Original Article

COMPARISON OF ONDANSETRON AND ONDANSETRON PLUS ALPRAZOLUM FOR PREVENTION OF NAUSEA AND VOMITING FOLLOWING ELECTIVE CAESAREAN SECTION

Md. Rafiqul Hasan Khan[1], S.N. Samad Choudhury[2]

SUMMARY

Pregnancy & operation both causes anxiety. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting. Prevention rather than treatment of postoperative nausea and vomiting should be the anesthetist's aim.

It was a prospective double blind comparative study of 60 parturient scheduled for elective caesarean section under subarachnoid block to see the effect of anxiolytic drug on per & PONV in LUCS. We have carried out comparative study with alprazolum as anxiolytic agent & compared the action of Ondansetron with Ondansetron +alprazolum. Parturient at term or elective caesarean section included in the study were ASA grade I & II.

A total of 60 cards, 30 in each group were prepared by another person who was blind for the study. Every parturient was allowed to draw one card and grouped accordingly. Group A: Inj. Ondansetron (8mg), Group B: Oral alprazolum (0.25mg) +inj. ondansetron (8mg). After 20 minutes of pre-hydration under all aseptic precaution lumber puncture was performed with 25 gauge Quincke's needle in the L3-L4 or L4-L5 space in sitting position and 0.5% Hyperbaric Bupivacaine 2.5 ml (12.5 mg.) was injected within 10-12 sec. Immediately after administration of spinal anaesthesia fetal heart rate was noted for any changes in pulse rate, blood pressure, rate of respiration, discomfort and occurrence of side effects: shivering, nausea, vomiting was recorded every 2 minute for first 10 minutes, then at 10 minutes interval for remainder of the operation. Per operative monitoring such as ECG, continuous SpO_2, non invasive arterial blood pressure was recorded each two minutes interval from time of intrathecal injection up to 10 minutes and then at 10 minutes interval until the end of operation. In the recovery room postoperative analgesia was provided with injection ketorolac tromethamine 30 mg IM on complaining pain and repeated in all patients if necessary. Presence of nausea and vomiting patients were interviewed at one hourly over the first 3 hours then at 3 hourly up to 24 hours postoperative period. Rescue antiemetic of prochlorparazine 10 mg I/M was given if vomiting occurs once, nausea for 10 minutes or at the patient request. Rest other parameters as for example; heart rate, BP, respiration and SpO_2 were also recorded at same interval. Patients were carefully observed for any adverse effects like headache, flushing, drowsiness or any other symptoms.

In the present study incidence of nausea and vomiting in group-A was one and in group-B was zero. Regarding hemodynamic changes (Pulse, Blood pressure) SpO_2, respiratory changes, during operation and 24 hours post operative period in some occasions significant changes were observed ($P<0.05$) but in other occasions no significant changes occur. No other adverse effect like headache, constipation and flushing during operation and 24 hours postoperative period were observed in this study.

In this study we have found that Ondansetron reduces peroperative and postoperative nausea and vomiting. But addition of Alprazolum (an anxiolytic) to Ondansetron, the chance of nausea and vomiting was less.

1. Assistant Professor, Department of Anaesthesia, Bangladesh Medical College, Dhanmondi, Dhaka
2. Professor & Head, Department of Anaesthesia, Dhaka National Medical College & Hospital

INTRODUCTION

Nausea is the subjective, unpleasant sensation of the desire to vomit but without any attempt at expulsive movement, frequently accompanied by salivation, sweating, tachycardia, and change in rate and depth of respiration.[1] It may be brief or prolonged, often occurring in waves and preceding vomiting or occurs in isolation.

Vomiting is a reflex mechanism integrated in the brain stem, by means of which the gastrointestinal tract rids itself of its contents in an attempt to rid the body of toxic harmful material when almost any part of the gastrointestinal tract becomes excessively irritated, over distended or even stimulated-by surgery, pregnancy, radiation, anesthesia, etc.[2]

Vomiting should not be confused with regurgitation or gastro oesophageal reflux neither of which is an active process like vomiting and retching. Emesis is a natural response that may be regarded as body's defense system against ingested toxins, But in spite of advancement in prevention and treatment, nausea and vomiting still occur in unacceptable frequency in association with surgery and anaesthesia and the description of it as "big little problem"[3] capsulate much of the general perception.

