ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Incidence And Risk Factors For Shivering During Caesarean Section Under Spinal Anaesthesia And Treatment With Ondansetron Versus Tramadol.

Krithika Ramamoorthy[1], Rahul Yadav[2], Binoy Michael[3]*, and Shradha Khatri[4].

[1]Graded Specialist, Department Of Anaesthesiology, Military Hospital Chennai, Defence Colony 1st Ave, Defence Colony, Guindy, Nandapakkam, Chennai, Tamil Nadu – 600032, India.
[2]Head Of Department, Department Of Anaesthesiology, Armed Forces Medical College, Wanowrie, Pune, Maharashtra – 411040, India.
[3]Graded Specialist, Department Of Anaesthesiology, Military Hospital Shimla, Circular Road, Sanjauli, Shimla, Himachal Pradesh – 171001, India.
[4]Graded Specialist, Department Of Psychiatry, Military Hospital Bhatinda, Bathinda Road, Cantonment, Bathinda, Punjab – 151004, India.

ABSTRACT

Shivering may be defined as an involuntary, repetitive activity in the skeletal muscle commonly occurs as a thermoregulatory response to hypothermia. Shivering increases perioperative heart rate and oxygen consumption by 5 times and increases the metabolic demand by 100–600%, thereby increasing probability of myocardial ischemia, hypoxia, hypoxemia and later lactic acidosis. Thus, shivering during caesarean section not only alters the patient's physiology but also affect the parturient's experience of childbirth. The cause of peri-operative shivering in a patient undergoing caesarean section is not fully understood. It is necessary to identify the risk factors associated with it for us to prevent them. There are various drugs which have been used for the prevention and treatment of post spinal shivering but many of them cause various side effects which can further lead to other complications. It is therefore necessary to study a drug which can be routinely used peri operatively with additional benefits and minimal adverse effects. In this study, we wanted to identify the potential risk factors for shivering during caesarean section and compare the efficacy of Ondansetron versus Tramadol as treatment options for the same. The study was conducted in an 850-bedded tertiary care hospital of the Indian armed forces after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants. This was a prospective, observational study conducted among 120 (n=120) pregnant patients who underwent elective caesarean section under spinal anaesthesia. Age (years), weight (kg), height (cm), Body Mass Index (BMI) in kg/m2, educational qualification, presence of anxiety {using hospital anxiety and depression scale (HADS) score}, number of previous deliveries, dermatome level of sensory block after subarachnoid block, temperature difference during surgery and American Society of Anaesthesiologists (ASA) score were investigated as potential risk factors for intra-operative shivering. Anxiety levels were evaluated using the Hospital Anxiety and Depression Scale (HADS) questionnaire. Patients who developed shivering (n=50) were divided into two groups by simple randomisation using coin flip method. Group 1 received Inj. Tramadol 0.5 mg/kg I.V and Group 2 received Inj. Ondansetron 8 mg I.V. Both drugs were diluted to 5 ml using Normal Saline (NS) before administration and disappearance of shivering was observed. The incidence of shivering was found to be 41.7% (n=50) in this study. Out of all the observed variables, association between age (p value 0.495), level of education (p value 0.188) and shivering was not statistically significant. There was significant corelation between the HADS score and shivering. With an increase in the HADS score, there was increase in the incidence of shivering (p value < 0.001). The incidence of shivering decreased with increase in gravida (p value 0.04). There was no significant association between the temperature difference of the patient during surgery and the incidence of shivering (p value 0.390).The incidence of shivering was 56.4% (n=31) in subjects with sensory block above T4 dermatome and it was 29.2% (n=19) in subjects with sensory block below T4 dermatome. With an increase in the level of sensory block, the incidence of shivering increased significantly (p value 0.003). IV Tramadol was found to be superior to IV Ondansetron for treatment of post spinal shivering (p value 0.01). IV Tramadol was found to be superior to IV Ondansetron for treatment of post spinal shivering (n=15,60% v/s n=6, 24%).
Keywords: Shivering, Thermogenesis, Ondansetron, Tramadol, Caesarean Section, Spinal Anaesthesia

https://doi.org/10.33887/rjpbcs/2024.15.6.8

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Temperature is one of the most important and closely maintained body parameter, as membrane fluidity, diffusion capacity and enzyme systems work optimally within a narrow temperature range. Shivering is defined as spontaneous, rhythmic, oscillatory, tremor-like muscular hyperactivity that occurs in response to core hypothermia in an attempt to raise the metabolic heat production [1-5].

Mammals are homeothermic. They need a nearly constant internal body temperature. Human core temperature normally ranges from 36.5° C to 37.5° C. Anterior hypothalamus integrates thermal inputs from different tissues of the body and compares peripheral information with a set point or threshold value. Temperature lower than this set point will result in responses to warm the body while temperatures higher will trigger reflexes to cool the body [6].

