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Efficacy of Ondansetron in the Control of Nausea and Vomiting During and After Caesarean Section under Spinal Anaesthesia

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Abstract: *Although much effort rightly has been placed on providing adequate pain relief after surgery, many physicians continue to view Post operative nausea and vomiting as a minor complication that posses little threat to the patient. In contrast many patients view post operative nausea and vomiting as more debilitating then the surgery itself. This complication is not only unpleasant and aesthetically displeasing to patients and their care givers, but, when severe, may also be associated with stress on suture lines, wound dehiscence, bleeding, electrolyte imbalance, dehydration and on rare occasions pulmonary aspiration of gastric contents. Post operative nausea and vomiting delays discharge and results in an increased use of resources which have financial implications. Yet this complication has been called the "big, little problem".Most antiemetics used currently have significant adverse effects such as sedation, dry mouth, dysphoria, extrapyramidal symptoms etc. Ondansetron, a selective 5-hydroxy tryptamine - 3 receptor antagonist is devoid of significant adverse effects and highly cost effective. It has been successfully used to control emesis in various clinical situations mainly during chemotherapy, radiotherapy and operative and postoperative conditions. Intra operative administration of ondansetron, single dose, during caesarean section significantly reduces the incidence of vomiting and the severity of nausea.*

I. Introduction

The first extensive description of postoperative nausea and vomiting was made by John Snow in 1848 in his book within 2 years of the demonstration of ether anaesthesia with W.T.G.Morton in 1846.

Although much effort rightly has been placed on providing adequate pain relief after surgery, many physicians continue to view Post operative nausea and vomiting as a minor complication that posses little threat to the patient. In contrast many patients view post operative nausea and vomiting as more debilitating then the surgery itself. This complication is not only unpleasant and aesthetically displeasing to patients and their care givers, but, when severe, may also be associated with stress on suture lines, wound dehiscence, bleeding, electrolyte imbalance, dehydration and on rare occasions pulmonary aspiration of gastric contents. Post operative nausea and vomiting delays discharge and results in an increased use of resources which have financial implications. Yet this complication has been called the "big, little problem".

Most mothers request and receive regional anaesthesia for caesarean section.Nausea and vomiting are important side effects both during and after caesarean section under spinal anaesthesia.They may distress the patient and decrease overall satisfaction with pain relief. Hence, the need to prevent nausea and vomiting during and after the surgery is very important.

Most antiemetics used currently have significant adverse effects such as sedation, dry mouth, dysphoria, extrapyramidal symptoms etc.

Ondansetron, a selective 5-hydroxy tryptamine - 3 receptor antagonist is devoid of significant adverse effects and highly cost effective. It has been successfully used to control emesis in various clinical situations mainly during chemotherapy, radiotherapy and operative and postoperative conditions. Intra operative administration of ondansetron, single dose, during caesarean section significantly reduces the incidence of vomiting and the severity of nausea.

II. Aim Of The Study

1. To evaluate the efficacy of single dose of Ondansetron 4 mg in the control of nausea, retching and vomiting during and after caesarean section under spinal anaesthesia.
2. To evaluate the safety of the drug by studying the Incidence of side effects.

III. Materials And Methods

This was a randomized, double blind, placebo controlled study conducted at the Coimbatore Medical college hospital,Coimbatore . A total of 50 Patients who were scheduled to undergo elective caesarean section were selected for the study. To be included in the study, these women were at full-term, 20-40 years of age ASA status 1 or 2, Without fetal distress, and able to understand and sign the informed consent form.

Since transmission of Ondansetron across the human placenta to the fetus and its effect on the neonate are still unknown, the drug was administered after delivery and Umbilical cord clamping.

Exclusion Criteria

Since the secretion of Ondansetron into colostrum / milk is still undetermined, women who have planned to breast feed were excluded. Exclusion criteria also included significant medical problems such as Cardiac, Gastrointestinal, hepatic, renal or known Psychiatric disease, Pregnancy induced hypertension, history of motion sickness, previous history of Post operative nausea and vomiting.

Informed consent was obtained from all the patients.

Method of Study:

The patients were randomised and divided into two groups each containing 25 patients to receive either Ondansetron 4 mg intravenously or placebo injection of Normal saline intravenously after delivery of the baby and Umbilical cord clamping. The Injections were loaded by an anaesthesiologist who was not involved in the assessment of the patients.

Preoperative Visit was done to reduce the anxiety of the patients. No Premedication was given to any of the patient.

