	108	108	82	84	82	82	80	78	78	76	70	70	68	68	66	99	35.5	2	3	4	NIL	S
16	SHAF	29	F	I	T	96	98	100	104	110	98	92	94	98	96	94	80	84	128	126	120	122	120	118	116	114	108	110	112	112	110	80	84	84	86	74	74	70	68	68	64	64	66	68	99	35.8	2	3	4	NIL	S
17	UDAY	22	F	I	T	90	94	90	92	92	98	94	92	90	88	88	86	86	126	124	120	118	120	118	108	106	104	108	108	110	110	82	82	80	78	76	74	70	70	76	66	66	64	64	99	35.5	2	3	3.8	NIL	S
18	UMA	30	F	II	T	90	98	90	92	80	84	84	88	84	80	88	92	90	130	128	126	122	122	120	118	116	106	112	108	112	112	68	68	70	72	72	74	70	74	70	64	64	66	68	98	35.6	2	3	3.8	YES	S
19	INDI	22	F	I	T	88	86	100	102	104	102	110	96	96	86	86	80	80	122	120	120	124	114	124	118	108	108	104	104	100	110	72	70	68	68	66	66	70	70	74	74	72	72	68	99	35.8	2	3	3.5	NIL	S
20	RADH	26	F	I	T	100	102	102	100	104	102	100	98	96	78	80	84	82	124	122	120	118	118	114	112	104	100	108	108	110	112	78	82	82	80	80	76	74	72	70	66	66	62	60	99	35.4	2	3	4	nil	S,N
21	RASI	25	F	II	T	84	86	88	84	80	86	86	88	88	90	90	94	94	120	122	124	124	108	104	100	112	118	120	122	120	120	86	84	84	80	80	78	78	76	76	74	74	70	70	99	35.5	2	3	4	NIL	S
22	MAN	26	F	I	T	88	88	84	78	76	74	70	68	70	74	74	70	72	130	130	128	124	124	120	120	118	108	104	104	108	110	80	84	80	80	78	78	74	74	70	70	68	68	70	99	35.8	2	3	4	NIL	S
23	RADI	24	F	II	T	96	96	94	94	90	90	92	92	78	74	74	72	70	122	120	120	118	104	108	110	102	102	108	110	110	112	82	82	82	80	80	78	74	70	68	68	64	64	60	99	35.4	2	3	4	NIL	S
24	USHA	26	F	I	T	96	98	100	102	100	98	94	94	88	74	70	70	74	128	128	126	124	124	120	120	108	108	104	102	104	108	84	84	82	80	78	70	70	68	64	66	60	62	60	99	35.5	2	3	4	YES	S
25	FATH	29	F	I	T	90	98	90	92	88	84	80	84	78	74	72	72	72	130	128	126	124	120	122	118	118	116	108	106	108	110	80	78	78	76	76	70	70	64	68	66	64	66	62	99	35.4	2	3	4	NIL	S
26	SELV	24	F	I	C	104	100	98	96	96	94	88	80	74	70	66	66	66	120	124	116	112	108	106	100	108	106	106	108	110	108	82	80	80	78	780	74	74	70	70	68	68	66	68	99	35.8	2	3	2.5	NIL	S
27	RADI	26	F	I	C	94	90	92	90	90	88	84	80	82	78	70	64	60	120	122	120	118	116	116	108	108	106	106	104	108	108	82	82	78	78	74	74	70	70	68	68	66	64	64	99	35.6	2	3	2	NIL	S
28	VIMA	28	F	I	C	98	96	96	90	90	88	88	80	84	84	88	90	98	120	122	120	122	120	118	118	116	108	108	108	106	104	84	84	82	82	80	82	78	78	74	74	72	72	70	99	35.8	2	3	2	NIL	S
29	ANUS	20	F	II	C	90	88	86	84	84	82	82	80	82	80	78	78	74	128	124	120	122	120	118	116	110	112	102	106	108	108	86	82	80	86	84	82	80	78	78	74	74	70	68	99	35.6	2	3	2.4	NIL	S
30	MAH	22	F	I	C	96	90	88	86	80	80	78	78	74	74	72	72	68	130	124	124	120	114	112	112	110	108	108	104	106	102	84	82	82	84	82	82	80	70	72	66	68	70	66	99	35.4	2	3	2	NIL	S
31	PALA	24	F	II	C	100	104	112	102	100	98	94	94	98	88	84	84	80	132	130	128	126	126	120	120	124	124	108	110	112	106	82	82	80	80	78	74	74	70	70	68	66	70	68	99	35.5	2	3	2	NIL	S
32	ROSY	26	F	I	C	78	78	78	82	82	80	78	78	76	74	74	70	68	122	120	124	110	114	118	118	120	116	114	112	110	108	86	84	82	82	80	76	76	74	70	68	66	64	62	99	35.6	2	3	2	NIL	S
33	ARO	28	F	I	C	80	84	84	80	80	74	74	70	70	68	68	66	66	132	130	128	128	124	124	120	118	118	116	116	110	112	88	86	80	74	70	70	68	68	68	64	64	66	99	35.5	2	3	2	NIL	S
34	AUGS	28	F	I	C	90	90	88	84	84	82	82	80	80	78	78	74	74	130	132	128	128	120	122	120	118	108	108	106	106	104	86	86	80	80	78	78	74	74	70	70	68	68	66	98	35.4	2	3	2	NIL	S
35	REVA	29	F	II	C	84	84	80	80	74	74	80	68	68	70	70	74	78	124	122	120	112	110	108	102	102	104	104	106	106	108	80	80	82	82	70	70	74	78	78	74	74	70	68	98	35.6	2	3	2.2	NIL	S
36	SUBA	29	F	I	C	90	92	94	96	90	88	86	84	84	80	80	78	78	128	126	126	120	122	124	120	108	108	108	108	106	106	82	82	82	80	80	80	78	78	76	76	74	74	70	99	35.8	2	3	2.5	NIL	S
37	AGIL	24	F	I	C	68	68	70	70	74	74	78	78	74	70	68	66	68	118	114	112	112	110	110	106	104	104	106	106	108	108	70	70	74	74	78	70	72	72	74	74	70	70	68	98	35.4	2	3	2	NIL	S
38	JEYA	24	F	I	C	78	74	74	70	70	72	68	68	68	64	64	64	64	122	120	120	118	118	114	114	112	102	104	104	108	106	84	84	82	82	80	80	78	78	74	74	70	70	68	99	35.6	2	3	2	NIL	S
39	MEN	26	F	II	C	80	78	78	72	72	74	74	70	70	68	68	64	66	122	120	116	116	110	112	104	104	102	106	106	108	108	72	72	74	74	70	70	68	66	66	68	68	64	64	98	35.4	2	3	2.7	NIL	S

