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ORIGINAL RESEARCH ARTICLE

A COMPARATIVE DOUBLE BLIND STUDY BETWEEN INTRAVENOUS GRANISETRON AND INTRAVENOUS TRAMADOL AGAINST PERIOPERATIVE SHIVERING AFTER SUBARACHNOID BLOCK IN LSCS

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ABSTRACT

BACKGROUND

Perioperative shivering is the most common problem encountered after subarachnoid block in 40-60% of the patients. Shivering can lead to psychological stress and slow down the recovery process. This study was performed to compare the effects of prophylactic intravenous granisetron and intravenous tramadol against perioperative shivering after subarachnoid block in lscs.

METHODS

After obtaining ethical committee clearance and parturient consent, sixty parturients posted for lscs under subarachnoid anaesthesia were divided into 2 groups of 30 each. Group G(n=30) received granisetron 40µg/kg intravenously and Group T(n=30) received tramadol 1mg/kg intravenously 5 minute a before the subarachnoid block. Perioperatively, vitals, shivering and sedation score was assessed using 5 point scale in intervals of 5 minutes for first 30 minutes and every 30 minutes till the return of modified bromage scale of 6 postoperatively.

RESULTS

Intraoperatively and postoperatively heart rate, blood pressure, mean arterial pressure, oxygen saturation and electrocardiography had no significant variation in both the groups. 20% of the parturients who received granisetron and 27% of the parturients who received tramadol had various grades of shivering, though the grade of shivering observed was low in tramadol group. 33% of the parturients who had received tramadol had nausea and vomiting perioperatively.

CONCLUSION

Granisetron and tramadol are both equally effects against prophylaxis of perioperative shivering after subarachnoid block in lscs. However, Granisetron seems to be the most suitable drug as it

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also helps in preventing the side effects to like sedation, nausea and vomiting caused by tramadol.

KEYWORDS
Perioperative Shivering, Granisetron, Tramadol, Subarachnoid Block, Parturient.

INTRODUCTION

Subarachnoid block is the most common preferred technique of anaesthesia for cesarean sections as it provides profound muscular relaxation and analgesia. However, it is also associated with unwanted side effects like hypotension, shivering, nausea and vomiting. The incidence of shivering is upto 40-60% in regional anaesthesia.[1]

The etiology in regional anaesthesia causing perioperative shivering is due to peripheral vasodilatation, reduced sympathetic tone, pyrogenic release, rapid heat loss and redistribution of the body heat.[2] Shivering leads to increase in tissue oxygen demand by 400%, increase in minute ventilation and cardiac output to maintain the aerobic metabolism.[3] It eventually leads to increased pulmonary ventilation capacity and cardiac workload, increase in metabolic rate up to 400%.[4] It can induce arterial hypoxemia, lactic acidosis, increased intraocular pressure and intracranial pressure.[5] Shivering also interferes with the monitoring of the patient by causing artefacts in electrocardiography, blood pressure and pulse oximetry. Furthermore, it can exacerbate postoperative pain due to incision stretch, slows down the patient recovery, prolong the discharge, thereby increasing the hospital stay and financial burden of the patient.[6]

Different modalities have been used for the control of shivering such and non-pharmacological and pharmacological. Non-pharmacological methods include the use of warmers, warm blankets, warm fluids, surgical drapes and also maintaining ambient operating theatre temperature.[7] Pharmacological methods include use of various drugs like opioids (pethidine, pentazocine, ketamine, tramadol), alpha-2 agonists (clonidine, ketanserine), 5-HT3 receptor antagonists (ondansetron, granisetron) and magnesium sulphate.[8]

Serotonin (5-HT3) is a biological amine found in the brain and the spinal cord which plays a pivotal role in the neurotransmission.[9] A serotonin 5-HT3 receptor antagonist inhibits the reuptake of the serotonin in the preoptic part of the anterior hypothalamus influencing both heat production as well as heat loss.

Granisetron is selective serotonin 5-HT3 receptor antagonist which has been used to prevent perioperative shivering caused by subarachnoid block. Tramadol is also known to inhibit the reuptake of 5-HT3 and norepinephrine at the spinal cord level which may help in preventing peroperative shivering.[10] Tramadol has been widely used as an analgesic for labour analgesia without affecting the mother and the newborn, has minimal respiratory depression and sedation effects.[11]

Thus in our study we have compared the prophylactic use of intravenous granisetron and intravenous tramadol for the prevention of perioperative shivering in parturients undergoing lscs after subarachnoid anaesthesia.