Unrelieved pain is a common cause of postoperative nausea and vomiting and opioids, widely used in pain relief are also cause of postoperative nausea and vomiting. Postoperative nausea and vomiting is multifactorial. Several other causes are age, sex (female are 2-4 times more prone to postoperative nausea and vomiting), mental status, obesity, gastro paresis, previous anaesthesia with postoperative nausea and vomiting, hypoxia, hypotension, site, duration and type of operation. The current incidence of postoperative nausea and vomiting varies from 10 to 60% depending on the patient, type of surgery, and anaesthetics. However, the incidence is as high as 85% has been observed after ophthalmic surgery in children and 75% after gynaecological surgery[4].

Although emesis is a common symptom of disease, side effect of many therapies, and result of natural stimuli (pregnancy, motion), the physiology of emetic mechanism has not been an area of particularly intense research since the classical studies of Wang and Borison in late 1940s and 1950s.[5]

The common cause of peroperative and PONV in LUCS under SAB is hypotension and vagal irritation. By using vasopressor and anticholinergic drugs we can control peroperative and PONV. Sedatives and anxiolytic often have an anti-emetic effect by reducing psychological component of the nausea[6]. Sedatives& hypnotics are often used to control anticipatory nausea & vomiting [7].

Though there is no such study available in LUCS under SAB but clinically we found that there are some possible factors such as physiological changes during pregnancy (distention of abdomen, compression of stomach, relaxation of lower oesophageal sphincter) which may contribute to PONV in LUCS under SAB. Though actual mechanism is not known but there may be some correlation between serotonin receptor (5HT3) with PONV in LUCS under SAB. Ondansetron is approved for use in the prevention of nausea and vomiting associated with surgery[8].

Pregnancy & operation both causes anxiety. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting [9].

Prevention rather then treatment of postoperative nausea and vomiting should be the anesthetist's aim. However, there is less agreed protocol as to which patients should receive preventive antiemetic therapy, but the relative indication for prophylaxis increases as the number of risk factors increase. Anti-emetics are occasionally used prophylactically to prevent postoperative nausea and vomiting, more often given postoperatively as treatment for postoperative nausea and vomiting. For prophylaxis to be acceptable, the drug must be effective, sufficiently long acting to last throughout the operative period, and especially without appreciable side effects[7].

The introduction of an effective well-tolerated antiemetic would allow the prevention of postoperative nausea and vomiting and its related consequences, particularly for high-risk patient. The efficacy of antiemetic therapy for the prevention or treatment of postoperative nausea and vomiting may be enhanced by combination therapy. It makes pharmacological sense to administer drugs, which act at different receptors. Presently, there is considerable interest in this and most studies have found combinations to be significantly more efficacious than a single drug[8]. No study is available on anxiolytic drug to prevent peroperative & PONV.

Aim and objectives:

We had become interested to see the effect of anxiolytic drug on per & PONV in LUCS. We have carried out comparative study with alprazolum as anxiolytic agent & compared the action of Ondansetron with Ondansetron +alprazolum.

MATERIAL AND METHOD

Subject:

It was a prospective double blind comparative study of 60 parturient scheduled for elective caesarean section under subarachnoid block in the department of Anaesthesiology, DNMH and Dhaka.

Parturient at term of elective caesarean section willing to be included in the study are ASA grade I & II.

Patient who are unwilling to be included in the study, Bleeding diathesis, Eclampsia, COPD, Patient having H/O motion sickness, hormonal imbalance, disturb mental state, Operation continued more than one hour are excluded from the study.

Grouping:

A total of 60 cards, 30 in each group were prepared by another person who is blinded for the study. Every parturient was allowed to draw one card and grouped accordingly.

Group A: Inj. Ondansetron (8mg)

Group B: Oral alprazolum (0.25mg) +inj. ondansetron (8mg)

Method:

After taking informed consent from each parturient during preoperative visit she was instructed for overnight fasting. After lottery, patients in group A received orally Vitamin B_1 and Inj. Ondansetron and group B received orally alprazolum and Inj. Ondansetron. All drugs were given 30 minutes before operation. In the operation room an intravenous cannula (18G) was inserted and the patient was received IV pre-hydration with 15ml/kg body weight- Ringers lactate solution within 20 minutes. Pulse rate, blood pressure, rate of respiration was recorded before spinal anaesthesia and catheterization was done.

