

Efficacy of Intravenous alpha₂ Agonists / Opioids to Attenuate Shivering in Parturients Undergoing Elective LSCS under Intrathecal Bupivacaine

Dr. Manisha Kapdi¹, Dr. Aishwariya Raj², Dr. Uma Santoki³

¹Associate Professor of Anaesthesia, AMCMET Medical College Ahmedabad Gujarat)
Ex - Associate professor of Anaesthesia, NHLM Medical College Ahmedabad Gujarat India,
Correspondence: [manisha_kapdi\[at\]yahoo.com](mailto:manisha_kapdi[at]yahoo.com)

²Resident in Anaesthesia AMCMET Medical College, Ahmedabad, Gujarat, India

³Resident in Anaesthesia, AMCMET Medical College, Ahmedabad, Gujarat, India

Abstract: ***Introduction:** Post spinal shivering is very unpleasant, uncomfortable to the 55% population of parturients. Shivering increases metabolic heat production upto 600% after general or regional anaesthesia. There are various methods available to control shivering during anaesthesia. We conducted study of 3 different drugs, 2 alpha agonists & 1 opioid to attenuate shivering after intrathecal bupivacaine. In present study to compare the relative efficacy of Dexmedetomidine, Clonidine and Tramadol for control of intraoperative shivering under spinal anaesthesia for Lower Segment Caesarean Section (LSCS) **Study design:** Randomised double blind Observation study. **Aims and Objectives:** The present study is undertaken to clinically compare the efficacy, haemodynamic effects, Adverse effects of Alpha₂ agonists, Dexmedetomidine, Clonidine & opioid Tramadol on control of postspinal shivering in parturients. **Methods:** After obtaining written informed consent, We conducted a randomised Observation study in 90 parturients (30 in each group) and compared the efficacy of intravenous Dexmedetomidine Clonidine and Tramadol for controlling postspinal shivering. Patients were given inj. Dexmedetomidine (Group D) 0.5 mcg/kg, injection Clonidine (Group C I.V Clonidine 0.5mcg/kg), Tramadol (Group T - I.V Tramadol 1mg/kg) when shivering of grade 2 to 4 was noted which lasted for minimum period of 2 minutes after spinal anaesthesia. **Conclusion:** Intravenous Tramadol is a better alternative than I.V Alpha₂ agonists (Dexmedetomidine & Clonidine) in treatment of postspinal anaesthesia shivering.*

Keywords: IV ALPHA₂AGONISTS (CLONIDINE, IV DEXMEDETOMIDINE), I.V TRAMADOL, LSCS, Parturients, Post Spinal Shivering

1. Introduction

Shivering in parturients undergoing LSCS is common. Almost 55-60% parturients suffer it worldwide, & very unpleasant, uncomfortable response which is spontaneous, involuntary, tremor-like muscle hyperactivity that increases metabolic heat production upto 600% after general or regional anaesthesia [1]. It is a potentially serious complication, resulting in increased metabolic rate; increased oxygen consumption along with raised carbon dioxide (CO₂) production; increase in lactic acidosis, increased intraocular and intracranial pressure, and interferes with pulse rate, blood pressure and ECG monitoring by causing artifacts [2, 3]. Hypothesis for reason of shivering is perioperative hypothermia, which occurs due to spinal anaesthesia-induced inhibition of temperature regulatory mechanism to maintain internal body temperature within a narrow range, thus optimising normal body function. There are various methods available to control shivering during anaesthesia, which include physiological and pharmacological methods using drugs which have anti-shivering properties.

Primary outcome is to assess Shivering parameters before & after study drug.

Secondary Outcome is to watch for complications and adverse effects. After study drug.

Aims & Objectives

The present study is carried out to assess the efficacy, haemodynamic stability, adverse effects of Dexmedetomidine, Clonidine & Tramadol to control postspinal shivering in parturients undergoing LSCS.