Spinal anaesthesia is the preferred method of anaesthesia in parturient undergoing both elective and emergency lower segment caesarean section. Spinal anaesthesia impairs the thermoregulatory system by inhibiting vasoconstriction, which plays an important role in temperature regulation. Spinal anaesthesia results in redistribution of core heat to the periphery from the trunk [(below the level of block). In the postoperative period, mechanisms like uninhibited spinal reflexes, sympathetic over activity, postoperative pain, adrenal suppression, pyrogen release and respiratory alkalosis may also be important [9]. The incidence of shivering has been reported to be about 8.15% to 70.7% after neuraxial anaesthesia [7, 8].

Shivering increases perioperative heart rate and oxygen consumption by 5 times and also increases the metabolic demand by 100- 600%, thereby increasing chances myocardial ischemia, hypoxia, hypoxemia and later lactic acidosis [2]. Traditionally researchers attributed shivering to intraoperative hypothermia but the mechanism remains unclear [13]. In addition, mean body temperature decreases in some patients and not in others [14]. On the other hand, evidence suggests that perioperative anxiety levels are affecting physiological behaviours in obstetric patients [15]. The neurotransmitter pathways involved in the mechanism of shivering are complex and still poorly understood. Serotonin (5-hydroxytryptamine [5-HT_3]), a biologic amine found in the brain and spinal cord, plays a part in neurotransmission of shivering. Many studies explained that the serotonergic system plays an important role in the pathogenesis of perioperative shivering [16, 17]. Serotonin antagonism seems to lower the human thermal set range, thereby reducing metabolic cold defences and discomfort associated with postoperative hypothermia. The cause of peri operative shivering in a patient undergoing caesarean section is not fully understood.

Consequences of hypothermia and shivering include: reversible coagulopathy (platelet dysfunction), increased blood loss, increased blood transfusion, impaired wound healing, increased risk of infection, delayed drug metabolism, left shift of haemoglobin – oxygen dissociation curve, altered mental status, cardiac arrhythmias and ischaemia, increased peripheral vascular resistance, increased myocardial oxygen consumption, increases basal metabolic rate and monitoring artefacts – shows aberrant values [18].

Shivering creates difficulty in monitoring the patients as most of the multi parameter monitors used for anaesthesia show erroneous values. Also, there can be delayed recovery from anaesthesia [19]. It may affect the autonomic nervous system and thus have an impact on hypotension after spinal anaesthesia during LSCS [20].

Treatment of shivering consists of both non-pharmacological and pharmacological methods. Non-pharmacological methods of treatment include external heating like use of blankets, forced air warmers and warmed fluids, maintaining operating room temperature etc. Pharmacological methods for treatment of hypothermia are the next resort to treat all these patients. A number of drugs were studied and are being used. Dexmedetomidine, Ketanserin, Pethidine, Magnesium Sulphate, Clonidine, Alfentanil, Tramadol, Granisetron, Ondansetron is some of the agents studied for the prevention and treatment of shivering.

Tramadol, an inhibitor of the re-uptake of serotonin and norepinephrine in the spinal cord is found to influence the thermoregulatory control mechanisms. Tramadol is emerging as a new and safe drug for treatment of post anaesthesia shivering [22]. Ondansetron, a selective $5HT_3$ receptor antagonist, is primarily used in PONV. In previous studies, mostly preventative effects of Ondansetron on post anaesthetic shivering has been studied, and useful results were obtained [23].

Ondansetron, 5-HT_3 antagonist, is a widely used antiemetic drug. It can be used safely during pregnancy and surgery. Some studies showed its anti-shivering effect following both general and regional anesthesia [24]. It has a potential advantage in obstetric anaesthesia because of its very low incidence of sedation, hypotension, bradycardia, or risk to the neonate. The mechanism of action of Ondansetron as anti-shivering is not clear, and it is proposed to act centrally at the level of the preoptic anterior hypothalamic region by inhibition of serotonin reuptake [25]. On the other hand, nausea and vomiting during spinal anaesthesia for caesarean section are very common but unpleasant complications. During spinal anaesthesia, Ondansetron has been shown to be effective in the prevention of nausea and vomiting [26].

This study also intends to identify risk factors causing shivering in patients undergoing caesarean section under spinal anaesthesia to prevent them. It also intends to study a drug which offers additional benefits but minimal adverse effects which can be routinely used peri operatively to treat this vexatious condition.

