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INTRAVENOUS GRANISETRON ATTENUATES HYPOTENSION DURING SPINAL ANAESTHESIA IN CESAREAN DELIVERY: A DOUBLE-BLIND, PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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ABSTRACT

AIM : To determine the effectiveness of intravenous (IV) granisetron in the prevention of incidence of hypotension and bradycardia during spinal anaesthesia in elective caesarean section.

MATERIALS AND METHODS : 80 ASA grade 1 or 2 patients undergoing elective cesarean section under spinal anaesthesia were included. GROUP I Patients received 1 mg Granisetron diluted in 10 ml of normal saline slowly IV (over 1 minute) 5 minute before spinal anaesthesia whereas. GROUP II Patients received 10 ml of normal saline (placebo) slowly IV (over 1 minute). The following parameters were noted. (1) Time of injection of subarachnoid block. (2) Time of onset of sensory block at T10 level. (3) Time of onset of motor block. (4) Time for sensory regression to T 12 dermatome. 5) Duration of surgical procedure. 6) Haemodynamic stability.

OBSERVATION AND RESULTS : The average time taken for the onset of motor block (Modified bromage score 3) was 2.20 minutes in Group I and 2.33 minutes in Group II. It was statistically not significant (p value 0.543 > 0.05).The time of sensory regression to T12 was shorter in Group I (102.30 ± 7.753) when compared with Group II (128.13 ± 8.401) & it was statistically significant (p value = 0.000 < 0.05).

CONCLUSION : Granisetron given as a dose of 1 mg intravenously before spinal anaesthesia in parturients who undergoing cesarean sections has the faster onset of sensory regression to T12 and reduced incidence of hypotension.

KEYWORDS : Granisetron, Spinal anaesthesia, Caesarean section.

INTRODUCTION

Many anaesthesiologist prefer to give spinal anaesthesia for women who will undergo caesarean section due to many advantages like avoiding risks of general anaesthesia, for better postoperative pain relief and also It is not associated with maternal or foetal risk for toxicity to local anaesthetics.

Although this can be achieved by spinal or epidural anaesthesia, spinal anaesthesia is a simple technique with low failure rate, rapid onset and low drug dose.

On the other hand, the anaesthesiologist is facing certain problems after giving spinal anaesthesia like hypotension, bradycardia and failure of block.

Various preventive methods are currently used to prevent or minimize hypotension, including left uterine displacement, crystalloids or colloid preloading, and utilizing compression stocking onto the lower extremities.

AIM OF THE STUDY

This study was conducted to determine the effectiveness of intravenous (IV) granisetron in the prevention of incidence of hypotension and bradycardia during spinal anaesthesia in elective cesarean section.

MATERIALS AND METHODS

Study design : A Double-blinded, prospective randomised control study.

After obtaining approval from the institutional ethical committee, Thanjavur medical college, Thanjavur, the study was conducted in 80 ASA grade 1 or 2 patients undergoing elective caesarean section under spinal anaesthesia..

INCLUSION CRITERIA:

Adult patients aged 18 - 30 years, ASA 1 and 2 patients , Primi or Multiparous women, Single live fetus, Uncomplicated pregnancy, Patients undergoing elective caesarean section

EXCLUSION CRITERIA:

Patient refusal, Patients with known contraindication for spinal anaesthesia, coagulation disorders or on anticoagulation therapy, cardiac disease history of allergy to study drugs,

The procedure was explained to the patients and written informed consent was obtained. They were allocated into following groups.

GROUP I

Patients received 1 mg Granisetron diluted in 10 ml of normal saline slowly IV (over 1 minute) 5 minutes before spinal anaesthesia.

GROUP II

Patients received 10 ml of normal saline (placebo) slowly IV (within 1 minute) 5 minutes before spinal anaesthesia.

PREOPERATIVE PREPARATION:

Patients were kept fasting overnight and oral ranitidine 150 mg at night and on the morning prior to surgery were given.

After routine preoperative assessment at the patients' waiting room in the OT, basal line readings of the vital parameters were recorded. Intravenous line started. The patients were randomly allocated into two groups of 40 each by using closed cover technique.

In the operating room, appropriate equipment for airway management and emergency drugs were kept ready.

Monitors were connected to the patient. Preoperative vital parameters were recorded. Patients were preloaded with 10ml/kg of Ringer lactate 15 minutes prior to the subarachnoid block. According to the randomization (closed cover technique) 10 ml of Normal saline with or without test drug was given intravenously over 1 minute 5 min before the procedure.

On sitting position, the skin over the back was prepared with antiseptic solution and draped with sterile towel. After skin's infiltration with 1 ml of 1% lignocaine, 25G Quincke's needle was inserted at the L3-4 interspace in the midline. After confirming free flow of CSF, 2ml (10 mg) of 0.5 % Inj. Bupivacaine was injected.