2. Material & Methods

After obtaining consent from Institutional review board & written and informed consent from patients, we conducted a randomised Observational study in 90 parturients and compared the efficacy of Dexmedetomidine, Clonidine, Tramadol for treatment of postspinal shivering. Parturients were divided randomly in three groups with 30 in each group.

A. Patient Inclusion and exclusion criteria:

Inclusion criteria:

Parturients for Elective LSCS of ASA grade I or II under subarachnoid block who developed shivering after anaesthesia, Patients with no prior medications, Shivering of grade 2 to 4, lasting for a minimum period of 2 minutes., Patients who have a valid informed written consent

Exclusion criteria:

- Parturients of emergency LSCS
- Patients who did not give a valid informed consent;
- Patient with coagulation abnormalities.

Volume 10 Issue 4, April 2021

www.ijrsr.net

Licensed Under Creative Commons Attribution CC BY

- Patients with fever, significant cardiovascular, renal, hepatic, respiratory, thyroid, neurological disorders, autonomic neuropathies, a need for blood transfusion during surgery.
- Patients with known hypersensitivity to Tramadol or Clonidine; Patients with known history of alcohol and substance abuse;
- Patients who develop shivering even before administering spinal anaesthesia; Patients requiring supplementation with general anaesthesia

Preanaesthetic evaluation:

Preanaesthetic evaluation of all patients consisted of detailed history, physical examination and routine investigation. A written informed consent was taken after proper counselling.

Preoperative preparation

All patients were Nil by mouth overnight, No sedatives or anxiolytics were given on previous night, Vital parameters noted in preoperative room were considered as baseline values

Study groups:

Group allocation was done randomised by randomisation numbering table. Number was given in sealed opaque envelopes.

Execution of Randomisation was done at time of giving drug when shivering occur.

Patients were randomly divided into three groups and each group consisted of 30 patients.

Patients were given study drug when shivering of grade 2 to 4 was noted which lasted for minimum period of 2 minutes after Intranasal Bupivacaine.

Group D- inj.I.V Dexmedetomidine 0.5mcg/kg

Group C - inj i.v Clonidine 0.5mcg/kg

Group T - inji.v Tramadol 1 mg/kg

Anaesthetic technique

The ambient temperature of operation theatre measured by a wall mounted thermometer was maintained at 24-26°C. All preloading IV fluids and drugs were stored and administered at room temperature. Baseline temperature of patient was recorded using a mercury thermometer in the axilla I.V access was obtained with 18G cannulae. preloading was done with lactated Ringer's solution 8ml/kg IV. On invasive monitors like-

- pulse oximeter, NIBP, ECG Monitors were applied.

Vital parameters noted and monitoring was done throughout the procedure

Subarachnoid block was instituted, under strict aseptic and antiseptic precaution in lateral position in L3-L4 intervertebral space with 25G quincke's spinal needle 10 mg, 2 ml of 0.5% hyperbaric Bupivacaine was used in all cases, to achieve a desirable level of sensory block (T4 dermatome)

Onset of sensory block was assessed by pinprick method.

Motor block was assessed according to Modified Bromage Scale.

Surgery was allowed once desired sensory block level of T4 and motor block of bromage grade 3 were achieved. Apgar score was noticed in each patient at 1&5 min after delivery of baby.

Parturients who have shivering after spinal anaesthesia were enrolled in present study. After sustain grade 2-4 shivering, study drug was given according to Group allocation. Randomisation was done at this time by randomisation numbering in sealed opaque envelope.

Intensity of shivering was graded according to WRENCH score.