Anaesthetic technique: Intrathecal Injection of 1.8-2ml (8-10mg) of hyperbaric bupivacaine 0.5% was used in all cases without any adjuvant like opioids which may initiate nausea and vomiting. Also the patient would be excluded if any opioid or an anaesthetic was required to control intra operative pain. After induction of spinal anaesthesia with the patient in lateral position. The uterus was tilted to the left, Oxygen was administed by plastic face mask and pulse oximeter placed. Vital signs (heart rate, Non invasive BP, respiratory rate) were recorded before anaesthesia and every 5 minutes there after. The preoperative values for the vital signs were the mean of three readings within 10 minutes of the spinal block. The sensory level as determined by pin prick was measured every 5 min.

One litre of lactated Ringer solution was administered within 20 min of the spinal block and another litre continued during surgery. More fluid was administered when required depending on the cardiovascular stability and clinical estimation of blood loss. To prevent hypotension ephedrine hydrochloride was given at dose of 6-12mg whenever necessary.

Hypotension was defined as decrease of the mean arterial blood pressure by 20%. When it occured it was treated promptly by additional fluids and intravenous increments of ephedrine.

In all patients the uterus was exteriorised during surgery. After delivery and umbilical cord clamping. 2ml containing either Ondansetron 4mg or 0.9% saline were injected intravenously. The study period continued for 24 hours. Following injectate to cover the period in the operating theatre, the recovery room and the immediate postoperative period. Before and at 15 min intervals following drug injection, the presence or absence and severity of nausea were recorded on a verbal analogue score extending from none = 0 to maximum nausea = 10.

The severity and frequency of vomiting, including retching were recorded before and after the injectate.

Post operative monitoring: The patients was assessed for nausea and vomiting at the time of recovery and then at 1 hour, 4 hours and 24 hours. Complaints of nausea and vomiting between the assessment period were recorded. All the patients were asked about other complaints like headache, dizzines, constipation etc.

Pain relief was given postoperatively with Inj Diclofenac im for all patients in both placebo and study group. Injection metoclopramide 10 mg iv was given as a rescue antiemetic for patients who had vomiting.

IV. Observation And Results

A total of 50 patients were taken for study. They were divided into two groups to receive either normal saline as placeho or Ondansetron. There were no significant differences between the two groups in terms of Age, Height, Weight or other parameters. The total duration of surgery was 45-60 minutes.

Summary Statistics Of Maternal Characteristics Mean (Sd)

	Placebo (n=25)	**Ondansetron (n=25)**
AGE (yrs)	24.24 (2.4)	24.12 (3.54)
WEIGHT (kg)	59.52 (3.74)	60 (4.18)
HEIGHT (cms)	159.84 (3.04)	160.08 (2.87)
GRAVIDITY	GI (7/25) 28% Multi (18/25) 72%	GI (9/25) 36% Multi (16/25) 64%
INITIAL MEAN BP (mm Hg)	92.17 (4.59)	92.8 (5.08)

The ranges of age, weight, Gravidity and initial mean BP were similar and statistically in significant.

Summary Statistics Of Surgical Variables Mean

	Placebo	**Ondansetron**
Surgical time (min)	42.2	45
Bupivacaine dose. In. mg.	8.96	9.28
Final sensory level	T4	T4
Incidence of Nausea and Vomiting before Injection	0	0
Hypotension Incidence	12%	8%
Ephedrine dose in mg	12	12

The incidence of nausea, retching and vomiting were observed in the 0-1hr, 1-4 hours, 4-24 hours the observation are as follows.

Number of patients with Nausea

Injectate	**0-1 Hours**	**1-4 Hours**	**4-24 Hours**
Placebo	9	3	1
Ondansetron	1	1	0

Prior to placebo or drug administration, the incidence of nausea and vomiting did not differ between the groups. Also, the time of occurence of nausea, retching and vomiting in regional anaesthesia for caesarean section, in contrast to general anaesthesia, is mainly intraoperative and in immediate post operative period. (In the 0-1 hr period 9 patients in the placebo group and 1 patient in the ondansetron group experienced nausea. In the 1-4 hours period, 3 patients in the placebo group and 1 patient in the Ondansetron group experienced nausea). 1 patient experienced nausea in the 4-24 hours period in the placebo group.

Number of patients with retching

Injectate	**0-1 Hours**	**1-4 Hours**	**4-24 Hours**
Placebo	7	3	0
Ondansetron	1	0	0

7 patients had retching in the placebo group in the first hour as compared to 1 patient in the Ondansetron group. In the immediate post operative period of 1-4 hours. 3 patients had retching in the placebo group and none in the ondansetron group. In the 4-24 hours period. None of the patient in both the groups had retching.