After the block was performed, the patients were made supine with 15-20 degree left displacement of uterus until delivery of baby by keeping wedge under the right buttock. Fluid therapy was maintained with ringer lactate 10 ml/kg/hr. Oxygen was supplemented through O2 mask 4L/minute. All patients in both groups have received. IM Tramadol 100 mg at the end of the surgery for post operative pain relief.

The following parameters were noted. 1) Time of injection of subarachnoid block, 2) Time of onset of sensory block at T10 level. 3)Time of onset of motor block. 4) Time for sensory regression to T 12 dermatome. 5) Duration of surgical procedure. 6) Haemodynamic stability.

HAEMODYNAMIC PARAMETERS

Heart rate, Systolic arterial pressure , and Mean arterial pressure were monitored at every 3rd minute for the first 30 minutes and then every 5th minute subsequently until 45 minutes or until completion of surgery.

Hypotension was treated with a rapid infusion of crystalloids 200 ml and a bolus of ephedrine 5mg iv. Bradycardia was treated with injection atropine 10mcg/kg intravenously.

SENSORY AND MOTOR BLOCK

Sensory block was assessed both sides by "loss of pinprick sensation" to 23 G hypodermic needle in the mid clavicular line. Time to reach T10 sensory level was taken as the time of onset of sensory block.

MOTOR BLOCK

Degree of motor block was assessed by "Modified bromage scale" as follows,

MODIFIED BROMAGE SCORE

Grade	Criteria	Degree of block
0	Able to move hip, knee, ankle.	Nil (0%)
1	Unable to move hip, but able move knee and ankle.	Partial (33%)
2	Unable to move hip and knee, but able to move ankle.	Almost complete (66%)
3	Unable to move hip, knee and ankle.	Complete (100%)

Motor block was assessed at the same interval as sensory block. Onset of motor block was assessed by time to reach modified bromage score 3.

RESPIRATION

Respiratory depression was defined as rate <10 breath/minute or Spo2 <92%.

Newborns APGAR scores were assessed at 1 minute and 5 minutes intervals.

OBSERVATION AND RESULTS

All 80 patients in two groups completed the study without any exclusion. we did inter group analysis and the results were as followed. Data were presented as Range, Mean , Standard Deviation using SPSS Statistics versions 16.0.

The collected data was analysed using chi square test, student T test and the probability value ' p' of less than 0.05 was considered as statistically significant. The above table shows the demographic data in terms of age, height, weight and duration of surgery and they are comparable in both groups.

The Mean time of onset of sensory block was (65.28± 6.831) in Group I and Group II (66.83 ± 4.624) and the p value was statistically not significant (0.238 > 0.05).

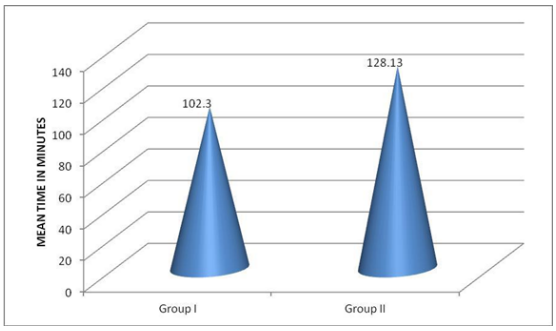
The average time taken for the onset of motor block (Modified bromage score 3) was 2.20 minutes in Group I and 2.33 minutes in Group II. It was statistically not significant (p value 0.543 > 0.05).

Table 1. Time of sensory regression to T12

Parameter	Time of sensory regression to T12 (in minutes)	
	Group I	Group II
Range	90-120	110-140
Mean	102.30	128.13
SD	7.753	8.401
'p' value	0.000 Significant	

The time of sensory regression to T12 was shorter in Group I (102.30 ± 7.753) when compared with Group II (128.13 ± 8.401). It was statistically significant (p value = 0.000 < 0.05). There was a delay in sensory regression of approximately 20% in Group II comparing to Group I. So faster sensory regression in Group I about 20 % compared to Group II.

Graph 1 . Time of sensory regression to T12



This graph shows the time of sensory regression to T12 between the Group I and Group II.