Grade 0: No shivering

Grade 1: No visible muscle activity but Piloerection, Peripheral vasoconstriction, or both are present (other causes excluded)

Grade 2: Muscular activity in only one muscle group

Grade 3: Moderate muscular activity involving two or more than two muscle groups but not involving whole body

Grade 4: Violent muscular activity that involves the whole body and bed shaking

Study drug was administered for shivering of grade 2 to 4 which persisted for minimum 2 minutes slowly over 5 min with running IV fluids, 100% Oxygen was given

Shivering response was defined as

Complete: When post treatment the shivering grade declined to grade 0

Incomplete: When post treatment the shivering grade declined but shivering did not cease completely

Failed: If no change in shivering grade was observed Time taken for cessation of shivering and haemodynamic changes were recorded at regular 5 minutes intervals upto 15 minutes postdrug administration.

Inj Dexamethasone 8 mg IV was taken as rescue drug for failed response of study drug for treatment of shivering.

Recurrence was defined as any rise in shivering score post treatment

Sedation score was assessed with a four-point scale as per Filos: (13)

1) Awake and alert

2) Drowsy, responsive to verbal stimuli

3) Drowsy, arousable to physical stimuli

4) Unarousable

Recurrence or incomplete response were treated with active warming measures using convective heaters, infusing moderately warm fluids and covering the patient. Complication and side effects were also noted and treated. Hypotension was defined as fall in systolic blood pressure (SBP) \geq 30% from baseline value or SBP < 90 mm of hg. If hypotension occurred, it was treated with injection i.v

Ephedrine 6 mg. Bradycardia was defined as fall in pulse rate $\geq 30\%$ from baseline value or pulse rate < 60 per minue

If bradycardia occurred, it was treated with injection i.v Atropine 0.6 mg

Nausea: it was evaluated using a 5 point scale 1 - no nausea and vomiting 2 - mild nausea 3 - moderate nausea 4 - severe nausea, treatment is necessary 5 - intractable nausea, patient complains despite treatment

Nausea & vomiting treated with injection i.v Ondansatrom 4 mg

Respiratory depression was defined as $SpO_2 < 90\%$ on room air and/or respiratory rate < 8 /minute.it was treated with oxygenation & airway intervention if needed.

Statistical analysis was done using ARMONK NY IBM statistical software version 20. Interpretation of observations and results were done using ANOVA test.categorical variables were analysed by Chi- square test.

P value of < 0.001 : highly significant, < 0.05 : significant, > 0.05 : non significant

3. Observation and Results

Table 1: Patients Characteristics

Patients Characteristics	Group D (n=30)	Group C (n=30)	Group T (n=30)	P value	Inference
Age in years (mean \pm SD)	27.2 \pm 10.2	27.8 \pm 9.8	26.8 \pm 10.07	> 0.05	NS
Height in Cms(mean \pm SD)	160 \pm 2.0	161 \pm 2.8	160 \pm 1.9		
Weight in Kg (mean \pm SD)	52.0 \pm 8.25	52.4 \pm 9.72	53.1 \pm 12.87	> 0.05	NS
ASA grade I/II	15/15	15/15	15/15	> 0.05	NS
Duration of surgery in mins (mean \pm SD)	49.5 \pm 8.46	50.1 \pm 10.27	49.6 \pm 10.88	> 0.05	NS
Grade of shivering (III/IV)	15/15	13/17	15/15	> 0.05	NS
APGAR Neonatal Score at 1 min	8 \pm 0.5	8 \pm 0.2	8 \pm 0.3	> 0.05	NS
APGAR Neonatal Score at 5 min	9 \pm 0.2	9 \pm 0.3	9 \pm 0.1	> 0.05	NS

No significant difference was seen in age, height,weight, ASA grade, duration of surgery and grade of APGAR Neonatal Score at 1 min was above 8 & comparable in each group ($p > 0.05$). APGAR Neonatal Score at 5 min was more than 9 & comparable in each group($P > 0.05$)

The axillary temperature in groups fall significantly during shivering compared with the baseline values, but the values between the groups did not differ significantly.