40	SIVA	24	F	II	C	88	86	86	84	80	80	74	70	68	66	66	64	64	120	118	116	110	114	112	110	108	108	106	104	104	110	82	82	82	80	80	78	78	74	74	60	62	68	64	99	35.6	2	3	2	NIL	S
41	SUMI	28	F	I	C	82	82	80	80	74	74	70	70	68	66	64	64	66	120	118	118	116	114	112	112	110	108	102	104	106	108	86	86	86	84	84	80	80	78	78	74	74	70	68	99	35.5	2	3	2.1	NIL	S
42	TAM	28	F	II	C	88	88	84	82	82	80	80	78	78	76	76	68	68	130	128	122	124	122	120	124	124	110	112	108	106	106	84	82	80	80	78	78	74	74	72	72	70	68	70	99	35.6	2	3	2	NIL	S
43	SULC	30	F	I	C	80	84	88	84	80	80	78	78	74	74	70	70	70	128	128	126	126	124	124	120	120	118	118	116	116	108	84	84	82	80	80	78	76	76	74	74	72	72	70	98	35.4	2	3	2.2	NIL	S
44	VASU	32	F	I	C	90	90	88	88	84	84	80	80	78	78	74	64	64	126	120	118	122	120	120	118	108	106	106	108	108	110	82	80	80	78	78	74	74	70	70	68	64	66	68	99	35.6	2	3	2.5	NIL	S
45	SARA	28	F	I	C	98	96	94	94	90	90	92	92	88	86	86	80	78	130	128	120	118	120	122	118	118	116	116	114	108	106	84	84	80	80	78	74	74	70	70	68	68	66	66	99	35.8	2	3	2	NIL	S
46	DEVI	23	F	II	C	88	84	84	82	82	80	78	78	74	74	70	68	68	120	120	112	112	108	108	118	104	104	106	106	108	108	80	80	84	80	68	68	70	70	74	70	74	70	68	99	35.8	2	3	2	NIL	S
47	CHITI	25	F	I	C	86	84	80	82	78	78	74	74	70	70	68	68	66	124	120	122	120	128	110	108	108	106	106	104	104	100	82	82	80	80	78	78	74	74	70	68	68	66	66	98	35.5	2	3	2.5	NIL	S
48	SHAN	25	F	I	C	78	74	74	70	70	68	64	70	70	74	74	68	68	128	128	126	122	122	120	112	108	110	104	104	106	106	82	84	80	80	78	78	72	72	70	64	64	66	68	99	35.6	2	3	2	NIL	S
49	DAN	26	F	I	C	102	100	90	88	86	86	84	84	80	80	84	78	78	130	132	128	126	124	124	122	120	122	114	112	112	110	78	78	74	74	70	70	74	74	70	70	64	64	68	99	35.4	2	3		NIL	S
50	SELV	29	F	II	C	98	98	90	90	92	92	84	84	80	80	74	70	74	128	126	126	124	124	120	120	118	118	116	116	108	108	84	84	80	80	78	78	76	74	74	70	70	70	70	98	35.8	2	3		NIL	S
51	MEN	30	F	I	N	84	88	82	90	94	96	78	74	70	74	70	68	68	110	110	108	106	104	100	112	112	118	116	110	110	110	70	74	70	72	68	66	66	64	64	68	70	70	70	99	35.6	2	3	3.5	NIL	S
52	KAN	29	F	I	N	104	104	100	98	98	94	94	90	86	88	78	74	70	120	122	122	124	124	120	118	118	114	114	112	112	110	78	74	74	70	70	68	66	66	68	68	70	74	72	99	35.6	2	3	4	NIL	S
53	SUSH	25	F	II	N	102	122	108	106	92	90	88	80	74	74	70	70	70	120	120	118	108	116	110	108	106	110	110	112	110	108	80	82	80	78	78	74	74	70	72	72	70	70	70	99	35.4	2	3	3	NIL	S
54	SALC	23	F	I	N	102	100	98	94	94	90	90	88	88	86	86	78	78	110	112	112	108	108	106	106	104	110	112	114	112	110	80	82	82	84	84	78	74	70	70	72	72	74	74	99	35.6	2	3	4	NIL	S
55	THIL	29	F	I	N	102	100	94	94	98	98	90	78	78	80	80	84	82	120	120	112	110	106	108	106	108	110	114	110	114	112	74	74	70	68	68	66	64	66	68	78	78	74	70	99	35.8	2	3	4	NIL	S
56	AMB	25	F	I	N	94	94	90	98	90	88	74	74	70	70	68	70	74	110	108	110	106	104	112	108	110	110	112	112	110	108	70	68	68	66	66	64	64	60	60	64	66	70	74	99	35.5	2	3	3	NIL	S
57	REGI	27	F	II	N	74	78	76	72	70	70	78	78	80	80	82	82	72	110	108	112	108	106	110	104	106	110	110	110	108	110	70	72	72	78	74	78	78	70	70	74	78	74	70	99	35.6	2	3	4	NIL	S