After 20 minutes of pre-hydration under all aseptic precaution lumber puncture was performed with 25 gauge Quincke's needle in the L3-L4 or L4-L5 space in sitting position and 0.5% Hyperbaric Bupivacaine 2.5 ml (12.5 mg.) was injected within 10-12 sec. After noting the time of injection, patient was immediately placed in supine position. A wedge was placed under the right hip. All patient were received supplemental O_2 (4 liter per minute) via mask or nasal cannula. Immediately after administration of spinal anaesthesia fetal heart rate was noted for any changes in pulse rate, blood pressure, rate of respiration, discomfort and occurrence of side effects: shivering, nausea, vomiting was recorded every 2 minute for first 10 minutes, then at 10 minutes interval for remainder of the operation.

Per operative monitoring such as ECG, continuous SpO_2, non invasive arterial blood pressure was recorded each two minutes interval from time of intrathecal injection up to 10 minutes and then at 10 minutes interval until the end of operation. Hypotension defined as a decrease in systolic BP to less than 90mm Hg or a decrease of 20% from the baseline. APGAR score was observed but at 1 and 5 minutes after delivery of baby.

In the recovery room postoperative analgesia was provided with injection ketorolac tromethamine 30 mg IM on complaining pain and repeated in all patients if necessary. Presence of nausea and vomiting patients were interviewed at one hourly over the first 3 hours then at 3 hourly up to 24 hours postoperative period. Rescue antiemetic of prochlorparazine 10 mg I/M was given if vomiting occurs once, nausea for 10 minutes or at the patient request. Rest other parameters as for example; heart rate, BP, respiration and SpO_2 were also recorded at same interval. Patients were carefully observed for any adverse effects like headache, flushing, drowsiness or any other symptoms.

STATISTICAL ANALYSIS:

The data was collected in a pre designed 'Data collection form'. All data was compiled and analyzed using't' test with the help of SPSS. The result was regarded as significant if $P<0.05$ or á Value of .05 with confidence interval 95%.

OBSERVATION & RESULTS:

All the observations were presented in a tabulated form. Observed parameters were expressed as mean±SEM.

The mean ages of Group-A and Group-B were 23.87 (± 0.96 SEM), 24.14 (± 0.67 SEM). The mean weight of Group-A, and Group-B were 62.63 (± 0.96 SEM) and 72.60 (± 0.93 SEM). The mean duration of surgery of Group-A and Group-B were 52.20 (±0.96 SEM) and 44.50 (± 0.61 SEM). All this data were subjected to't'test. The difference in two groups regarding age was not significant (P>0.05), but it was significant (P<0.05) regarding weight and duration of surgery.

Mean values of pulse rate at different occasions during surgery and 24 hours postoperative period were compared in two groups. The mean changes of heart rate per minute varied in group-A from 74.07 ± 0.40 SEM to 105.13 ± 0.93SEM, In group-B from 83.87 ± 1.42 SEM to 92.67 ± 1.31 SEM. Significant changes were observed at 2 min, 8 min, 10 min, 20 min, 30 min, 40 min, 50 min, 12 hour, 15 hours, 18 hours, 21 hours, 24 hours, (P < 0.05). In other occasions no significant changes were observed (P> 0.05).

Mean values of SBP at different occasions during surgery an 24 hours post operative period compared in two groups. The mean changes of SBP varied in group A from 94.10 ± 0.82 SEM to 119.00± 0.56 SEM, In group – B from 103.17 ± 1.93 SEM to 126.00 ± 1.89 SEM. Significant changes were observed at 4 min, 10 min, 20 min, 30 min , 40 min, 50 min, at 1st hour, 2nd hour, 3rd hour (p<0.05). In other occasions no significant changes were observed (P>0.05).

Mean values of DBP at different occasions during surgery and 24 hours post operative period were compared in three groups. The mean changes of DBP per minute varied in group-A 60.00 ± 0.00 SEM to 76.00 ± 0.91 SEM. In group-B from 67.67 ± 1.57 SEM to 82.83 ± 1.72 SEM. Significant changes were observed at 10 min, 20 min, 30 min, 40 min, 50 min, 2nd hr, 24th hr (p< 0.05). In other occasions no significant changes were observed (P>0.05) were compared in three groups. the mean changes of DBP perminute voried in group-Ave (P>0.05).e mean cha

