Comparison of Intravenous Ondansetron and Tramadol for Control of Shivering during Spinal Anaesthesia: A Prospective, Observer Blind Study

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ABSTRACT

Introduction: Post spinal shivering is a frequent problem in parturient undergoing lower segment caesarean section. We conducted a study in parturient undergoing lower segment caesarean section, to compare the efficacy of Ondansetron and Tramadol for control of shivering under regional anaesthesia.

Material and Methods: A randomised prospective double blinded single hospital comparative study was conducted Gauhati Medical College and Hospital, Guwahati, Assam, from a period of August 2016 to July 2017. 124 ASA I and II patients planned for lower segment caesarean section were randomly classified into two groups A and B, Group A received 0.5mg/kg tramadol and Group B received 8mg bolus ondansetron.

Result: The complete disappearance of shivering took a mean of 3.4 minutes in Group A while 5.1 minutes in Group B (p value ≤0.05).

Conclusion: I.V Tramadol is superior to ondansetron for control of shivering with early onset.

Keywords: Shivering, Ondansetron, Tramadol

INTRODUCTION

Temperature is one of the most important and closely maintained body parameter as membrane fluidity, diffusion capacity and enzyme systems works optimally within a narrow temperature range.[1]

Shivering defined as spontaneous, rhythmic, oscillatory, tremor-like muscular hyperactivity occurs in response to core hypothermia in an attempt to raise the metabolic heat production[2]

Spinal anaesthesia is the preferred method of anaesthesia in parturient undergoing both elective and emergency Lower segment caesarean section. The incidence of shivering has been reported to be about 19-33% after neuraxial anaesthesia.[3,4]

Shivering may be defined as an involuntary, repetitive activity in the skeletal muscle commonly occurs as a thermoregulatory response to hypothermia. However, in the postoperative period, mechanisms like uninhibited spinal reflexes, sympathetic over activity, postoperative pain, adrenal suppression, pyrogen release and respiratory alkalosis[5] may also be important.

Shivering increases perioperative heart rate and oxygen consumption by 5 times and also increases the metabolic demand by 100- 600%.[6,7] thereby increasing chances myocardial ischemia, hypoxia, hypoxemia and later lactic acidosis. Also there can be delayed recovery from anaesthesia.[8] Moreover, it may lead to artefacts in the monitor readings. Therefore, prevention and control of shivering is vital

Tramadol, is an inhibitor of the re-uptake of serotonin (5-HT) and norepinephrine in the spinal cord found to influence the thermoregulatory control mechanisms. Tramadol is emerging as a new and safe drug for treatment of post anaesthesia shivering.[9] Ondansetron, a selective $5HT_3$ receptor antagonist, primarily used in PONV. In previous studies, mostly preventative effects of ondansetron on post anaesthetic shivering has been studied, and useful results were obtained.[10]

This study aimed to compare the efficacy of Ondansetron and Tramadol for control of shivering in patients undergoing lower segment caesarean section under spinal anaesthesia and to evaluate any other relevant observation, if they arise.

MATERIAL AND METHODS

The present prospective clinical study was carried out in pregnant patients at term, scheduled for elective low-risk lower segment caesarean section under spinal anaesthesia at Gauhati Medical College and Hospital, Guwahati, Assam, from a period of August 2016 to July 2017.

The patients who developed intra-operative shivering following spinal anaesthesia for caesarean section were included in the study.

Sample size calculation: As unpublished clinical experience in our institute 70% of patients gets relived of shivering within 3 minutes of 0.5 mg/kg of IV tramadol. Therefore, to detect a 20% increase in efficacy, 55 samples in each group is required with the power of 80% and significance level of 0.05. considering an attrition rate of 10%, a sample size of 62 per group will be required.

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Method of collection

After obtaining approval from the ethical review committee and taking informed consent, 124 cases posted for elective lower segment caesarean section and developing shivering of grade 2 or more were selected for the study.