MATERIALS AND METHODS

Aims of study:

- To investigate the incidence of shivering during caesarean section under spinal anaesthesia
- To investigate the correlation between preoperative anxiety and the risk of shivering during caesarean section
- To examine the relationship between potential risk factors and the incidence of intraoperative shivering during caesarean section
- To compare the efficacy of Ondansetron and Tramadol for control of intraoperative shivering.

Place of study: The material and data for the study were collected from all the patients undergoing elective caesarean section under spinal anaesthesia at a tertiary care hospital in the department of anaesthesiology for a period of 2 years (Sep 2019 to Aug 2021).

Study design: The current study was a prospective observational study.

Sample size: The sample size (N) was calculated to be 120 using the following formula:

$$\mathbf{N = (Z\ alpha)^2\ [p * q]\ /\ e^2}$$

Where,

p = prevalence of shivering in LSCS under spinal anaesthesia i.e. 8.5% based on previous studies
q = 100 - p *i.e.* 91.5%
e = margin of error i.e. 5%
Z alpha = 1.96 with 95% confidence interval with 2 standard deviations of the mean

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Inclusion criteria: The patients were included in the study if they satisfied the following criteria:

- Over 18 years of age undergoing elective caesarean section under spinal anaesthesia.
- ASA classification I – II

Exclusion criteria: The patients were the exclusion criteria:

- Refusal by patient
- History of anxiolytic or psychotropic drug use
- Those with any surgical or anaesthetic complication (massive haemorrhage, conversion to general anaesthesia, intravenous sedation, etc)
- ASA classification more than II

Study Methodology: Written informed consent to participate in the study was taken from each parturient during the pre-anaesthetic consultation. On the day of surgery, each participant was provided with the

Hospital Anxiety and Depression scale (HADS) questionnaire and was asked to fill it 30 mins before transfer to the operation theatre. Age (years), weight (kg), height (cm), BMI (kg/m^2), anxiety level (HADS Score), number of previous deliveries, sensory block level, level of education, temperature difference during surgery (ºC) and ASA score were noted down.

Ambient temperature of the OT was maintained between 21ºC to 24 ºC. Intravenous access was obtained with 18 G intravenous (IV) cannula. The volume of the local anaesthetic, volume of preloading IV fluid, use of vasopressors was at the discretion of the attending anaesthesiologist. Baseline preoperative axillary temperature was noted in all the patients using a skin probe placed in the axilla in the vicinity of the axillary artery. Intra-operative patient monitoring as per Standards for Basic Anesthetic Monitoring issued by American society of Anesthesiologists (last affirmed on December 13, 2020) were used.

All patients received spinal anaesthesia with Bupivacaine heavy (2.2ml to 2.5ml) according to departmental protocol. The level of maximum block height was assessed after 5 min using cotton wool soaked in alcohol. Oxygen at rate of 6 L/min was administered through face mask to all the parturient.

Shivering, if appeared, was assessed as Grade 0 = no shivering; Grade 1 = piloerection/peripheral vasoconstriction, no visible shivering; Grade 2 = muscular activity in one muscle group; Grade 3 = muscular activity in >1 muscle group, but not generalised; Grade 4 = generalised shivering [21].

Patients who develop shivering were divided into two groups by coin flip method. Group 1 received Inj Tramadol 0.5 mg/kg intravenous and Group 2 received Inj Ondansetron 0.1 mg/kg intravenous. Both drugs were diluted to 5 ml using normal. All the patients were assessed for shivering and graded using the shivering classification [21], its disappearance and complications (if any). Those patient in which the shivering was not controlled within 10mins were considered as treatment failure.

Statistical method of analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Ethical considerations: The study was approved by the institutional human ethics committee. Informed written consent was obtained from all the participants, and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

RESULTS

The flow of patients in our study has been depicted in Figure 1. Out of 145 patients enrolled in the study, 120 patients completed the study. 15 patients were excluded from the study since they did not meet the inclusion criteria and 10 patients opted out of the study.

Out of the 120 patients who participated in this study, 50 patients (41.7%) developed shivering after receiving spinal anaesthesia for elective caesarean section. Out of this, 09 patients (7.50%) developed grade 1 shivering, 4 patients (3.30%) developed Grade 3 shivering and 37 patients (30.80%) developed Grade 4 shivering (Figure 2).

ISSN: 0975-8585

Figure 1: Consolidated flowchart of patient recruitment, randomization and observation.