HEMODYNAMIC VARIABLES

Table . 2 Mean Arterial Pressure

Time Interval	Group I (Mean ± SD)	Group II (Mean ± SD)	P value
0 min	81.25 ± 7.772	79.53± 7.543	0.156
3 min	78.30 ± 7.068	67.58 ± 11.593	0.000
6 min	76.03 ± 7.859	65.40 ± 7.964	0.000
9 min	73.78 ± 8.297	65.80 ± 8.567	0.000
12 min	72.97 ± 7.960	68.05 ± 9.126	0.012
15 min	72.80 ± 7.680	68.53 ± 9.356	0.028
18 min	72.50 ± 6.702	68.43 ± 8.003	0.016
21 min	72.80 ± 7.233	68.33 ± 7.381	0.008
24 min	73.53 ± 7.093	70.80± 7.875	0.108
27 min	73.47 ± 6.320	71.40 ± 7.537	0.186
30 min	75.38 ± 5.856	72.10 ± 7.249	0.029
35 min	75.80 ± 6.947	72.58 ± 7.769	0.054
40 min	77.53 ± 7.602	73.00 ± 7.154	0.008
45 min	79.00 ± 7.729	74.63 ± 8.273	0.017

The mean arterial pressure was monitored from preoperative basal to 45th minute of the procedure (14 intervals), out of which three intervals (24, 27, 35th minute) were statistically not significant. (Table.2 Graph 2)

Graph 2. Comparison of Mean Arterial Pressure

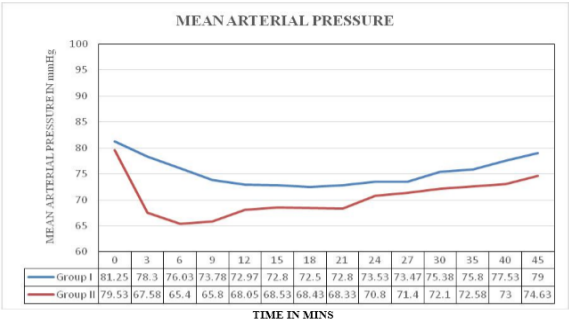
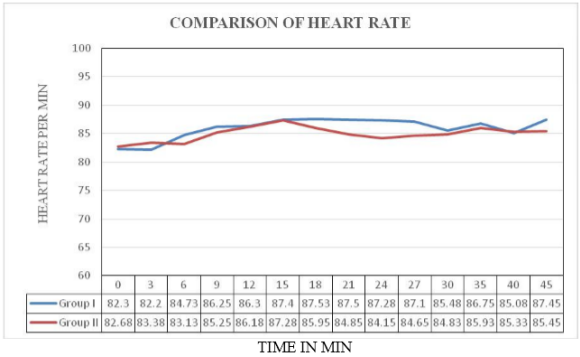


Table .3 Heart Rate

Time Interval	Group I (Mean ± SD)	Group II (Mean ± SD)	P value
0 min	82.23 ± 6.455	82.68± 5.907	0.746
3 min	82.20 ± 7.321	83.38 ± 5.808	0.429
6 min	84.73 ± 6.880	83.13 ± 6.022	0.272
9 min	86.25 ± 7.847	85.25± 7.608	0.564
12 min	86.30 ± 7.035	86.18 ± 6.714	0.935
15 min	87.40 ± 6.706	87.28 ± 7.387	0.937
18 min	87.53 ± 7.197	85.95 ± 6.127	0.295
21 min	87.50 ± 8.045	84.85 ± 6.183	0.103
24 min	87.28 ± 8.111	84.15± 7.533	0.078
27 min	87.10 ± 7.759	84.65 ± 7.185	0.147
30 min	85.48 ± 7.766	84.83 ± 6.201	0.680
35 min	86.75 ± 8.189	85.93 ± 8.988	0.669
40 min	85.08 ± 8.247	85.33 ± 7.774	0.889
45 min	87.45 ± 10.064	85.45 ± 5.870	0.418

In this study, heart rate less than 50 beats was considered as bradycardia while collecting the data. Heart rate was recorded in 14 intervals. None of the intervals had statistically significant.

Graph 3: COMPARISON OF HEART RATE



35% (14 patients) had nausea and vomiting and 5% (2 patients) shivering in group II whereas none of the patients had nausea , vomiting and shivering in group I.

DISCUSSION

We conducted a randomized double blinded control study in Govt. Raja Mirasudhar Hospital, an obstetrics and Gynaecology speciality unit of Thanjavur Medical College, to evaluate the hemodynamic changes with administration of intravenous Granisetron and intravenous normal saline in elective caesarean section after spinal anaesthesia.

After spinal anesthesia, reduced preload may initiate vagally mediated cardiac-depressant reflexes. Later, decreased heart rate and blood pressure from stimulation of cardiac chemoreceptor and mechanoreceptor were established.

In the present study, the Bupivacaine dose of spinal anaesthesia in both groups was 10 mg (2ml) which was very similar to **Ahmed A. Eldaba et al** and **Omyma Sh M Khalifa et al.**

Parameters were recorded for 45 minutes as basal and 14 intervals after spinal anaesthesia which was similar to **Ahmed A. Eldaba et al.** But these were recorded into 6 intervals for 30 minutes in **Omyma Sh M Khalifa et al.**

The results of the present clinical study are discussed under the following headings 1) Onset of sensory and motor block , 2)Time for sensory regression to T12 , 3) Hemodynamic stability and 4) Adverse effects.