Total patient participating in the study were randomized into two groups intraoperatively at the occurrence of shivering. Sealed brown envelopes containing either of alphabet A or B were put in a box and reshuffled. The total number of sealed envelopes was equal to the number of sample size plus attrition (n=124).

One group assigned as Group A received Tramadol 0.5 mg/kg diluted to 5ml with distilled water and other group assigned as Group B received Ondansetron 8 mg diluted to 5ml with distilled water intravenously slowly over 1 minutes.

Study Design: A randomised prospective double blinded single hospital comparative study

Methodology: Informed written consent was obtained from the patients participating in the study.

Anaesthetic management

Ambient temperature was maintained between 25 to 28^{O}C. Baseline vital parameters like Heart Rate, Mean Arterial Pressure and SPO2 were recorded. IV access was obtained with 18 G cannula and IV fluids started. The volume of the local anaesthetic, volume of preloading fluid, use of vasopressors were determined by the attending anaesthesiologist, and was not affected by inclusion in the study.

Monitoring of NIBP, Pulse Oximetry, ECG, was done throughout the procedure. Baseline preoperative axillary temperature was noted in all the patients using a skin probe kept in the axilla near the vicinity of axillary artery.

All patients received spinal anaesthesia according to department protocol with Bupivacaine heavy 12 – 15 mg along with inj. buprenorphine 50µg. The level of maximum block height was assessed after 5 min using cotton wool soaked in alcohol. Oxygen at rate of 5 L/min was administered through face mask to all the parturient.

Patients who developed shivering after the spinal anaesthesia were included in the study and were randomly divided into one of the two groups.

Group A (62 patients) received 0.5mg/kg Tramadol I.V made up to 5ml using sterile water.

Group B (62 patients) received 8mg ondansetron I.V made up to 5 ml using sterile water.

Parameters compared

Shivering if appeared was graded as follows.

1. Grade 0: No shivering,
2. Grade 1: Piloerection or peripheral vasoconstriction but no visible shivering.
3. Grade 2: Muscular activity in only one muscle group,
4. Grade 3: Muscular activity in more than one muscle group but not generalized.
5. Grade 4: Shivering involving whole body.

The drug was administered by anaesthesia personnel who was not involved in the study and was blinded to the groups and to whether the drug contains Tramadol or Ondansetron. The same anaesthesia resident who administered the drug, assessed the effect of the drug administered based on the proforma. All the patients were assessed for shivering grades, its disappearance, haemodynamic status, sedation score and complications if any.

Patients were observed at intervals of 0 min, 1 min, 2 mins, 3mins, 5 minutes, and thereafter at 10, 20, 30, 40, and 60 minutes. Adverse effects such as nausea and vomiting were documented. Any other adverse effect if occurred was also noted.

Those patient in which the shivering is not controlled within 10mins were considered as treatment failure and in these patients the same drug which was previously given are administered at half the earlier dose.

Recurrence of shivering was also noted and an additional dose of either Tramadol or Ondansetron in a dose of 0.25 mg/kg iv and 4 mg iv was given in the respective groups.

STATISTICAL ANALYSIS

Descriptive statistical analysis has been carried out in the present study. Statistical analysis was done using Microsoft excel 2016 student edition, and online calculators available at https://graphpad.com/scientific-software/instat.

The Data was expressed as mean and standard deviation for weight, age, height, parity, time taken to control shivering etc. The data was tested for normality using Kolmogorov–Smirnov test. Comparison of continuous data between the Groups A and B was done using independent t-test. Nominal data in both groups was compared using Chi-square test and P value < 0.05 was considered statistically significant.

RESULTS

The two groups were comparable with respect to demographic profile, Parity, body mass index (Table 1).

The two Groups were also comparable with respect to baseline axillary temperature (P value 0.74). The mean temperature at which shivering occurred in our study groups was 97.37^{0}f.

Shivering grade: The maximum shivering grade was compared with unpaired t test and was comparable in two groups with a p value of 0.608743 (TABLE 2).