Table 2: Changes in Heart Rate (MEAN \pm SD)

HR at Time of	Group D (n=30)	Group C (n=30)	Group T (n=30)	P value	Inference
Preoperative	84.5 \pm 8.2	82.6 \pm 10.5	88.5 \pm 14.7	> 0.05	NS
During shivering	86.8 \pm 6.5	84.5 \pm 11.5	90.2 \pm 15.0	> 0.05	NS
5 min post study drug	77.8 \pm 7.9	81.3 \pm 11.1	90.6 \pm 16.0	< 0.001	HS
10 min post study drug	76.5 \pm 8.2	82.9 \pm 11.9	91.4 \pm 17.4	< 0.001	HS
15 min post study drug	80.5 \pm 9.5	84.1 \pm 10.1	91.7 \pm 15.8	< 0.001	HS

At the onset of shivering, the haemodynamic variables were comparable in both groups. After receiving the study drug treatment, a propensity toward a slight fall in pulse

rate was observed in Dexmedetomidine & Clonidine groups in contrast to Tramadol group, in which no significant haemodynamic changes were observed.

Table 3: Changes in Systolic Blood Pressure (mm of Hg) (Mean)

SBP at Time	Group D (n=30)	Group C (n=30)	Group T(n=30)	P value	Inference
Preoperative	114.2 \pm 6.80	116.3 \pm 8.03	112.8 \pm 7.46	> 0.05	NS
During shivering	116.4 \pm 3.40	113.3 \pm 5.73	111.6 \pm 7.95	> 0.05	NS
5 min post study drug	102.6 \pm 5.23	107.9 \pm 8.73	113.8 \pm 7.79	< 0.05	S
10 min post study drug	100.4 \pm 10.2	106.1 \pm 11.89	112.1 \pm 7.0	< 0.05	S
15 min post study drug	108.6 \pm 9.7	109.9 \pm 10.1	112.5 \pm 7.50	> 0.05	NS

Comparison of SBP (mm of Hg) at Different Time Intervals in Study Groups

After receiving the study drug treatment, a propensity towards a slight fall in SBP was observed in Dexmedetomidine & Clonidine group in contrast to Tramadol group, in which no significant haemodynamic

changes were observed. Christina Lamontagne (21) have used Dexmedetomidine to prevent shivering in parturients as preventive measure as 55% of parturients experience shivering,they have given Dexmedetomidine after cord clamping.

Table 4: Shivering Parameters

Shivering parameters	Group D		Group C		Group T		P value
Onset of shivering after spinal anesthesia in minutes (mean \pm sd)	31.5 \pm 5.26		32.5 \pm 6.42		30.9 \pm 7.89		>0.05 (NS)
Time taken for cessation of shivering in minutes (mean \pm sd)	3.25 \pm 0.25		3.52 \pm 0.52		2.58 \pm 0.55		<0.001 (HS)
Type of response	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Complete response	27	90	24	80	30	100	
Incomplete response	3	10	4	13.3	0	0	
No response	0	0	2	6.6	0	0	
Recurrence	0	0	8	26.6	2	6.6	

Time for onset of shivering after spinal anaesthesia was not statistically significantly different between the groups. ($P>0.05$) It was after delivery of newborn in each group. So, effect of study drug on neonatal outcome is out of question. APGAR Neonatal Score was more than 8 in each group. ($P>0.05$)

The time taken for complete cessation of shivering was significantly higher in Group C than in Group D & Group T for which p value was <0.001 indicating that difference is highly significant. The complete response rate was significantly higher for patients treated with Tramadol. The Incomplete response rate, failure rate, recurrence rate was significantly higher for patients treated with Clonidine.

Table 5: Complications in groups

Complications	Group D (n=30)		Group C (n=30)		Group T (n=30)	
	No. of patient	%	No. of patient	%	No. Of patient	%
Nausea	0	0	0	0	15	50
Vomiting	0	0	0	0	6	20
Bradycardia	1	3.3	2	6.6	0	0
Hypotension	4	12	6	20	0	0
Sedation score 2 or more	10	33	12	40	2	6.6

Incidence of Nausea and vomiting were significantly higher in Tramadol group, whereas Bradycardia and hypotension were higher in clonidine group. Tramadol was found to have less sedation. Episodes of oxygen desaturation or respiratory depression were not detected in any patient of any group during the study.