ONSET OF SENSORY AND MOTOR BLOCK

Time of onset of sensory blockade was very similar and comparable in both Group I (granisetron) and II (normal saline) (65.28 ± 6.83 seconds versus 66.83 ± 4.62 seconds) in the present study. In **Ahmed A. Eldaba et al** study mean time to sensory blockade was 6 ± 4 minute and 7 ± 4 minute respectively. The fastest onset time in their study might be explained by the level of onset of blockade was T 10. whereas it was T 6 in **Ahmed A. Eldaba et al.**

The mean onset of motor block in group I was 2.20 ± 0.883 minutes whereas in group II, 2.33 ± 0.944 minutes. It was not statistically significant.

TIME FOR SENSORY REGRESSION TO T12

In the present study Time of sensory regression to T12 was 102.30 ± 7.753 minutes in Group I when compared to Group II (128.13 ±8 . 4 0 1 minutes). It was statistically significant (p value < 0.000). Sensory regression was faster in **granisetron group (20%)** comparing to Normal saline group.

Omyma Sh M Khalifa et al observed prophylactic use of i.v. granisetron , ondansetron, or ephedrine reduced the severity of spinal-induced hypotension, nausea, and vasopressor need. They also observed faster recovery of sensory block with granisetron comparing to all other groups .These findings agree with prior study by **Mowafi et al.**

HEMODYNAMIC STABILITY

MEAN ARTERIAL PRESSURE:

In the present study, most of the intervals (except 24th,27th,35th minute interval) group I had higher MAP compared to group II and statistically significant. The 3rd minute (first reading after spinal anaesthesia) was highly significant and showed only 4 % reduction in MAP in group I whereas 15 % reduction in group II.

But with **Ahmed A. Eldaba et al,** in all the 14 intervals after the spinal anaesthesia the MAP was significantly higher in granisetron group than the normal saline group.

In the present study, the total doses of ephedrine (1.07 ± 2.57 mg vs 7.51 ± 6.41 mg respectively) consumed were significantly less in group I compared to group II which is similar to **Ahmed A. Eldaba et al** study(4.07 ± 3.87 mg versus 10.7 ± 8.9 mg).

HEART RATE:

In the present study heart rate was recorded in 14 intervals after spinal anaesthesia. None of the intervals were statistically significant in both the group.These findings agree with those of **Tsikouris et al.**

ADVERSE EFFECTS

In the present study,the total of ephedrine (1.07±2.57 mg Vs 7.51 ±6.41 mg respectively) consumed were significantly less in group I compared to Group II, thereby the incidence of hypotension was reduced by 57% in group I. This is similar to Ahmed A.Eldaba et al study. 35% (14 patients) had nausea and vomiting in group II whereas none of the patients had nausea and vomiting in group I and the difference was not statistically significant.

Gupta et al. they found that both granisetron and ondansetron are better than the metoclopropamide for prophylactic therapy for postoperative nausea and vomiting (PONV).

APGAR score at 1, 5 minute was comparable between the groups .

CONCLUSION

Granisetron, the selective serotonin receptor antagonist (5 HT-3) given as a dose of 1 mg intravenously before spinal anaesthesia in parturients undergoing cesarean sections has faster sensory regression and reduced incidence of hypotension.

REFERENCE:

(1) Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anesthesia for cesarean section. Cochrane Database Syst Rev 2006; 1 8:4.
(2) Mark AL. The Bezold-Jarisch reflex revisited: Clinical implications of inhibitory reflexes originating in the heart. J Am Coll Cardiol 1983;1:90-102.
(3) Ahmed A. Eldaba, Intravenous granisetron attenuates hypotension during spinal anesthesia in cesarean delivery, Jr of Anaesthesiology and clinical pharmacology.2015, 329-332.
(4) Rashad MM, Farmawy MS. Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section. Egypt J Anaesth 2013; 29:369– 374.
(5) Omyma Sh. M. Khalifa, A comparative study of prophylactic intravenous granisetron, ondansetron, and ephedrine in attenuating hypotension and its effect on motor and sensory block in elective cesarean section under spinal anesthesia,Ain Shams J of Anaes. 2015, 08, page 166-172.
(6) Mowafi HA, Arab SA, Ismail SA, Al-Ghamdi A. The effects of intravenous granisetron on the sensory and motor blockade produced by intrathecal bupivacaine. Anesth Analg 2008; 106:1322–5.
(7) Iqbal A, Ahmed A, Rudra A, Wankhede RG, Sengupta S, Das T, Roy D. Prophylactic granisetron vs pethidine for the prevention of postoperative shivering: a randomized control trial. Indian J Anaesth 2009; 53:330– 334.