58	DAM	23	F	I	N	76	76	78	78	74	70	70	68	68	66	66	70	70	110	112	114	110	112	110	108	108	106	104	104	112	112	70	76	76	74	72	68	66	60	74	72	72	74	70	99	35.6	2	3	4	NIL	S
59	RATH	27	F	I	N	78	76	78	70	70	78	78	80	80	84	84	82	82	120	118	120	118	116	114	112	112	110	108	108	108	110	74	66	68	68	70	72	72	74	70	70	66	64	68	98	35.8	2	3	4	NIL	S
60	SAVI	25	F	I	N	88	86	90	90	92	92	94	94	90	90	94	92	92	120	118	122	118	114	116	116	120	118	116	112	114	110	78	78	74	74	70	70	70	68	68	66	68	70	72	99	35.6	2	3	4	NIL	S
61	PADI	28	F	I	N	98	98	96	96	94	94	90	90	94	88	84	88	84	110	112	110	108	108	106	106	110	112	108	106	110	110	74	76	84	80	80	82	84	84	74	74	70	72	72	99	35.8	2	3	4	NIL	S
62	PRIY	29	F	II	N	86	86	84	84	88	88	92	92	94	90	90	94	94	120	110	110	112	112	114	114	116	114	114	108	108	110	80	84	84	82	82	84	84	80	70	72	72	74	70	99	35.5	2	3	3	NIL	S
63	MAH	23	F	I	N	98	96	92	84	84	88	88	86	86	80	80	84	84	110	112	112	108	108	106	106	104	104	108	108	110	112	70	74	74	70	68	66	70	78	78	74	74	70	66	98	35.8	2	3	3	NIL	S
64	KALA	30	F	I	N	86	86	80	80	84	84	88	90	90	94	94	96	96	122	120	112	118	110	108	106	110	120	118	116	114	110	70	68	64	64	68	70	72	72	70	74	70	74	68	99	35.6	2	3	4	NIL	S
65	JOTH	23	F	I	N	74	78	78	74	70	70	68	68	74	74	70	70	68	120	118	116	114	112	108	108	106	106	110	112	112	110	80	84	86	84	82	80	74	74	70	70	74	72	72	99	35.8	2	3	4	NIL	S
66	ARUL	27	F	I	N	90	88	88	86	86	84	84	82	82	80	78	78	76	124	120	118	118	120	120	122	120	118	110	114	110	112	84	80	80	68	68	64	64	66	66	78	74	74	70	99	35.6	2	3	3	NIL	S
67	DHIV	29	F	I	N	96	98	98	90	90	88	88	84	84	70	70	74	74	110	108	112	112	110	108	108	106	108	110	110	112	114	80	84	82	80	84	80	74	74	70	70	74	70	78	99	35.4	2	3	4	NIL	S
68	CHAI	27	F	II	N	88	96	98	90	74	74	78	78	80	80	82	84	84	110	108	112	110	118	120	112	118	120	120	124	124	118	78	74	74	76	76	78	78	80	80	82	82	84	80	98	35.6	2	3	4	NIL	S
69	RADI	26	F	I	N	90	98	98	100	102	100	96	96	94	94	90	90	94	120	122	120	118	118	120	124	124	122	120	122	120	118	78	74	70	74	70	76	74	74	74	72	72	70	70	99	35.8	2	3	4	YES	S
70	ANAI	27	F	II	N	96	98	98	88	84	80	82	82	78	78	78	88	90	118	120	120	108	108	116	116	114	118	118	124	120	120	80	82	82	70	74	66	68	68	70	70	74	72	72	99	35.8	2	3	4	NIL	S
71	MUTI	25	F	I	N	104	104	100	100	96	96	94	94	90	90	88	88	86	120	120	112	118	118	116	118	116	114	110	110	112	124	80	80	80	78	78	76	76	70	70	68	68	74	74	99	35.6	2	3	4	YES	S
72	RAM	30	F	I	N	94	94	96	96	90	78	78	70	70	74	72	72	74	120	124	122	122	118	118	108	108	106	106	108	108	110	80	78	78	74	74	70	70	68	68	74	74	70	70	98	35.8	2	3	4	NIL	S
73	GANI	28	F	I	N	80	80	84	84	88	88	90	90	92	92	94	94	94	130	128	124	124	1220	120	110	112	108	108	110	110	112	80	76	76	74	78	78	74	74	70	70	72	74	74	99	35.4	2	3	4	NIL	S
74	VANI	27	F	II	N	86	88	86	84	84	80	80	78	78	74	74	78	78	128	128	124	124	120	120	118	118	116	116	114	114	110	78	74	74	70	70	70	82	82	80	74	72	72	70	98	35.6	2	3	4	NIL	S
75	PERI	29	F	I	N	98	98	92	92	90	90	88	80	78	94	98	96	96	124	124	112	110	118	122	120	122	118	118	114	114	112	78	78	74	74	70	70	72	72	74	70	74	70	74	99	35.8	2	3	4	NIL	S