4. Discussion

Postspinal Shivering is a common problem faced by anaesthesiologist, incidence being 19% to 33% in General surgeries, while in parturients it is noticed 55% after spinal anaesthesia for LSCS. Probable mechanisms could be decrease in core body temperature secondary to sympathetic block; peripheral vasodilatation; increased cutaneous blood flow; which leads to increased heat loss through skin; cold temperature of operation theatre, rapid infusion of cold i.v fluid; and effects of cold anaesthetic drugs upon the thermosensitive receptors in the spinal cord (1,9).

Pharmacological intervention resets the shivering threshold to a lower level, thereby decreasing rigors and its episodes. The neurotransmitter pathways involved in shivering involve opioids, α -2 adrenergic, serotonergic, and anticholinergic receptors (6,14) In present study, we compared the efficacy of Clonidine and Tramadol for

postspinal shivering. Atakshkхой(2) et al, Reddy et al (19) have treated parturients for shivering.

Tramadol is a novel analgesic. It has opioid effect mediated by the mu receptor, with minimal effect on kappa and delta receptors. It also inhibits synaptosomal noradrenaline reuptake. It also activates the monoaminergic receptors of the descending neuraxial inhibiting pain pathway. The antishivering action of Tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both. (5)

Dexmedetomidine is α 2-adrenoceptor agonist which has potency of Clonidine is an α 2-adrenoceptor agonist. It exerts its anti-shivering effects at three levels: Hypothalamus where it decreases the thermoregulatory threshold for vasoconstriction and shivering, at locus coeruleus - a pro-shivering centre in pons, it reduces spontaneous firing, and at the spinal cord level, it activates the α 2-adrenoreceptors and release of dynorphine, norepinephrine and acetylcholine. It is highly lipid-soluble and easily crosses the blood-brain barrier and provides a significant reduction in the incidence of post-extradural shivering without clinically relevant adverse side effects. (8, 17).

Gaffar et al (22) have used Dexmedetomidine to prevent shivering after spinal anaesthesia.

Perioperative Environment

- Potential risk factors for hypothermia in spinal anaesthesia include aging, level of sensory block, temperature of operation theatre and i.v solutions.
- V.Aarvind et al (12), Usha Shukla et al. (20), Cristiana (21), Gaffar (22) In their studies, temperature of i.v fluids, drugs and temperature of operating room were not tightly controlled. However, in our study, the ambient temperature was maintained at 24-26 C. All preloading fluids and drugs were stored and administered at room temperature. Demographic factors such as age, gender, duration of surgery and anaesthesia have also been matched to reduce any confounding bias.

Study Drug and Dose

We have compared Dexmedetomidine 0.5 mcg/kg, Clonidine 0.5mcg/kg, Tramadol 1 mg/kg to prevent shivering.

V.Aarvind et al (12), compared efficacy of 1mg/kg Tramadol i.v and 1mcg/kg i.v Clonidine on post spinal shivering. We compared the effect of 0.5 mcg/kg

Dexmedetomidine, 0.5 mcg/kg of Clonidine vs 1mg/kg of Tramadol on postspinal shivering.

Cristina et al (21) used Dexmedetomidine 1 mcg/kg in parturients to prevent shivering. Gaffar et al (22) different doses of Dexmedetomidine to prevent shivering as 0.5 mcg/kg, 0.3 mg/kg, 0.2 mg/kg, & concluded 0.3 mcg/kg control shivering with minimum haemodynamic response.

Shivering parameters

Niranjan Kumar et al (24) used Dexmedetomidine 0.5mcg/kg, Clonidine 0.5mcg/kg-Tramadol 2 mg/kg to prevent postspinal Shivering.