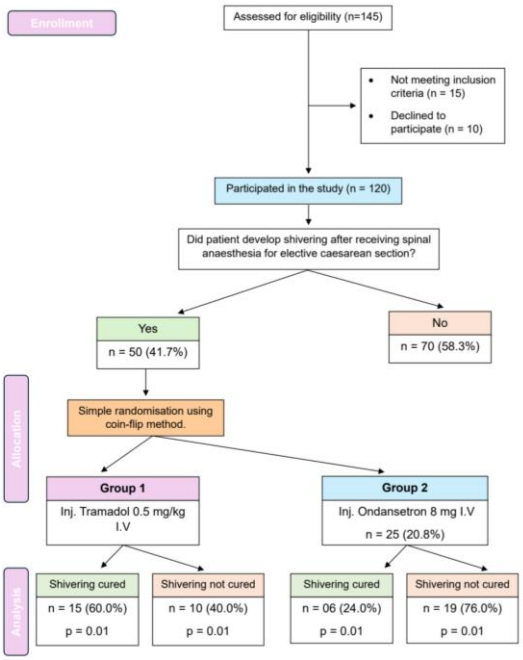
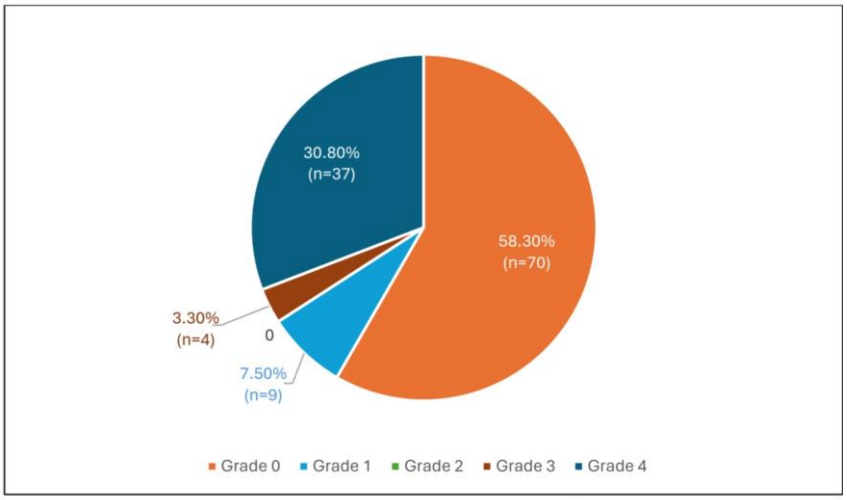


Figure 2: Percentage distribution of grade of shivering amongst study participants



DISCUSSION

Childbirth is a germane event in a woman's life. It is a moment that will be cherished throughout a person's life. Shivering is an undesirable effect which can lead to both physical and mental impediment in a parturient's experience of childbirth. It is therefore necessary to identify the factors responsible for it, so that it can be prevented. We designed this study in a way that the patients faced minimal hassle while participating in it. Hospital Anxiety and Depression Scale (HADS) questionnaire was given to them to be filled out 30 mins prior to the study and all clinical parameters were noted down in the study proforma intraoperatively.

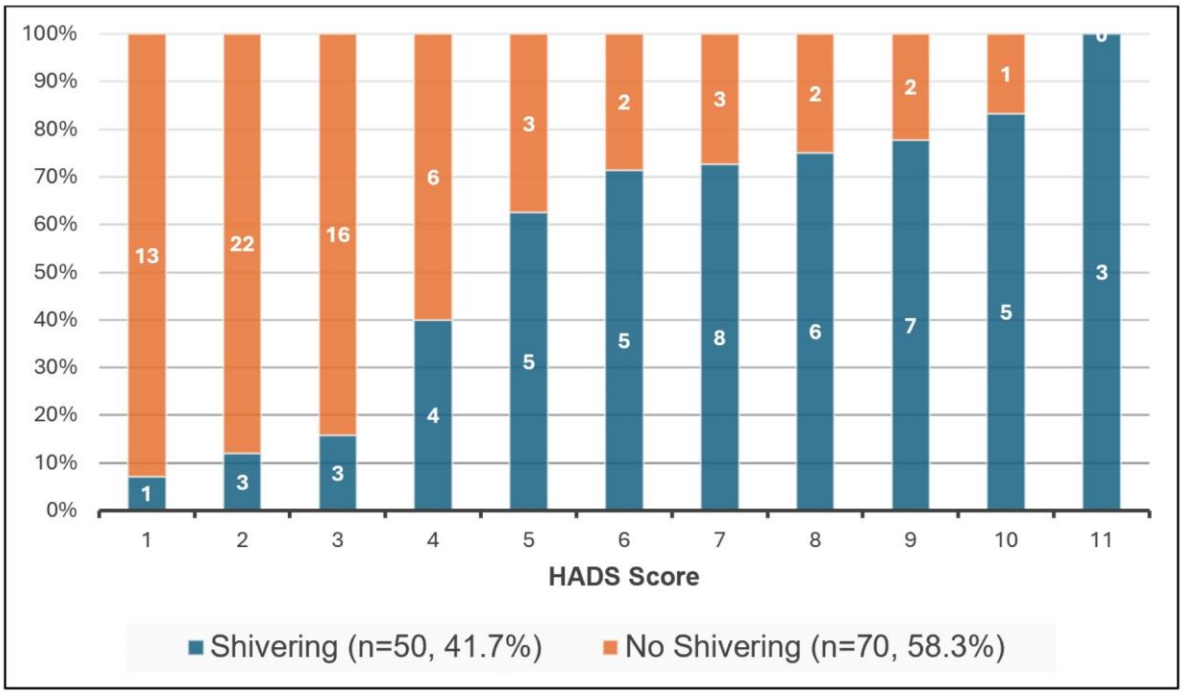
The incidence of shivering amongst patients undergoing elective caesarean section in this study was 41.7% (n=50) which is not dissimilar to previous studies which have reported incidence ranging from 8.15% to 70.7%. Kelsaka et al [27] reported an incidence of 36%, whereas Buggy et al [6] have reported the incidence of shivering in their study to be 8.15%. Lema et al [7] have reported a high incidence of 70.7%. Wodarski et al [28] had an incidence of 21.9% shivering in their study. The wide variation in the prevalence

