

A Randomized Double Blind Study On Antiemetic Effect Of Ondansetron And Glycopyrrolate During Cesarean Section

Syed Safiullah Ghori¹, Sabila Fatima¹, Pathan Amanulla Khan², Hafsa Khalid¹

¹Department of Pharmacology, Anwar-ul-Uloom College of Pharmacy, New Mallepally
Hyderabad 500016, Telangana, India

²Department of Pharmacy Practice, Anwar-ul-Uloom College of Pharmacy, New Mallepally
Hyderabad 500016, Telangana, India

*Corresponding Author E-mail: safiullahghori@gmail.com

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Abstract

In this randomized double blind study anti-emetic effect of ondansetron and glycopyrrolate was evaluated in parturients during cesarean section. In spite of number of antiemetics available, their effectiveness and fetal safety profile when used in parturients remains debatable. This comparative study of randomized double-blind was designed with an aim to compare the antiemetic effects of Ondansetron and glycopyrrolate during cesarean section. Twenty-four parturients scheduled for elective cesarean section was randomized to receive intravenous ondansetron 4 mg (Group O, n=24) or glycopyrrolate 0.2 mg (Group G, n=23) before spinal anesthesia. Data on postoperative episodes of hypotension, bradycardia and pain was measured till 10 h. The data was analyzed by using statistical analysis method. Statistically there was no significant difference between nausea and vomiting at all the study intervals between the two groups. There was no difference in patients of hypotension, but patients of bradycardia were significantly less in glycopyrrolate group than in ondansetron group, glycopyrrolate shows the incidence of dry mouth with more significant as compared to ondansetron group. The effect of glycopyrrolate in nausea and vomiting patients during cesarean section are comparable to ondansetron, but with an increased incidence of dry mouth. Glycopyrrolate has no effect on hypotension, but the incidence of bradycardia is significantly less.

KEYWORDS: Nausea, vomiting, cesarean section, glycopyrrolate, ondansetron

INTRODUCTION:

Pregnancy is the term used to describe the period in which a fetus develops inside a women's womb or uterus. The condition between conception till birth, during which the fertilized egg develops in the uterus. Pregnancy last for about 40 weeks or just over 9 months, as measured from the last menstrual period to delivery¹. Nausea and vomiting are most common symptoms of pregnancy which usually resolved by 16-20 weeks of gestation period. In 80% of patients it has been reported that nausea and vomiting lasts for the whole day. Therefore nausea and vomiting generally considered as a good sign of healthy pregnancy². The pregnancy is divided into three trimesters. The first trimester starts from the first day of the last menstrual period till the twelfth week of pregnancy. In this stage the egg and sperm combine and get attached to the uterine wall. This stage is very crucial for both the mother and fetus as the chances of miscarriage are high in this period. The second trimester begins from the thirteenth week till the twenty seventh weeks. During this period the mothers feel very active and the abdomen grows significantly. The third trimester begins from twenty eighth week till the delivery of baby. During this period the mothers experience swollen feet, frequent urination, difficulty getting up and walk, backache, insomnia, discomfort in the pelvis and fatigue, morning sickness^{3,4}. Cesarean section or C-section is used to deliver a baby through surgical incision made in the abdomen and uterus. This procedure is performed to save the life of fetus and sometimes to save the life of the women. This procedure is performed when a vaginal delivery is not possible or saved for both the baby and mother. A cesarean section generally takes 45 minutes to an hour by spinal block. The prevalence of cesarean section is generally agreed to be higher than needed in many countries⁵.

Anti-emetic drugs are used to prevent or relieve nausea and vomiting, so in the post-operative period it is not just an unpleasant and distressing experience but may be a major factor in upsetting the post-operative convalescence. A number of studies prevent emesis and continued research for newer drug to treat emesis. Anti-emetic drugs work by blocking one or more chemical messengers⁶. Ondansetron is most commonly used for the empiric treatment of nausea and vomiting. This drug is most commonly used for the prevention of post-operative nausea and vomiting. It is a potent anti-emetic agent, is a 5-hydroxytryptamine receptor 3 antagonist that blocks the effect of serotonin. It acts as both centrally and peripherally to prevent and treat nausea and vomiting. This drug is very effective that works by blocking the action of chemicals in the body that trigger nausea and vomiting. The women who are experiencing nausea and vomiting during pregnancy have been treated with this drug⁷. Glycopyrrolate is also known as glycopyrronium. This drug is widely used as a preoperative medication to inhibit salivary gland and respiratory secretions. It creates a sedative and amnesic effect by preventing the reflexion of bradycardia. This drug is mainly used as preoperatively as a muscarinic receptor antagonist. The incidence of this drug for nausea and vomiting has been minimized successfully during spinal anesthesia for cesarean section without affecting the neonatal outcome⁸.