Mean values of MBP at different occasions during surgery and 24 hours postoperative period were compared in two groups. The mean changes of MBP per minute varied in group-A from 71.53 ± 0.31 SEM to 90.60 ± 0.53 SEM, In group-B from 79.50 ± 1.57 SEM to 97.22 ± 1.61 SEM. Significant changes were observed at 10 min, 20 min, 30 min, 40 min, 50 min, 1st hr, 2nd hr, 3rd hr (P<0.05). In other occasions no significant change were observed (P> 0.05)

Mean values of SpO_2 at different occasions during surgery and 24 hours postpositive period were compared in two groups. The mean changes of SpO_2 per minute varied in group-A from 96.63 ± 0.13 SEM to 99.03 ± 0.08 SEM, In group – B from 97.30 ± 0.12 SEM to 97.40 ± 0.10 SEM. Significant changes were observed at 2 min, 4 min, 6 min, 30 min, 40 min, 50 min, at 9th hr, 15th hr, 18th hr, 21st hr, 24th hr (P<0.05). In other occasions no significant changes were observed (P>0.05).

Mean values of respiratory changes at different occasions during surgery and 24 hours post operative period were compared in two groups. The mean changes of respiratory rate per minute varied in group-A from 14.00 ± 0.14 SEM to 15.57 ± 0.10 SEM, In group B from 13.30 ± 0.20 SEM to 14.00 ± 0.26SEM. Significant changes were observed at 2nd min, 4th min, 6th min, 8th min, 10th min, 20th min, at 6th hr, 12th hr, 15th hr, 18th hr, 21st hr, 24th hr (P<0.05). In other occasions no significant changes were observed (P>0.05).

In the present study incidence of nausea and vomiting in group-A is one and in group-B is zero.

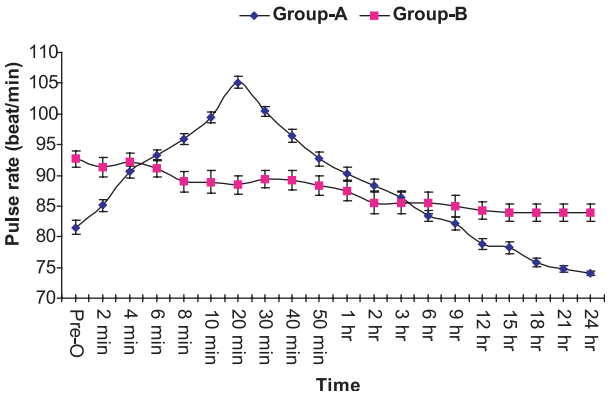

Fig.-1: *Intra operative and post operative pulse rate changes of different groups*

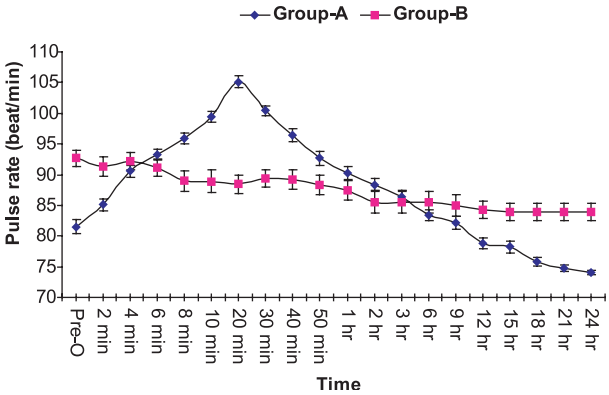

Fig.-2: *Intra operative and post operative mean blood pressure changes of different groups*