MATERIALS AND METHODS

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This prospective comparative double blind study was conducted after obtaining ethical committee clearance and written informed consent.A total of 60 (n=30 in each group) parturients scheduled for lscs under subarachnoid block were randomised in 2 groups using computer generated sampling after obtaining written informed consent.

Parturients aged 19-40years, ASA PS-II, Body mass index of 20-30kg/m^2, lscs with singleton pregnancy were included in the study.Parturients with known hypersensitivity to the study drugs, who had received the study drug 24 hours before the surgery, parturients with emetic episodes 24 hour prior to the surgery, parturients who are of opioids, requiring sedation, intraoperative blood transfusion, parturients with preoperative temperature >38°C or < 36.6°C and parturients having Parkinson's disease of any movement disorders of seizure history were excluded from the study.

After a detailed pre-anaesthetic evaluation parturients fulfilling the above inclusion criteria were explained in detail about the anaesthetic procedure, surgery and the study protocol. A written informed consent was obtained and the parturients willing to participate in the study were kept nil per orally 8 hour a before the surgery. On arrival to the preoperative room, all parturients were given Inj.Pantoprazole 40mg and Inj.Metoclopramide 10mg intravenously over 10 minutes and made to wear a cotton gown covered with a single cotton bed sheet. The parturients were administered with either Inj.Granisetron 40µg/kg or Inj.Tramadol 1mg/kg intravenously over 5 minutes, 5 minutes prior to the subarachnoid block and coloaded with warm intravenous fluids like ringer lactate at 7-10ml/kg.

In the operation theatre, the ambient temperature was set between 22-24℃, parturients were connected to the standard ASA monitors like pulse oximetry, non- invasive blood pressure, spo2 and electrocardiogram. Under aseptic precautions, subarachnoid block was performed using 25G Quincke's spinal needle and 2ml of 0.5% bupivacaine heavy at the rate of 0.3ml/second after ensuring satisfactory flow and aspiration of csf. The parturients were immediately placed in supine position and handed over to the obstetrics team and covered by surgical drapes and one layer of cotton blanket is placed over the chest and arms. No other active warming methods were used. Intraoperatively, vitals, shivering, sedation and other side effects were noted. Any shivering observed were graded u sing a 5 point scale by CROSSLEY AND MAHAJAN[12] at regular 5 minutes for the first 30 minutes and every 30 minute a till the return of modified bromage scale of 6 postoperatively.

0	No shivering
1	Piloerection or peripheral vasoconstriction but no visible shivering
2	Muscular activity in and one muscle group
3	Muscular activity in more than one muscle group but not generalised shivering
4	shivering involving the whole body

Table 1: 5 Point scale by CROSSLEY AND MAHAJAN

1	Completely awake
2	Awake but drowsy
3	Asleep but responsive to verbal commands
4	Asleep but responsive to tactile stimulus
5	Asleep and not responsive to and stimulus

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Table 2: Sedation if any was evaluated by a 5 point numerical score

Shivering score ≥3 after subarachnoid block and extraction of the foetus was treated with Inj.Pethidine 25mg intravenously. Any side effects and complications was noted and treated accordingly.

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in our study. The continuous measurements are presented as Mean±SD and results on categorical measurements are presented as number (%). Significance is assessed at 5% level of significance. Chi- square/ Fischer test has been used to find the significance of the study parameters.

RESULTS

The present study had 60 parturients with 30 in each study group. The demographic parameters are described in table-3 and both the groups were comparable with respect to age, weight, height and body mass index. Table- 4 depicts the baseline clinical variables with respect to heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation.

Table-5 represents the incidence of shivering in both the groups and shows that there is no statistical significance in both the groups. However, the percentage of incidence of perioperative shivering is low with granisetron group than the tramadol group. Totally, shivering was observed in about 6 (20%) out of 30 parturients in the granisetron group and 8(27%) out of 30 parturients in the tramadol group. 10(33%) parturients from the tramadol group had nausea and emetic episodes and was treated appropriately. There was no evidence of sedation in any parturients of the 2 groups.