List of Statistical formulae used

1. Mean = $\frac{\sum x}{n} = \frac{\text{Sum of All values}}{\text{Number Of values}}$

2. SD $= \sqrt{\frac{\sum (x-\bar{x})^2}{n-1}}$

3. $t = \frac{\text{Difference of means}}{\text{SE of mean}}$

4. $\chi^2 = \frac{(O-E)^2}{E}$

O – Observed values

E – Expected values

Anova is a statistical test which analyzes variance. It is helpful in making comparison of two or more means which enables a researcher to draw various results and predictions about two or more sets of data. Anova test includes one-way anova, two-way anova or multiple anova depending upon the type and arrangement of the data. One-way anova has the following test statistics:

$$F = \frac{MST}{MSE}$$

Where,

F = Anova Coefficient

MST = Mean sum of squares due to treatment

MSE = Mean sum of squares due to error.

Formula for MST is given below:

$$MST = \frac{SST}{p-1}$$
$$SST = \sum n(x - \bar{x})^2$$

Where,

SST = Sum of squares due to treatment

p = Total number of populations

n = Total number of samples in a population.

Formula for MSE is given below:

$$MSE = \frac{SSE}{N-p}$$
$$SSE = \sum (n-1)S^2$$

Where,

SSE = Sum of squares due to error

S = Standard deviation of the samples

N = Total number of observations.

CONSENT FORM

I _____ hereby give consent to participate in the study conducted by **Dr.J.VASANTHY,** Post Graduate in Anaesthesia, Department of Anesthesiology,Thanjavur Medical College and hospital,Thanjavur and to use my personal clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations

Place :