of shivering could be due to the different protocols followed in different institutes regarding administration of spinal anaesthesia.

Some used intrathecal fentanyl that resulted in a lower incidence rate. The use of vasoconstrictors also altered the incidence of shivering. In some studies, the temperature of the operation theatre was not constant which was a major confounding factor. We standardized the ambient temperature of the operation theatre between 21ºC to 24ºC. Intrathecal opioids were not administered. Spinal anaesthesia was given with hyperbaric Bupivacaine only.

In this study, the major risk factor associated with shivering was anxiety. There was significant relationship between the Hospital Anxiety and Depression Scale (HADS) Score and incidence of shivering (Figure 3). Patients with HADS score of 1 had the least incidence of shivering of 7.1% (n=1). To avoid any bias, patients with known psychiatric disorders like anxiety, psychosis, depression with history of taking anxiolytic medications regularly were not included in this study. As the HADS score increased, so did the incidence of shivering. This proved that anxiety was a risk factor for intraoperative shivering during spinal anaesthesia. This is consistent with other studies. Wodarski et al reported that peri operative stress was a major risk factor for intra operative shivering [28]. Detailed discussion about the delivery plan, including analgesia and anaesthesia techniques with the patient should be an important part of preoperative anaesthetic workup and would help in reducing incidences of shivering among patients undergoing caesarean section under subarachnoid block.

Figure 3: Percentage distribution of incidences of shivering according to HADS score.



We observed that as the number of deliveries increased, incidence of shivering decreased. In this study, majority of shivering was observed in primigravida with an incidence of 46.6% (n=27) (Table 1). The fact that the risk of shivering in our study was lower with each subsequent delivery is very interesting. This may be since multiparous parturients are less stressed, having had previous experiences which they can relate to. Such interpretation is related with the transactional theory of stress by Lazarus [29]. According to his work, patient's previous experiences and their cognitive appraisal may help in coping with stress. Being in a familiar situation of labour and delivery can affect parturient's physiological reactions. Such interpretation was supported by the role of another predictor – patient's anxiety level.

The level of sensory block was also significantly associated with post spinal shivering. Higher the level of block, more was the incidence of shivering. Patients who had sensory block above T_4 dermatome

had 56.4% (n=31) incidence of shivering while patients who had sensory block below T 4 dermatome had an incidence of 29.2% (n=19) **(Table 1)**.

Some studies have reported correlation between temperature change during surgery and shivering. Sultan et al [12] studied the effects of patient warming during LSCS on maternal and neonatal outcomes and reported that there was significant relation between the two. De White et al [13] and Mullington et al [14] reported that change in mean body temperature was associated with shivering. In this study, we did not find any significant association between difference in temperature and shivering. There was no significant correlation between age and shivering. There was also no association between the level of education and shivering.

Kranke et al opined that with pharmacological shivering prophylaxis many patients receive a drug they didn't need and in process are unnecessarily exposed to adverse drug effects [32].