Usha Shukla et al, (20) included those patients who developed shivering of grade 3 or 4 in their study. In our study, patients with shivering of grade 2 to 4 lasting for min period of 2 minutes were included. Usha Shukla et al (20), defined response rate as shivering ceasing within 15 minutes after treatment. In our study, shivering control was defined according to grade of shivering after drug administration as either complete, incomplete or failed response.

V. Aarvind et al, (12) treated recurrence with additional doses of Clonidine 1mcg/kg i.v or Tramadol 1mg/kg i.v in respective groups. In our study, recurrence or incomplete response were treated with active rewarming measures using convection heaters & infusing moderately warmed i.v fluids. We avoided additional doses of study drug and/or multimodal treatment for recurrence so that it does not interfere with intraoperative vital parameters.

Time of Shivering After Subarachnoid Block

In all groups Shivering was observed 30 min after spinal anaesthesia. so no effect on neonatal outcome.

Time for cessation of shivering

-In study by Perna Attal et al, (16) Tramadol took less time (4.58 ± 0.59 min) than Clonidine (8.02 ± 5.15 min) to control shivering. In our study, cessation of shivering with Tramadol was achieved earlier (2.58 ± 0.55 min) than with Clonidine (3.52 ± 0.52 min). Contradictory to this result, Usha Shukla noticed longer time with Tramadol (5.01 ± 1.02 min) as compared to Clonidine (2.54 ± 0.76 min) for control of shivering.

Response Rate

-V. Aarvind et al (12), found Tramadol has significant advantage (100%) over Clonidine (85%) for stopping shivering early i.e at 10 min post shivering. We too found higher incidence of complete response with Tramadol (100%) as compared to Dexmedetomidine (90%) & Clonidine (80%). In contradiction, Usha Shukla et al (20) noticed higher success rate in Clonidine group (97.5%) as compared to Tramadol group (92.5%).

Incomplete Response

Pranav Bansal et al (15) found lower incidence of incomplete response of Tramadol group (26.6%) compared to Clonidine group (46.6%). We too observed incomplete response in 0% in Dexmedetomidine group, 13.3% patients of Clonidine group whereas 0% in patients in Tramadol

group. No response was seen in 0% in Dexmedetomidine & Tramadol groups, 6.6% patients of Clonidine group.

Recurrence

Perna Attal et al, (16) found a higher recurrence rate in Clonidine group (13.3%) than in Tramadol group (6.6%). Our study shows similar findings with higher recurrence in Clonidine group (26.6%) than Tramadol group (6.6%).

Niranjan Kumar et al (24) had compare Dexmedetomidine, clonidine, Tramadol for postspinal shivering & found that Tramadol is superior to prevent shivering than alpha agonists. (24)

5. Complications

Bradycardia

- Gaffar et al (22) showed Dexmedetomidine in 0.3mcg/kg provide very less haemodynamic response & prevent shivering effectively.
- Cristina et al (21) used Dexmedetomidine 1mcg/kg in LSCS patients & showed that Dexmedetomidine produces hypotension & bradycardia.
- Niranjan Kumar et al (24) also find Bradycardia & hypotension with dexmedetomidine & Tramadol.
- Usha Shukla et al, (20) observed incidence of bradycardia was higher in Clonidine group (5%) compared to Tramadol group (0%). Our incidence of bradycardia was also higher in Clonidine group (6.6) than in Tramadol group (0%).

Hypotension

Cristina et al (21) used Dexmedetomidine 1mcg/kg in LSCS patients & showed that Dexmedetomidine produces hypotension & bradycardia.

Hypotension was seen more frequently in Dexmedetomidine & Clonidine group (7.5 %) than Tramadol group (0 %) in Usha Shukla et al (20) observations. We observed even higher incidence of hypotension with Clonidine (20%) compared to Tramadol (0%).

Nausea and Vomiting

Gaffar et al (22) have not found Nausea or vomiting with dexmedetomidine group.