Date : Signature of Participant

			Systolic Blood p													Diastolic Blood pressure (mmHg)																			
50	55	60	0	5	10	15	20	25	30	35	40	45	50	55	60	0	5	10	15	20	25	30	35	40	45	50	55	60	SPo2	Mean body temperature	Sedation score	Shivering score	Shivering stops	Shivering recurs	Complications
86	86	86	120	122	124	108	102	102	100	110	112	112	120	120	118	80	88	80	76	72	68	66	68	68	66	70	70	72	99	35.8	2	3	3.5	NIL	NO
88	80	84	130	134	128	122	120	118	108	106	106	100	106	104	110	80	86	82	78	76	74	70	70	68	68	72	72	70	99	35.7	2	3	4	NIL	N
94	90	92	130	128	126	124	104	106	108	110	112	108	106	106	106	84	82	82	78	76	76	68	68	66	66	64	64	64	98	35.6	2	3	3	NIL	N
78	74	74	132	130	130	124	120	110	110	116	118	106	106	108	112	74	74	78	78	70	74	74	68	66	64	64	66	68	99	35.7	2	3	4	NIL	NO
84	84	86	120	122	124	124	126	106	104	100	104	108	108	108	110	78	76	74	70	70	68	68	66	66	60	66	68	68	98	35.5	2	3	4	NIL	NO
84	86	88	130	132	130	132	130	110	110	106	108	108	106	106	108	80	76	76	74	74	70	68	62	62	64	64	66	66	98	35.5	2	3	3.5	NIL	S
84	86	80	124	120	120	120	118	118	112	112	110	110	108	108	106	80	80	80	78	70	68	68	62	64	66	64	68	60	98	35.8	2	3	4	NIL	S
90	86	86	120	112	110	112	112	110	108	108	106	106	104	104	106	82	82	84	80	78	78	76	74	70	68	66	68	66	99	35.5	2	3	4	NIL	S
98	94	96	124	124	120	120	122	110	112	112	110	108	104	106	108	82	82	80	72	72	74	70	70	68	66	60	60	66	99	35.6	2	3	4	NIL	S
88	86	84	122	120	120	118	110	110	108	108	112	110	108	106	106	80	78	76	76	74	70	70	72	68	66	70	72	72	99	35.7	2	3	4	NIL	S
80	86	88	120	122	118	118	116	116	114	112	112	110	108	108	106	80	78	78	74	74	60	66	66	68	68	66	68	70	99	35.8	2	3	4	NIL	S
94	90	90	130	128	122	122	120	120	118	118	116	110	110	108	110	80	80	76	78	78	74	74	70	70	68	66	64	66	99	35.8	2	3	4	NIL	S
70	70	74	128	122	120	112	114	118	112	122	120	124	120	118	118	82	82	82	80	84	78	74	72	72	70	70	68	68	99	35.7	2	3	3.5	NIL	S,N
96	112	100	128	124	124	120	122	118	120	122	116	118	118	116	110	84	86	86	84	84	80	80	78	76	74	72	74	70	99	35.7	2	3	4	NIL	S
78	80	80	130	130	124	124	122	120	120	118	118	116	116	108	108	82	84	82	82	80	78	78	76	70	70	68	68	66	99	35.5	2	3	4	NIL	S
94	80	84	128	126	120	122	120	118	116	114	108	110	112	112	110	80	84	84	86	74	74	70	68	68	64	64	66	68	99	35.8	2	3	4	NIL	S
88	86	86	126	124	120	118	120	118	108	106	104	108	108	110	110	82	82	80	78	76	74	70	70	76	66	66	64	64	99	35.5	2	3	3.8	NIL	S
88	92	90	130	128	126	122	122	120	118	116	106	112	108	112	112	68	68	70	72	72	74	70	74	70	64	64	66	68	98	35.6	2	3	3.8	YES	S
86	80	80	122	120	120	124	114	124	118	108	108	104	104	100	110	72	70	68	68	66	66	70	70	74	74	72	72	68	99	35.8	2	3	3.5	NIL	S
80	84	82	124	122	120	118	118	114	112	104	100	108	108	110	112	78	82	82	80	80	76	74	72	70	66	66	62	60	99	35.4	2	3	4	nil	S,N
90	94	94	120	122	124	124	108	104	100	112	118	120	122	122	120	86	84	84	80	80	78	78	76	76	74	74	70	70	99	35.5	2	3	4	NIL	S
74	70	72	130	130	128	124	124	120	120	118	108	104	104	108	110	80	84	80	80	78	78	74	74	70	70	68	68	70	99	35.8	2	3	4	NIL	S
74	72	70	122	120	120	118	104	108	110	102	102	108	110	110	112	82	82	82	80	80	78	74	70	68	68	64	64	60	99	35.4	2	3	4	NIL	S