Table 1: Summary of Association between Risk factors and Shivering

		Shivering				P value
		Yes		No		
		Count	Row N %	Count	Row N %	
Age	21 to 25 years	5	29.4%	12	70.6%	0.495
	26 to 30 years	29	45.3%	35	54.7%	
	31 to 35 years	16	41.0%	23	59.0%	
Education	10th standard	3	21.4%	11	78.6%	0.188
	12th standard	11	37.9%	18	62.1%	
	Graduate	36	46.8%	41	53.2%	
HADS Score	Normal (1-7)	38	40.0%	57	60.0%	0.001
	Borderline (8-11)	12	48.0%	13	52.0%	
Gravida	1	27	46.6%	31	53.4%	0.046
	2	15	30.0%	35	70.0%	
	3	8	66.7%	4	33.3%	
Level of Sensory block	Above T_4 dermatome	31	56.4%	24	43.6%	0.003
	Below T_4 dermatome	19	29.2%	46	70.8%	
Temperature difference	0.1 ° C	3	37.5%	5	62.5%	0.390
	0.2 ° C	7	36.8%	12	63.2%	
	0.3 ° C	13	48.1%	14	51.9%	
	0.4 ° C	13	59.1%	9	40.9%	
	0.5 ° C	13	31.7%	28	68.3%	
	0.6 ° C	1	33.3%	2	66.7%	

This study was designed to compare the efficacy of intravenous Ondansetron and Tramadol for control of shivering in patients undergoing lower segment caesarean section under spinal anaesthesia and the planned drugs were given only if the patient developed shivering. Ondansetron is a commonly used drug during caesarean section with minimal adverse effects. We designed our study to standardise the possible confounding factors. The temperature in the operating room was maintained constant. IV fluids were warmed and drugs were given at room temperature.

In our study Tramadol was given in dose of 0.5mg/kg based on previous studies that used Tramadol in a dose of 0.5mg/kg and found it safe and effective for control of shivering. Intravenous Ondansetron was given in a dose of 0.1mg/kg and was selected based on the study by Mahoori et al [33] which concluded that Ondansetron and Pethidine have similar effects on shivering and that 8 mg of intravenous Ondansetron can control shivering and is the dose of choice.

In our study, Tramadol was found to be significantly superior to Ondansetron in the treatment of post spinal shivering. Of the 50 patients who developed shivering, 25 (50%) were given Tramadol and 25

(50%) were given Ondansetron. Simple randomisation using coin-flip method was implemented. 60% (n=15) of patients who were given Tramadol in our study had effective reduction in shivering. This is substantially less than 100% response rate in the control of shivering with Tramadol by studies done by Mittal et al [34], Kaparati et al [35], and Manouchehrian et al [36].

In the Ondansetron group, 24% (n=6) patients had effective reduction in shivering. P value was 0.001. The efficacy of Tramadol was found to be significantly superior to Ondansetron in our study. Mahoori et al [33] had reported response rate of 81% in control of shivering with Ondansetron. However, Joshi et al [38] had found a response of 23.52% in their study group treated with Ondansetron. The said study had used low dose Ondansetron of 0.06mg/kg vs 0.1mg/kg in our study.

Onyekwulu et al reported time taken to control shivering with Tramadol as 3.1mins ± 1.1 [37]. Manouchehrian et al found the time taken to control the shivering with Tramadol to be 2.57min ± 2.2 [36]. Study done by Kaparti et al28 showed control of shivering with Tramadol within 2 minutes in all patients (n=20, 100%), they however used Tramadol in dose of 1mg/kg.

No patients developed nausea or vomiting in the Ondansetron group. This finding was similar to the finding by Joshi et al [38]. The incidence of nausea in the Tramadol group of our study was found to be 24% (n=6). This is same to the findings of Mahoori A. et al [33]. However, it is a little higher than that reported in studies by Manouchehrian et al [36]. The incidence rate of vomiting in the Tramadol group in our study was 8% (n=2). This result is similar to studies done by Onyekwulu et al [37].

Limitation of the Study

This is a single-centre study with sample size not large enough to make recommendations. However, larger, multi-centric studies may draw recommendations pertinent to Indian tertiary hospitals. External validity of the study is limited, as the study included only armed forces personnel and their families. No validation or calibration exercise was conducted between the different doctors who were filling the data forms. As few variables were collected from patient records, they were prone to information bias.

CONCLUSION

A total of 120 subjects were included in the final analysis, of which 50 subjects were observed to have shivering, with 25 in the Tramadol group and 25 in the Ondansetron group. The prevalence of shivering was 41.7% (n=50). There was significant corelation between the HADS score and shivering. With an increase in the HADS score by 1, there was increase in the prevalence of shivering (p value < 0.001). In this study, the incidence of shivering decreased with increase in gravida. The result was statistically significant. Highest incidence of 46.6% (n=27) was noted in primigravida (p value 0.04). The incidence of shivering was 56.4% (n=31) in subjects with sensory block above T4 dermatome and it was 29.2% (n=19) in subjects with sensory block below T4 dermatome. With an increase in the level of sensory block, the incidence of shivering increased significantly (p value 0.003). Age of the patient was not significantly associated with shivering (p value 0.495). Association between level of education and shivering was not statistically significant (p value 0.188). There was no significant association between the temperature difference of the patient during surgery and the incidence of shivering (p value 0.390).