Hemodynamic variations after giving medication

Vital parameters like Heart rate, Mean arterial pressure and Body temperature did not show any significant change with the administration of medication and was comparable between two groups (figure 1). There was a significant increase in the HR in the Tramadol group in the 5th minute (figure 1), other vital parameters were well maintained with Tramadol.

Temperature variability: -There was no statistical difference in the two groups. However the patient in both the group showed a rise in temperature by 1^{0}f after shivering.

Shivering Control: The mean time required to control shivering was significantly lesser in Group A as compared to Group B (table 3) (p value=0.0000470283). Whereas

Demographic variable	Group A	Group B	P value
Number of patients	62	60	
Age (mean ± S.D)	24.8±4.59	25.5±4.71	0.755
Weight (mean ± S.D)	56.81±6.99	57.23±10.6	0.2749
Height (mean ± S.D)	147.8±6.17	148.2±6.06	0.8503
BMI (mean ± S.D)	26.02±3.45	26.1±4.38	0.5901
Parity(multipara/Primipara)	32/30	33/27	0.7077

Table-1:

Shivering grade	Group A	Group B
Mean ±SD	3.387±0.553	3.333± 0.601

Table-2:

Group A	Group B
3.4 MINS±0.98	5.1 MINS±2.89

Table-3:

Response rate	Group A	Group B
Yes	62	58
No	0	2
Recurrence rate	Group A	Group B
Yes	5	10
No	57	50

Table-4:

Nausea	Group A	Group B	Vomiting	Group A	Group B
Yes	8	0	Yes	6	0
No	54	60	No	56	60

Table-5:

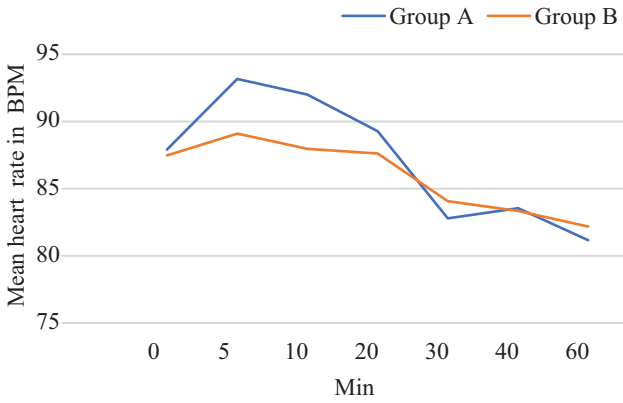

Figure-1: Mean heart rate

Time	Group A (Ramsay sedation score)						Group B (Ramsay sedation score)						P value
	1	2	3	4	5	6	1	2	3	4	5	6	
0 Mins	6	53	3	0	0	0	4	55	1	0	0	0	0.55
5 Mins	3	55	4	0	0	0	1	58	1	0	0	0	0.24
10 Mins	0	55	7	0	0	0	0	57	3	0	0	0	0.323
30 Mins	0	48	14	0	0	0	0	55	5	0	0	0	0.04
60 Mins	0	46	16	0	0	0	0	57	3	0	0	0	0.002

Table-6:

the success of controlling shivering was comparable in two groups (table 4) (P value= 0.239). Recurrence of shivering was significantly higher in Group B than Group A (table 4).

Incidence of nausea and vomiting: The incidence of nausea and vomiting was significantly higher in group A as compared to Group B (table 5). The P value calculated using Fisher's Exact test is <0.006.

Sedation score: Sedation score was comparable between the two groups except at 30th minute during which higher number of patients in Group A had higher sedation score (table 6).

DISCUSSION

Shivering, is an undesirable side effect in both regional and general Anesthesia and should be prevented. However, Kranke et al., in 2004, commented that with pharmacological shivering prophylaxis many patients receive a drug they didn't need and be unnecessarily exposed to adverse drug effects.[11]

Therefore, the present study was designed to evaluate the compare the efficacy of 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 develops shivering. We designed our study to standardise the possible compounding factors while reflecting the customary practice in our institution. The temperature in the operating room was maintained constant at 25°C - 28°C. IV fluids and drugs were given at room temperature.