70	70	74	128	128	126	124	124	120	120	108	108	104	102	104	108	84	84	82	80	78	70	70	68	64	66	60	62	60	99	35.5	2	3	4	YES	S
72	72	72	130	128	126	124	120	122	118	118	116	108	106	108	110	80	78	78	76	76	70	70	64	68	66	64	66	62	99	35.4	2	3	4	NIL	S
56	66	66	120	124	116	112	108	106	100	108	106	106	108	110	108	82	80	80	78	780	74	74	70	70	68	68	66	68	99	35.8	2	3	2.5	NIL	S
70	64	60	120	122	120	118	116	116	108	108	106	106	104	108	108	82	82	78	78	74	74	70	70	68	68	66	64	64	99	35.6	2	3	2	NIL	S
88	90	98	120	122	120	122	120	118	118	116	108	108	108	106	104	84	84	82	82	80	82	78	78	74	74	72	72	70	99	35.8	2	3	2	NIL	S
78	78	74	128	124	120	122	120	118	116	110	112	102	106	108	108	86	82	80	86	84	82	80	78	78	74	74	70	68	99	35.6	2	3	2.4	NIL	S
72	72	68	130	124	124	120	114	112	112	110	108	108	104	106	102	84	82	82	84	82	82	80	70	72	66	68	70	66	99	35.4	2	3	2	NIL	S
84	84	80	132	130	128	126	126	120	120	124	124	108	110	112	106	82	82	80	80	78	74	74	70	70	68	66	70	68	99	35.5	2	3	2	NIL	S
74	70	68	122	120	124	110	114	118	118	120	116	114	112	110	108	86	84	82	82	80	76	76	74	70	68	66	64	62	99	35.6	2	3	2	NIL	S
58	66	66	132	130	128	128	124	124	120	118	118	116	116	110	112	88	86	80	74	70	70	68	68	68	68	64	64	66	99	35.5	2	3	2	NIL	S
78	74	74	130	132	128	128	120	122	120	118	108	108	106	106	104	86	86	80	80	78	78	74	74	70	70	68	68	66	98	35.4	2	3	2	NIL	S
70	74	78	124	122	120	112	110	108	102	102	104	104	106	106	108	80	80	82	82	70	70	74	78	78	74	74	70	68	98	35.6	2	3	2.2	NIL	S
80	78	78	128	126	126	120	122	124	120	108	108	108	108	106	106	82	82	82	80	80	80	78	78	76	76	74	74	70	99	35.8	2	3	2.5	NIL	S
58	66	68	118	114	112	112	110	110	106	104	104	106	106	108	108	70	70	74	74	78	70	72	72	74	74	70	70	68	98	35.4	2	3	2	NIL	S
54	64	64	122	120	120	118	118	114	114	112	102	104	104	108	106	84	84	82	82	80	80	78	78	74	74	70	70	68	99	35.6	2	3	2	NIL	S
58	64	66	122	120	116	116	110	112	104	104	102	106	106	108	108	72	72	74	74	70	70	68	66	66	68	68	64	64	98	35.4	2	3	2.7	NIL	S
56	64	64	120	118	116	110	114	112	110	108	108	106	104	104	110	82	82	82	80	80	78	78	74	74	60	62	68	64	99	35.6	2	3	2	NIL	S
54	64	66	120	118	118	116	114	112	112	110	108	102	104	106	108	86	86	86	84	84	80	80	78	78	74	74	70	68	99	35.5	2	3	2.1	NIL	S
76	68	68	130	128	122	124	122	120	124	124	110	112	108	106	106	84	82	80	80	78	78	74	74	72	72	70	68	70	99	35.6	2	3	2	NIL	S
70	70	70	128	128	126	126	124	124	120	120	118	118	116	116	108	84	84	82	80	80	78	76	76	74	74	72	72	70	98	35.4	2	3	2.2	NIL	S
74	64	64	126	120	118	122	120	120	118	108	106	106	108	108	110	82	80	80	78	78	74	74	70	70	68	64	66	68	99	35.6	2	3	2.5	NIL	S
86	80	78	130	128	120	118	120	122	118	118	116	116	114	108	106	84	84	80	80	78	74	74	70	70	68	68	66	66	99	35.8	2	3	2	NIL	S
70	68	68	120	120	112	112	108	108	118	104	104	106	106	108	108	80	80	84	80	68	68	70	70	74	70	74	70	68	99	35.8	2	3	2	NIL	S
68	68	66	124	120	122	120	128	110	108	108	106	106	104	104	100	82	82	80	80	78	78	74	74	70	68	68	66	66	98	35.5	2	3	2.5	NIL	S
74	68	68	128	128	126	122	122	120	112	108	110	104	104	106	106	82	84	80	80	78	78	72	72	70	64	64	66	68	99	35.6	2	3	2	NIL	S
84	78	78	130	132	128	126	124	124	122	120	122	114	112	112	110	78	78	74	74	70	70	74	74	70	70	64	64	68	99	35.4	2	3		NIL	S