Parameters	Group G	Group T	Total	p value
Age (in years)	25.57±2.96	24.4±3.02	24.98±3.02	0.136
Height (in cm)	164.9±4.99	165.8±4.6	165.35±4.78	0.471
Weight (in cm)	66.9±7.02	66.6±6.73	66.75±6.82	0.886
BMI (kg/m^2)	24.53±2.35	24.2±2	24.37±2.17	0.564

Table 3: Depicting demographic characteristics of both groups

Parameters	Group G	Group T	Total	p value
Heart rate	80.5±11.63	83.73±6.7	82.12±9.55	0.192
SBP (mm Hg)	117.03±8.11	118.6±6.66	117.82±7.4	0.417
DBP (mm Hg)	73.7±10.01	72.77±7.77	73.23±8.9	0.688
MAP (mm Hg)	88.14±8.62	88.04±0.89	88.09±7.74	0.961
SpO2	98±0.59	98.2±0.55	98.01±0.57	0.179

Table 4: Depicting baseline clinical variables in 2 groups of parturients

Time	Shivering	Group G (n =30)	%	Group T (n =30)	%	Total	p value
0 min	No	30	100%	30	100%	60	1
	Yes	0	0%	0	0%	0	

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5 min	No	30	100%	30	100%	60	1
	Yes	0	0%	0	0%	0	
10 min	No	27	90%	29	97%	56	0.1620
	Yes	3	10%	1	3%	4	
15 min	No	26	87%	29	97%	55	0.3533
	Yes	4	13%	1	3%	5	
20 min	No	25	83%	27	90%	52	0.7065
	Yes	5	17%	3	10%	8	
25 min	No	25	83%	25	83%	50	>0.9
	Yes	5	17%	5	17%	10	
30 min	No	25	83%	24	80%	49	0.7386
	Yes	5	17%	6	20%	11	
60 min	No	24	80%	24	80%	48	>0.99
	Yes	6	20%	6	20%	12	
90 min	No	24	80%	23	77%	47	0.754
	Yes	6	20%	7	23%	13	
120 min	No	24	80%	22	73%	46	0.5416
	Yes	6	20%	8	27%	14	
150 min	No	24	80%	22	73%	46	0.5416
	Yes	6	20%	8	27%	14	
180 min	No	24	80%	22	73%	46	0.5416
	Yes	6	20%	8	27%	14	

Table 5: Depicting incidence of shivering in both groups

Parameters	**Group G (n=30)**	**Group T (n=30)**	**p value**
Shivering (%)			0.5416
No	24 (80%)	22 (73%)	
Yes	6 (20%)	8 (27%)	
Severity of shivering (%)			0.5416
Grade 1	3 (10%)	5 (16.87%)	
Grade 2	1 (3.33%)	2 (6.75%)	
Grade 3	2 (6.66%)	1 (3.37%)	
Grade 4	0	0	

Table 6: Depicting severity of shivering in both groups

p value >0.05= Non significant, p value<0.05= significant

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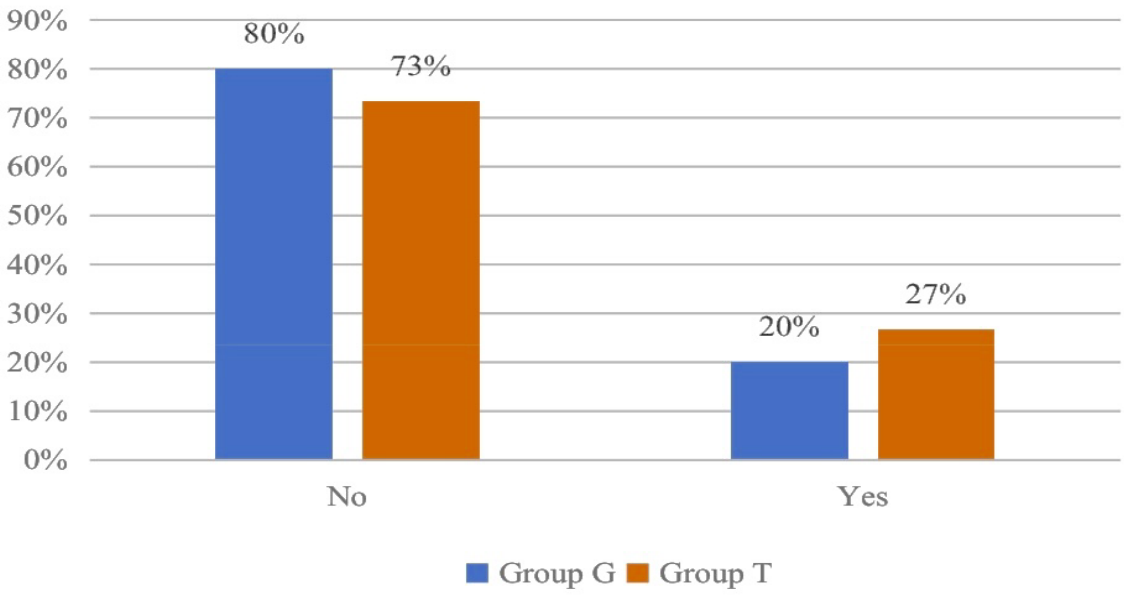