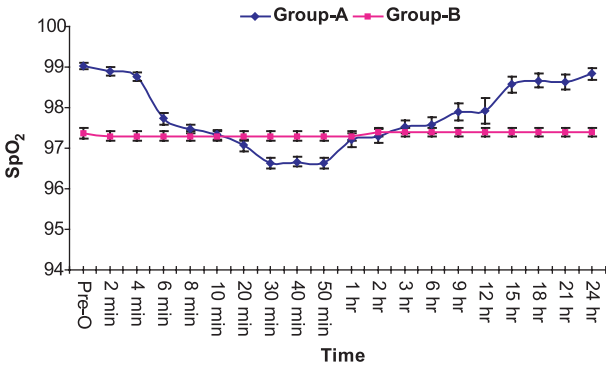

Fig.-3: *Intra operative and post operative SpO_2 changes of different groups*

DISCUSSION

Nausea and vomiting are common and sometimes dangerous side effects following surgery. Most of the incidence of nausea and vomiting occur during the first two hours of recovery from anaesthesia. The etiology of postoperative nausea and vomiting is multi-factorial. Many factor associated with anaesthesia and surgery may contribute to nausea and vomiting. In the present study concern factors are type of anesthesia, female patient and gynecological surgery. Incidence of nausea and vomiting is two to three times more in female due to changing endocrine environment which sensitize the brain stem emetic mechanism. During LUCS the regional anaesthesia as well as some traction of vagal innervated gut may play role in triggering emesis. The reported overall incidence of nausea and vomiting after gynecological surgery is 75%[12]. In lower uterine caesarean section the incidence of nausea and vomiting is relatively more then other gynaecological procedure[13, 14, 15]. The antiemetics are now mainstay of therapy to prevent PONV.

In the present study incidence of nausea and vomiting in group-A is one and in group-B is zero. In one study M Naguib[16] with his co-worker shows that prophylactic antiemetic treatment with ondansetron resulted in a lower incidence of PONV than with metochlopramide and placebo in a randomized double blind comparative study on laparoscopic cholecystectomy.

In our study the incidence of PONV occurred within first two hours after surgery in group-A but in rest of the period no nausea and vomiting occur which is similar with the study of Dr. Bridges[17]. It has some dissimilarity with the study of Dr. Naguib[18] and Dr. Dipasri Bhattacharya[19]. Most of the operations in previous study done under general anaesthesia. The aggravating factor for PONV in general anaesthesia are anaesthetics agents, distention by gas, per and postoperative use of narcotics. But in our study the possible aggravating factor are female patient hormonal changes, regional block, and vagal irritation. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting [20]. Sedatives& hypnotics are often used to control anticipatory nausea & vomiting [21]. Pregnancy & operation both causes anxiety. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting [22].

Prevention rather then treatment of postoperative nausea and vomiting should be the anaesthetist's aim. However, there is less agreed protocol as to which patients should receive preventive antiemetic therapy, but the relative indication for prophylaxis increases as the number of risk factors increase. Anti-emetics are occasionally used prophylactically to prevent postoperative nausea and vomiting, more often given postoperatively as treatment for postoperative nausea and vomiting. For prophylaxis to be acceptable, the drug must be effective, sufficiently long acting to last throughout the operative period, and especially without appreciable side effects[23].

The introduction of an effective well-tolerated antiemetic would allow the prevention of postoperative nausea and vomiting and its related consequences, particularly for high-risk patient. The efficacy of antiemetic therapy for the prevention or treatment of postoperative nausea and vomiting may be enhanced by combination therapy. It makes pharmacological sense to administer drugs, which act at different receptors. Presently, there is considerable interest in this and most studies have found combinations to be significantly more efficacious than a single drug[24].

No study is available on anxiolytic drug to prevent peroperative & PONV.

Regarding hemodynamic changes (Pulse, Blood pressure) SpO_2, respiratory changes, during operation and 24 hours post operative period in some occasions significant changes were observed ($P<0.05$) but in other occasions no significant changes occur.

No other adverse effect like headache, constipation and flushing during operation and 24 hours postoperative period were observed in this study.

Pain as well as commonly used analgesic pethidine may cause nausea and vomiting. For this reason postoperative control of pain we used ketorolac tromethamine as required instead of pethidine. We chose a single oral dose because it is easier to give one dose before operation. Involution of the uterus may not be affected by single dose of ketorolac. The study confirmed the previous study regarding the safety of the patient as side effects were mild.

Considering the above discussions, we have observed that Ondansetron reduces peroperative and postoperative nausea and vomiting. But addition of Alprazolum (an anxiolytic) to Ondansetron, the chance of nausea and vomiting is less.

However further work is required to compare between ondansetron and ondansetron plus alprazolum about their efficacy for prevention of PONV in LUCS under SAB.

CONCLUSION

As emesis is not caused by a single mechanism at a special site, remedies with various combinations of antiemetic and different mechanism of action may be promising.

In this study we have found that Ondansetron reduces peroperative and postoperative nausea and vomiting. But addition of Alprazolum (an anxiolytic) to Ondansetron, the chance of nausea and vomiting is less.

There was no evidence of any adverse side effects and whole of the operative period was smooth.

However, further work is required to compare the efficacy between ondansetron and ondansetron plus alprazolum for prevention of PONV in large scale.

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