74	70	74	128	126	126	124	124	120	120	118	118	116	116	108	108	84	84	80	80	78	78	76	74	74	70	70	70	70	98	35.8	2	3		NIL	S
70	68	68	110	110	108	106	104	100	112	112	118	116	110	110	110	70	74	70	72	68	66	66	64	64	68	70	70	70	99	35.6	2	3	3.5	NIL	S
78	74	70	120	122	122	124	124	120	118	118	114	114	112	112	110	78	74	74	70	70	68	66	66	68	68	70	74	72	99	35.6	2	3	4	NIL	S
70	70	70	120	120	118	108	116	110	108	106	110	110	112	110	108	80	82	80	78	78	74	74	70	72	72	70	70	70	99	35.4	2	3	3	NIL	S
86	78	78	110	112	112	108	108	106	106	104	110	112	114	112	110	80	82	82	84	84	78	74	70	70	72	72	74	74	99	35.6	2	3	4	NIL	S
80	84	82	120	120	112	110	106	108	106	108	110	114	110	114	112	74	74	70	68	68	66	64	66	68	78	78	74	70	99	35.8	2	3	4	NIL	S
58	70	74	110	108	110	106	104	112	108	110	110	112	112	110	108	70	68	68	66	66	64	64	60	60	64	66	70	74	99	35.5	2	3	3	NIL	S
82	82	72	110	108	112	108	106	110	104	106	110	110	110	108	110	70	72	72	78	74	78	78	70	70	74	78	74	70	99	35.6	2	3	4	NIL	S
56	70	70	110	112	114	110	112	110	108	108	106	104	104	112	112	70	76	76	74	72	68	66	60	74	72	72	74	70	99	35.6	2	3	4	NIL	S
84	82	82	120	118	120	118	116	114	112	112	110	108	108	108	110	74	66	68	68	70	72	72	74	70	70	66	64	68	98	35.8	2	3	4	NIL	S
94	92	92	120	118	122	118	114	116	116	120	118	116	112	114	110	78	78	74	74	70	70	70	68	68	66	68	70	72	99	35.6	2	3	4	NIL	S
84	88	84	110	112	110	108	108	106	106	110	112	108	106	110	110	74	76	84	80	80	82	84	84	74	74	70	72	72	99	35.8	2	3	4	NIL	S
90	94	94	120	110	110	112	112	114	114	116	114	114	108	108	110	80	84	84	82	82	84	84	80	70	72	72	74	70	99	35.5	2	3	3	NIL	S
80	84	84	110	112	112	108	108	106	106	104	104	108	108	110	112	70	74	74	70	68	66	70	78	78	74	74	70	66	98	35.8	2	3	3	NIL	S
94	96	96	122	120	112	118	110	108	106	110	120	118	116	114	110	70	68	64	64	68	70	72	72	70	74	70	74	68	99	35.6	2	3	4	NIL	S
70	70	68	120	118	116	114	112	108	108	106	106	110	112	112	110	80	84	86	84	82	80	74	74	70	70	74	72	72	99	35.8	2	3	4	NIL	S
78	78	76	124	120	118	118	120	120	122	120	118	110	114	110	112	84	80	80	68	68	64	64	66	66	78	74	74	70	99	35.6	2	3	3	NIL	S
70	74	74	110	108	112	112	110	108	108	106	108	110	110	112	114	80	84	82	80	84	80	74	74	70	70	74	70	78	99	35.4	2	3	4	NIL	S
82	84	84	110	108	112	110	118	120	112	118	120	120	124	124	118	78	74	74	76	76	78	78	80	80	82	82	84	80	98	35.6	2	3	4	NIL	S
90	90	94	120	122	120	118	118	120	124	124	122	120	122	120	118	78	74	70	74	70	76	74	74	74	72	72	70	70	99	35.8	2	3	4	YES	S
78	88	90	118	120	120	108	108	116	116	114	118	118	124	120	120	80	82	82	70	74	66	68	68	70	70	74	72	72	99	35.8	2	3	4	NIL	S
88	88	86	120	120	112	118	118	116	118	116	114	110	110	112	124	80	80	80	78	78	76	76	70	70	68	68	74	74	99	35.6	2	3	4	YES	S
72	72	74	120	124	122	122	118	118	108	108	106	106	108	108	110	80	78	78	74	74	70	70	68	68	74	74	70	70	98	35.8	2	3	4	NIL	S
94	94	94	130	128	124	124	1220	120	110	112	108	108	110	110	112	80	76	76	74	78	78	74	74	70	70	72	74	74	99	35.4	2	3	4	NIL	S
74	78	78	128	128	124	124	120	120	118	118	116	116	114	114	110	78	74	74	70	70	70	82	82	80	74	72	72	70	98	35.6	2	3	4	NIL	S
98	96	96	124	124	112	110	118	122	120	122	118	118	114	114	112	78	78	74	74	70	70	72	72	74	70	74	70	74	99	35.8	2	3	4	NIL	S