Number of patients with vomiting

Injectate	**0-1 Hours**	**1-4 Hours**	**4-24 Hours**
Placebo	6	2	0
Ondansetron	0	0	0

No patients had vomiting four hours after surgery 6 patients from the placebo group had vomiting in the first hour and 2 in the immediate post operative period. The incidence in the ondansetron group is none in the 24 hours period. Rescue antiemetic Injection metoclopramide 10 mg was given to patients who had vomiting.

24 Hours occurence of Nausea, Retching, vomiting

	Placebo	**Ondansetron**
Nausea	13	2
Retching	10	1
Vomiting	8	0

Table shows the overall occurance of nausea, retching and vomiting in 24 hours observation period. There is statistically significant difference among the placebo group and ondansetron group in control of nausea and vomiting during and after caesarean section under spinal anaesthesia as detected by chi square test by which the probability was < 0.01 which means that there is significant difference between the two groups.

The study results show that the

1. Incidence of Nausea was 52% in the placebo group and 8% in the ondansetron group.
2. Incidence of retching was 40% in the placebo group and 4% in the ondansetron group.
3. Incidence of vomiting was 32% in the placebo group and 0% in the ondansetron group.

In the 24 hours observation period the overall incidence of Nausea, retching and vomiting was 52% in the

placebo group and 8% in the Ondansetron group. A statistically significant difference exist between the two group as tested and proved by Chi square test by which the `P' value is < 0.01.

Thus a single dose of intraoperative intravenous administration of Ondansetron 4mg, after clamping of the cord, during caesarean section reduces the incidence of nausea retching and vomiting by 44%

V. Discussion

Nausea, retching, and vomiting are a common and distressing problem which are not only unpleasant and aesthetically displeasing to the patient and their care givers, but, when severe, may also be associated with other potentially dangerous and even lethal complication, such as pulmonary aspiration of gastric contents.

Intra operative nausea, retching, and vomiting during caesarean section under regional anaesthesia can be problematic and effort should be made to control them.

Chestnut DH, Owen CL et al studied the incidence of nausea and vomiting during epidural anaesthesia. They tried drugs like metaclopramide and droperidol and found them to be effective but with some side effects.

Pan PH, Moore CH et al compared the older drugs like droperidol with newer $5HT_3$ antagonist ondansetron and found it very effective and safe in caesarean section under epidural anaesthesia.

Our study showed ondansetron to be an effective antiemetic drug during the intra-operative and immediate post operative period for prevention and control of nausea, retching and vomiting during and after caesarean section under spinal anaesthesia. This confirms the beneficial effects of ondansetron as reported by Pan and moore et al in patients under going caesoran section under epidural anaesthesia and E.I Abouleish et al study similar to ours on which this study is based.

We have used a smaller dose of ondansetron, 4 mg instead of 8mg, based on the work of Pearman and Claybon. In our study we have excluded those patient with factors that might influence nausea and vomiting, for example opiods, antacids, history of gastro intestinal disease and morbid obesity.

The incidence of emesis in our study is higher than previously published in studies conducted by Kang YG et al and santos A Datta. The possible reasons for this difference are the

(1) Routine exteriorisation of the uterus
(2) Use of spinal Vs epidural anaesthesia as reported in other studies.
(3) The routine administration of oral antacids in most of them.
(4) The possibility of racial influence.

The time of occurence of nausea and vomiting in regional anaesthesia for caesarean section, in contrast to general anaesthesia is mainly intra operative, therefore the timing of anti emetic administration is important. After intravenous injection, the maximum effect of ondansetron is reached in 6-20 min and its half life is 3.5 hours in healthy volunteers as proved in studies conducted by Claybon et al and Fortney JY et al. Therefore, it seems preferable to inject the drug before the spinal block. However, since the transmission of ondansetron across the placenta and its effects on fetus and neonate are still unknown. We had to administer the drug after delivery and umbilical cord clamping. Also since it is unclear whether ondansetron is secreted into maternal milk, we had to include only those women who did not breast feed their efforts until 4 hours have elapsed from the surgery.

In conclusion, in women undergoing caesarean section under spinal anaesthesia, the intravenous administration of 4 mg ondansetron significantly reduced the incidence of vomiting and severity of nausea. It was also found to be very safe with only minimal adverse effects.

VI. Conclusion

Intraoperative Intravenous Injection of Ondansetron 4 mg is highly efficacious in reducing the incidence of vomiting and the severity of nausea during and after caesarean section under spinal anaesthesia.

It is also very safe with minimal side effects. Thus ondansetron stands out as a near ideal drug for reducing the incidence of nausea and vomiting along with more distressing and potentially lethal complications during caesarean section under spinal anaesthesia.

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