In our study Tramadol is given in dose of 0.5mg/kg based on previous studies that used tramadol in a dose of 0.5mg/kg

and was found safe and effective for control of shivering.[12-15] Ondansetron is given in a dose of 8mg was selected based on the study by Mahoori et. al,[16] in year 2014 where they 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.

We randomly administered tramadol 0.5mg/kg IV and Ondansetron 8mg IV to a group of 124 patient who were posted for elective caesarean section under spinal anaesthesia, and who in the due course of anaesthesia and surgery developed shivering. Two patients from Group B (Ondansetron) were excluded from the study due to lack of adequate data. Powell et al.[20] compared the effect of 4 mg and 8 mg Ondansetron with placebo and reported that administration of 8 mg Ondansetron before the induction of anaesthesia could reduce the incidence of Post Anaesthesia Shivering

The mean temperature at which shivering occurred in our study groups was 97.37^{0}f. This results were similar to the earlier study done by A. Dhimar et al.[21]

In our study, the mean time required to control shivering in Group Tramadol is 3.4 mins. This result is comparable to study done by Onyekwulu et al.[19] Manouchehrian et al.[13] where they found to control the shivering with tramadol in 3.1mins ± 1.1 and 2.57min ± 2.2 respectively. Study done by Kaparti et al.[18] showed control of shivering with tramadol within 2 minutes in all patients(n=20), they however used tramadol in dose of 1mg/kg

There was statistically significant difference between the mean time of stopping of shivering between group Tramadol when compared to group Ondansetron. We could not find any study comparing Tramadol and Ondansetron for the treatment of shivering.

Vital parameters like Heart rate, Oxygen Saturation, mean arterial pressure and Body temperature did not show any significant change with the administration of ondansetron. There was a significant increase in the HR in the Tramadol group in the 5th minute.

Response rate (control of shivering within 10mins) in Group A (tramadol) in our study is 100%. This result is similar to the studies done by Mittal et al.[14], Kaparati et al.[18], and Manouchehrian et al.[13] In contrast ondansetron showed a response rate of 93.3%, this result was different from the study done by Mahoori et al.[16] where they have found response rate of 81%. The difference can be attributed to the difference in the study protocol. Joshi et al.[17] have found a response of 23.52% in there study group treated with ondansetron, the cause for such low response rate may be due to low dosing of ondansetron 0.06mg/kg vs 8mg in our study.

In the Ondansetron group recurrence was seen in 10/60 (16%) patients whereas it was 5 out of 62 patients (8.0%) with Tramadol. The percentage of recurrence in tramadol in our study is similar to studies by Mohammad et al.[15] Mittal et al.[14] and Shukla et al.[5], they found a recurrence rate of 6.6%, 8%, and 5% in their studies. The probable reason for recurrence of shivering could be result of low concentration of the active drug. In our study, more patients in Group A were sedated with Ramsay sedation scoring of 3 at 30 mins and 60 minutes of the drug administration. Sedation scoring showed no difference between the two group at 0, 5 and 10 minutes.

No patients developed nausea or vomiting in the ondansetron group. This finding was similar to the finding by Joshi et al.[17] and Mahoori A. et al.[16] In the tramadol group, the incidence of nausea was 8/62(12%) which is similar to the study reported by Manouchehrian et al.[13] the incidence of vomiting in tramadol group in our study was 6/62(9.6%) this result is similar to studies did by Onyekwulu et al.[19]

CONCLUSIONS

I.V Tramadol is qualitatively superior to ondansetron for control of shivering. Ondansetron is also effective in reducing shivering but the onset is delayed. However, Ondansetron renders the patient more stable haemodynamically and reduces effectively the incidence of postoperative nausea and vomiting. So, we conclude that, though the efficacy of tramadol is superior to Ondansetron, both can be used as effective agents for shivering after post-spinal anaesthesia.

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