A comparative study of the Effect of Clonidin...

By 201320207 .md Anesthesiology Dr J Vasanthy

anesthesia (spinal anaesthesia)

ly performed technique for Caesarean section due to its quick onset, 10

local anaesthetic usage in both elective and emergency caesarean section. The incidence of shivering after spinal section is about 40 -50% which is an unpleasant and physiologically stressful condition for the patient. "Shivering is a ponse to early hypothermia in warm blooded animals. When the core temperature drops, the shivering reflex is triggered Shivering is a serious complication leading to increased metabolic rate, increased oxygen consumption, increased CO2 rterial hypoxemia, lactic acidosis, increased intraocular Pressure, increased intracranial pressure, increased surgical and it interfers with pulse rate, blood pressure, and ECG monitoring. It is detrimental to patients with low cardio respiratory

ermia is the primary cause for shivering 22

xial blockade induced inhibition of thermoregulatory centre, peripheral vasodilatation due to sympathetic blockade, cold iv fluids .Various non pharmacological and pharmacological interventions are used to control post spinal anesthesia ogical methods includes convection warming system and radiant heat system which uses specialized equipments to g which are often expensive and are not practical in all clinical settings. Pharmacological agents used to control shivering e, tramadol, nalbuphine, ondasetron, ketanserin, magnesiumsulphate, propofol, alfentanil, sufentanil, physostigmine, te, ketamine, etc. Among them pethidine is the commonly used drug to treat shivering, but it has its own limitation. So we andomized clinical study to compare