Graph 1: Depicting comparison of perioperative shivering percentage between granisetron and tramadol

DISCUSSION

Sixty parturients were enrolled in our study. The baseline demographic and clinical parameters like age, weight, height, BMI, core temperature before subarachnoid block, room temperature, fluid input, and duration of surgery were matched. This showed that the parturients in our study were relatively homogenous and comparable.

Subarachnoid block is the preferred choice of anaesthesia for caesarean section when compared with general anaesthesia as it prevents general anaesthesia related complications like neurotoxicity, as well its easy to perform in nature and post-operative pain management.[13] However it poses to side effects such and hypotension, bradycardia, shivering. Perioperative shivering is often described by the patients as an extremely unpleasant feeling, which leads to numerous physiological as well as psychological disturbances.[14]

Over the past decade, many pharmacological agents and non-pharmacological methods have been employed in preventing shivering after subarachnoid block. In our study we have compared granisetron and tramadol for their antishivering property. The result of our study showed that the administration of granisetron 40µg/kg can decrease the incidence and degree of shivering similar to the administration of tramadol 1mg/kg. Although, 30% of the parturients who received tramadol had side effects like nausea and vomiting which was not seen in the parturients receiving granisetron.

According to the monoamine thermoregulation theory proposed by Felberg and Meher's, 5HT3 serotonin receptor located in the preoptic part of the anterior hypothalamus may have a significant role in the thermoregulation and shivering.[15]Granisetron, a 5HT3 receptor antagonist is known to prevent shivering by inhibiting serotonin reuptake in the preoptic area and tramadol in the spinal cord level.

Sajedi et al in 2008, conducted a placebo controlled study comparing tramadol 1mg/kg, granisetron 40µg/kg, meperidine 0.4mg/kg and saline 0.9%. The study was concluded with

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granisetron 40μg/kg being as effective as tramadol 1mg/kg and meperidine 0.4mg/kg in preventing postanaesthetic shivering[16] in accordance with our study.

Maruf et al in 2014, conducted a study to evaluate the efficacy and effects of tramadol 0.5mg/kg and pethidine 0.5mg/kg intravenously in preventing shivering during caesarean section under spinal anaesthesia. The study was concluded that both tramadol and pethidine are effective but tramadol offered rapid onset of antishivering action, less recurrence and fewer side effects like nausea and vomiting.[17] This observation was in contrast to our study where tramadol had significant number of side effects like nausea and vomiting as when compared to granisetron.

Mohammadi et al in 2015, compared efficacy of granisetron of prevention of shivering, nausea and vomiting during caesarean delivery under spinal anaesthesia with saline as a control group. The study was concluded as granisetron to be an effective drug to prevent shivering and other side effects[18] as same our study.

Kabade et al in 2018, conducted a comparative study of granisetron versus pethidine for prevention of perioperative shivering, nausea and vomiting during caesarean delivery under spinal anaesthesia. They found out prophylactic granisetron 40μg/kg was as effective as pethidine 0.4mg/kg in preventing perioperative shivering following spinal anaesthesia and also reduces the need of antiemetics[19] yielding the same result as our study.

Jouryabi et al in 2021, compared the effects of low dose ketamine, tramadol, ondansetron and normal saline and placebo in prevention of post spinal anaesthesia shivering in caesarean section. The found out that the incidence of shivering in placebo group was high and tramadol was the most effective drug in preventing shivering followed by ketamine and ondansetron.[20]

Wahid et al in 2021 conducted a comparative research between granisetron 10μg/kg versus 40μg/kg of granisetron for prophylaxis of shivering after spinal anaesthesia for lower abdominal surgery and concluded that 40μg/kg granisetron reduces the incidence and severity of shivering and maintains a better core temperature compared to granisetron 10μg/kg, which also coincided with our study.[21]

CONCLUSION

Our study found out that prophylactic administration of intravenous administration of granisetron 40μg/kg before subarachnoid block in parturients undergoing caesarean section did not significantly decrease shivering as compared to intravenous tramadol but granisetron was found to be a more suitable drug as compared to tramadol due to lesser side effects like nausea and vomiting which seems to be the dilemma with most of the drugs employed for prevention of peri operative shivering

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