Niranjan Kumar (24) et al found Nausea vomiting in Tramadol group.

Usha Shukla et al (20) found a higher incidence of nausea (77.5%), vomiting (20%) and dizziness (55.5%) with Tramadol group than Clonidine (0%). Our observation also correlates with above studies. Incidence of nausea and vomiting with Tramadol was 50% and 20% respectively which is higher than Dexmedetomidine, (0%), Clonidine (0%).

Sedation

Gaffar et al (22) have used different doses of Dexmedetomidine to prevent shivering & showed that Dexmedetomidine produces dose dependant sedation.

Prerna Attal et al (16) observed sedation score of ≥ 2 in more number of patients with Clonidine group (60%) than Overall quality of control of shivering was excellent with Tramadol as compared to Dexmedetomidine & Clonidine in our study, but in Tramadol Group Nausea, vomiting are very commonly observed.

Reddy et al (19) also compare both drugs to control shivering in LSCS, they also shown comparable results, they concluded in same way to us, as Tramadol more effective but with more adverse effects, whereas Clonidine less effective, but with less adverse effects than Tramadol.

6. Limitation

A limitation of this study is that we could not measure the core body temperature as the probe needs to be put in the oesophagus or near the tympanic membrane. Both these are uncomfortable and unacceptable to the patient who has been given spinal anaesthesia.

To summarise Dexmedetomidine, Clonidine and Tramadol effectively treated patients with post spinal shivering, but time taken for complete cessation of shivering was earlier in Tramadol than Dexmedetomidine & Clonidine; difference being statistically highly significant.

Incidence of complete response was more in Tramadol compared to Dexmedetomidine & Clonidine.

Incidence of failure rate, incomplete response and recurrence was less with Tramadol compared to Dexmedetomidine & Clonidine. Incidence of Complications like nausea & vomiting were higher in Tramadol, whereas bradycardia & hypotension were higher in Clonidine. Tramadol was found to have less sedation than Clonidine. From our study.

7. Conclusion

In nutshell we conclude that, intravenous Dexmedetomidine, Clonidine, Tramadol are good in treatment of postspinal anaesthesia shivering in parturients. Tramadol provide better response to prevent shivering but with adverse effects of Nausea, vomiting whereas α_2 agonists provide almost equally good control of shivering but vigilant haemodynamic monitoring is needed.