In this study, the efficacy of Tramadol was found to be significantly superior to Ondansetron for the treatment of post spinal shivering (p value 0.01). Among patients who received intravenous Tramadol, 60% of patients (n=15) responded to treatment while only 24% (n=06) of patients who received intravenous Ondansetron responded to treatment. However, Ondansetron was found to have fewer side effects and has added benefit of reducing the incidences of postoperative nausea and vomiting.

Having identified anxiety as a potential risk factor for shivering makes it crucial to develop a good rapport between medical staff and the patient. It is particularly important to highlight how familiarity with the delivery plan and the actual LSCS procedure could help in coping with stress and anxiety. Discussing about the delivery plan, including analgesia and anaesthesia techniques with the patient should be an important part of preoperative anaesthetic workup. 'Patient-centred' relates to not only the patient and her family's involvement into therapeutic decisions, but also relates to making emotional well-being a top priority [37]. It is proven that preoperative anxiety has an impact on many crucial physiological factors such as hypotension during surgery or postoperative pain [38]. That means that we, as part of perioperative

care professionals should focus more on psychological support and well-being, thus, creating a more friendly environment.

REFERENCES

[1] Crowley LJ, Buggy DJ. Shivering and neuraxial anesthesia. Reg Anesth Pain Med 2008 ;33(3):241-52.

[2] Hazarika R, Choudhury A. Comparison of weight-adjusted dose versus fixed dose ondansetron in preventing shivering following spinal anaesthesia for caesarean deliveries. Journal of Evolution of Medical and Dental Sciences 11(12): 898–903.

[3] Wódarski B, Chutkowski R, Banasiewicz J, Moorthi K, Wójtowicz S, Malec-Milewska M, Iohom G. Risk factors for shivering during caesarean section under spinal anaesthesia. A prospective observational study. Acta Anaesthesiol Scand 2020;64(1):112-116.

[4] Morrison SF, Nakamura K. Central neural pathways for thermoregulation. Frontiers In Bioscience 2011; 16:74-104.

[5] Ozaki M, Kurz A, Sessler DI, Lenhardt R, Schroeder M, Moayeri A, et al. Thermoregulatory thresholds during epidural and spinal anaesthesia. Anaesthesiology 1994; 81:282-8.

[6] Buggy DJ, Crossley AW. Thermoregulation, mild perioperative hypothermia and postanesthetic shivering. Br J Anaesth 2000; 84:615-28.

[7] Lema GF, Gebremedhn EG, Gebregzi AH, et al. Efficacy of intravenous tramadol and low-dose ketamine in the prevention of post-spinal anesthesia shivering following cesarean section: a double-blinded, randomized control trial. Int J Womens Health 2017; 9:681-688.

[8] Luggya TS, Kabuye RN, Mijumbi C, Tindimwebwa JB, Kintu A. Prevalence, associated factors and treatment of post spinal shivering in a Sub-Saharan tertiary hospital: a prospective observational study. BMC Anesthesiol. 2016 Oct 18;16(1):100.

[9] Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. Indian Journal of Anaesthesia 2011; 55:242-6.

[10] Badjatia N, Strongilis E, Gordon E, et al. Metabolic impact of shivering during therapeutic temperature modulation: the Bedside Shivering Assessment Scale. Stroke 2008; 39(12):3242–7.

[11] Rai S, Verma S, Pandey HP, Yadav P, Patel A. Role of butorphanol and ondansetron premedication in reducing postoperative shivering after general and spinal anesthesia: A randomized comparative study from North India. Anesth Essays Res 2016; 10:319–23

[12] Sultan P, Habib AS, Cho Y, Carvalho B. The effect of patient warming during Cesarean delivery on maternal and neonatal outcomes: a meta-analysis. B J Anaesth 2015; 115:500-510.

[13] De White, Sessler D. Perioperative shivering: physiology and pharmacology. Anaesth 2002; 96:467-84

[14] Mullington CJ, Barlett RE, Terry JE, et al. Is the mean body temperature a cause of shivering during elective cesarean section under spinal anaesthesia? A pilot study. IJOOA 2016.

[15] Orbach-Zinger S, Ginosar Y, Elliston J, et al. Influence of preoperative anxiety on hypotension after spinal anaesthesia in women undergoing Caesarean delivery. Br J Anaesth 2012; 109:943-949

[16] Tie HT, Su GZ, He K, Liang SR, Yuan HW, Mou JH. Efficacy and safety of ondansetron in preventing postanesthesia shivering: a meta-analysis of randomized controlled trials. BMC Anesthesiol 2014; 14:12.