References

- [1] Ozaki M, Kurz A, Sessler DI, Lenhardt R, Schroeder M, Moayeri A, et al. Thermoregulatory thresholds during spinal and epidural Anaesthesia. *Anesthesiology* 1994;81:282-8.
- [2] Atashkhoyi S, Negargar S. Effect of Tramadol for prevention of shivering after spinal anaesthesia for cesarean section. *Research Journal of Biological Sciences*. 2008;3:1365-1369.
- [3] Bhatnagar S, Saxena A, Kannan TR, Punj J, Panigrahi M, Mishra S. Tramadol for postoperative shivering: A double blind comparison with Pethidine. *Anaesth Intensive care*. 2001;29:149-54.
- [4] Bhattacharya PK, Bhattacharya L, Jain RK, Agarwal RC. Post anaesthesia shivering (PAS); A Review, *Indian journal of anaesthesia* 2003; 47(2):88-93
- [5] Bilotta F, Pietropaoli P, Sanita R, Liberatori G, Rosa G. Nefopam and Tramadol for the prevention of shivering during neuraxial anaesthesia. *Regional anaesthesia pain med* 2002;27:380-4
- [6] Brauchi S et al. A hot sensing cold receptor: C-terminal domain determines thermosensation in transient receptor potential channels. *J Neuroscience* 2006; 26 : 4835 - 40
- [7] Buggy DJ, Crossley AWA. Thermoregulation, mild perioperative hypothermia and post anaesthetic shivering. *British Journal of Anaesthesia* 2000; 84 (5) :615-2
- [8] Capogna GI, Celleno D : I.V Clonidine for extradural shivering in parturients : a preliminary study . *Br J Anaesth*. 1993 Aug;71(2):294-5
- [9] Chaturvedi S, Domkondwar G . Control of shivering under regional anaesthesia using Tramadol. *Asian archives of anaesthesiology and resuscitation* 2002;57:491-6
- [10] De Witte, Sessler DI. Perioperative shivering: Physiology and Pharmacology. *Anesthesiology*. 2002;96:467-84.
- [11] Dhimar AA, Patel MG, Swadian VN. Tramadol for control of shivering: comparison with Pethidine. *Indian J Anaesthesia*. 2007;51:28-31.
- [12] V Aravind, M. Dhakshinamoorthy, C. Dhanasekharan: Comparison of clonidine/ Tramadol for post Spinal Anaesthesia shivering . *International Journal of Modern Research & Review: Volume 2, October 2014 issue 10, PP 379-384*
- [13] Filos KS, Goudas LC, Patroni O, Polyzou V. Hemodynamic and analgesic profile after intrathecal Clonidine in humans. A dose-response study. *Anesthesiology*. 1994;81:591-601.
- [14] Hervey GR, Thermoregulation. In : Emsile-Smith D, Paterson C, Scatcherd T, Read N, eds . *Textbook of physiology*, 11th edition. Edinburgh : Churchill-Livingstone, 1988;510-33.
- [15] Pranav Bansal, Gaurav Jain: control of shivering with clonidine, Buterophenol, Tramadol under spinal anaesthesia, A comparative study. *Local Regional anaesthesia*, 2011;4:29-34
- [16] Attal Prerna, Akhilesh Chhaya, Ram Upadhyay: Comparison of clonidine/ Tramadol for control of shivering under Spinal anaesthesia. *International journal of Biomedical & Advanced Research* 2015;6(01):25-31
- [17] Mercadante S, De Michele P, Letterio G, Pignataro A, Sapio M, Villari P : effect of Clonidine on postpartum shivering after epidural analgesia ; a randomised, controlled, double blind study. *J Pain symptom manage*. 1994 Jul;9(5):29
- [18] Anne Miu Han Chan, Kwok Fu. Control of shivering under regional anaesthesia in obstetric patients with Tramadol. *Can J Anaesth* 199; 46(3):253-8
- [19] Reddy VS, Chiruvella S. Clonidine versus Tramadol for postspinal shivering during caesarean section: A randomized double blind clinical study. *J Obstet Anaesth Crit Care* 2011;1:26 -29.

- [20] Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of Clonidine and Tramadol on post spinal anaesthesia shivering. *Indian J Anaesth* 2011;55:242 - 6.
- [21] Christina Lamontagne . Sandra Lesage, Edith Villeneuve, Elsa Lidzborski, Alex Derstenfeld, .Chantal Crochetie`re . Intravenous dexmedetomidine for the treatment of shivering during Cesarean delivery under neuraxial anesthesia: a randomized-controlled trial *Can J Anesth/J Can Anesth* (2019) 66:762–771 <https://doi.org/10.1007/s12630-019-0>
- [22] Abdel-Ghaffar HS, Mohamed SA, Fares KM, Osman MA. Safety and efficacy of dexmedetomidine in treating post spinal anesthesia shivering: a randomized clinically controlled dose finding trial. *Pain Physician* 2016; 19: 243-53.
- [23] Rajagopalan Venkatraman et al. A prospective, randomized, double-blinded control study on comparison of tramadol, clonidine and dexmedetomidine for post spinal anesthesia shivering] *Rev Bras Anesthesiol*. Jan-Feb 2018.
- [24] Dr. Niranjan Kumar Verma , Dr. Mahesh Kumar . Comparison of Clonidine, Dexmedetomidine and Tramadol for Control of Post Spinal Shivering: A Randomized Double Blind Clinical Study, November 2016 *International Journal of Pharmaceutical and Life Sciences* 2(6):658-664.