[17] Mohammadi SS, Jabbarzadeh S, Movafegh A. Efficacy of granisetron on prevention of shivering, nausea and vomiting during cesarean delivery under spinal anesthesia. J Obstet Anaesth Crit Care 2015; 5:22–6.

[18] Kander T, Schött U. Effect of hypothermia on haemostasis and bleeding risk: a narrative review. J Int Med Res 2019;47(8):3559-3568.

[19] Lopez MB. Postanaesthetic shivering - from pathophysiology to prevention. Rom J Anaesth Intensive Care 2018;25(1):73-81.

[20] Šklebar I, Bujas T, Habek D. Spinal anaesthesia-induced hypotension in obstetrics: prevention and therapy. Acta Clin Croat 2019;58(Suppl 1):90-95.

[21] Crossley AW, Mahajan RP. The intensity of postoperative shivering is unrelated to axillary temperature. Anaesthesia 1994; 49:205–7.

[22] Bhatnagar S, Saxena A, Kannan TR, Punj J, Panigrahi M, Mishra S. Tramadol for postoperative shivering: a double-blind comparison with pethidine. Anaesthesia And Intensive Care 2001; 29:149-54.

[23] Dawson NJ, Malcolm JL. Initiation and inhibition of shivering in the rat: interaction between peripheral and central factors. Clinical And Experimental Pharmacology & Physiology 1982; 9:89-93.
[24] Shakya S, Chaturvedi A, Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. J Anaesthesiol Clin Pharmacol 2010; 26:465–9.
[25] Asl ME, Isazadefar K, Mohammadian A, Khoshbaten M. Ondansetron and meperidine prevent postoperative shivering after general anesthesia. Middle East J Anaesthesiol 2011; 21:67–70.
[26] Choi DK, Chin JH, Lee EH, Lim OB, Chung CH, Ro YJ, et al. Prophylactic control of post-operative nausea and vomiting using ondansetron and ramosetron after cardiac surgery. Acta Anaesthesiol Scand 2010; 54:962–9.
[27] E. Kelsaka, S. Baris, D. Karakaya, B. Sarihasan. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. Reg Anesth Pain Med 2006; 31: 40-45)
[28] B Wódarski, R Chutkowski, J Banasiewicz, K Moorthi, M Malec-Milewska, G Iohom. Risk factors for shivering during cesarean section under spinal anaesthesia: are there any? A prospective observational study. International Journal of Obstetric Anesthesia 2018; 35(S1): 26
[29] Lazarus R, Folkman S. Transactional theory and research on emotions and coping. European Journal of Personality 1987; 1:141-169.
[30] Bardes Ch, Defining "Patient-Centered Medicine". N Eng J Med 2012; 366;9: 782-783.
[31] Sobol-Kwapinska M, Babel P, Plotek W. Psychological correlates of acute postsurgical pain: A systematic review and meta-analysis. Eur J Pain 2016; 20(10):1573-1586
[32] Kranke P, Eberhart LH, Roewer N, Tramer MR. Single dose parenteral pharmacological interventions for the prevention of postoperative shivering: a quantitative systematic review of randomised controlled trials. Anesthesia and Analgesia 2004; 99: 718–27.
[33] Mahoori A, Noroozinia H, Hasani E, Soltanahmadi M. Comparison of Ondansetron and Meperidine for Treatment of Postoperative Shivering: A Randomized Controlled Clinical Trial. Iranian Red Crescent Medical Journal 2014;16(8).
[34] Mittal G, Gupta K, Katyal S, Kaushal S. Randomised double-blind comparative study of dexmedetomidine and tramadolfor post-spinal anaesthesia shivering. Indian J Anaesth 2014; 58:257-62.
[35] T M, Kaparti L. A randomised trial comparing efficacy, onset and duration of action of pethidine and tramadol in abolition of shivering in the intra operative period. J Clin Diagn Res 2014 ;8(11): GC07-9.
[36] Manouchehrian N, Mohammadian A, Sanie Jahromi MS, Faridi Tazeh kand N, Sanatkar M. A Comparison of the Therapeutic Effect of Tramadol and Meperidine for Treatment of Shivering after Spinal Anesthesia in Elective Caesarean Section. Archives of Anesthesia and Critical Care (Spring 2015); 1(2): 50-54.
[37] Onyekwulu FA, Agu EE, Amucheazi AO. Efficacy of intravenous tramadol in the control of shivering following spinal anaesthesia for caesarean section. Niger Postgrad Med J 2016 ;23(3):116-20.
[38] Joshi SS, Arora A, George A, Shidhaye RV. Comparison of intravenous butorphanol, ondansetron and tramadol for shivering during regional anesthesia: A prospective randomized double-blind study. Anaesth Pain & Intensive Care 2013;17(1):33-39.