MATERIAL AND METHODS

The present research work was done in Om Sai hospital, after taking Institutional Ethical Committee clearance, 24 patients scheduled for elective cesarean section under spinal anesthesia were randomized to receive Intravenous injection of ondansetron 4mg having volume of 2ml (Group O, n=24) or Glycopyrrolate 0.2 mg diluted to 2ml with normal saline (Group G, n=23) before spinal anesthesia. Drugs were prepared by an anesthesiologist based on the nature of study. At the time of drug administration both the investigator and patient were unaware⁹. At the time of surgery the patients were preoperatively injected to ranitidine intravenously at least 2 hours prior to the surgery. In the operation theater baseline heart rate, blood pressure and oxygen saturation of the patient were noted. ECG was monitored throughout the duration of surgery. Intravenous infusion of ringer lactate 500 ml was started to be over within 20-30 min. Spinal anesthesia was administered under all aseptic precautions in left lateral positions with 2.5ml of 0.5% hyperbaric bupivacaine.

After the delivery of baby oxytocin 5 units were injected with the infusion to last for 30-60 minutes. Post operatively patients were injected to diclofenac 75mg for every 8 hours till the patient is shifted to ICU. If the pulse saturation was dropped to 95% supplemental oxygen was administered till the delivery of baby. In the post-operative period the drug studied for 10 hours¹⁰ from the time of administration during the study interval of emesis. In dichotomous variable the incidence of nausea and vomiting was recorded at the end of intraoperative period and in the end the post-operative period of time 0-5 and 5-10 hours were recorded.

To measure the severity of emesis a visual analog scale of 10 cm was used for 0 being no emesis and for 10 being worst possible emesis. Subsequently for the treatment of nausea and vomiting¹¹ injection metoclopramide 10mg was given intravenously. A score of more than 3 was treated with tramadol 100mg injection. If there was no improvement injection pentazocine 30mg and promethazine 25mg was administered intravenously. Continuous data were expressed as mean and median range. Continuous evaluation of data was done by using t-test or Mann Whitney test, categorical data was done using chi-square test or Fishers exact test whichever was applicable depending upon the normality of data.

Statistical analysis:- Software used was Microsoft Excel and Epi Info 7 (Glycopyrrolate-neon Laboratories Ltd, Palghar, Thane, Ondansetron-intas Pharmaceutical Ltd, Ahmadabad). $P < 0.05$ were taken as statistically significant. Sample size calculation was done with significance level (alpha) of 5% and power of 80%. Sample size calculation was done taking into account the percentage decrease from actual incidence reported¹², in either of the experimental groups. Assuming that antiemetic was able to decrease the incidence of nausea by 25% over the actual incidence of reported nausea in cesarean section and taking difference between the two groups to be more than 33% to be clinically relevant, we calculated the sample size to be 10 per group. In order to compensate for drop-outs, we increased the sample size to 13 per group.

RESULTS:

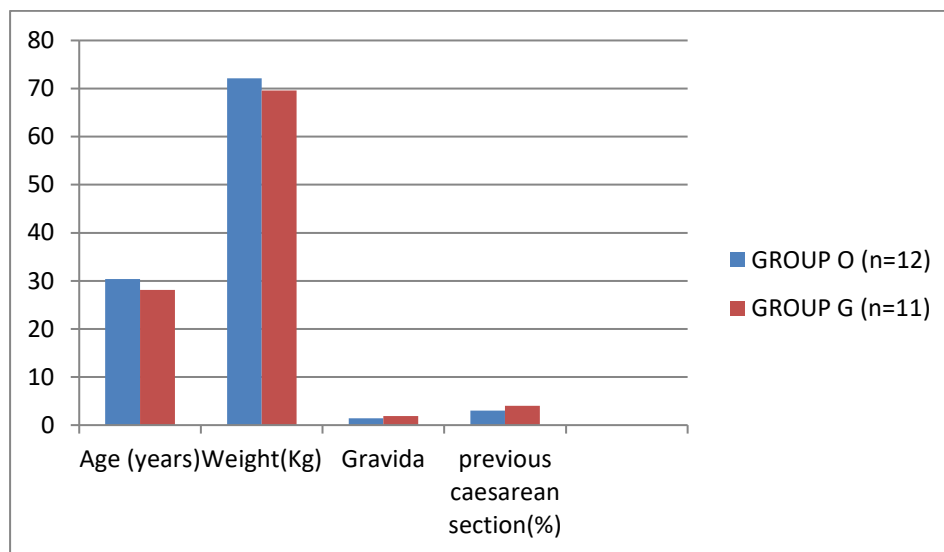
The number of women patients participated for ondansetron group was 12 and their mean age was recorded as 30.4 ± 4.21 , whereas in the glycopyrrolate group the women patients participated was 11 and their mean age was recorded as 28.14 ± 5.24 . Similarly, the weight of the ondansetron patients was 72.10 ± 11.5 and for glycopyrrolate the weight of the patients was found to be 69.58 ± 10.28 respectively.

The result of gravida for ondansetron patients was 1.4 and for glycopyrrolate it was found to be 1.9. Meanwhile the percentage of previous cesarean section in the patients of ondansetron group was 3 and for glycopyrrolate group it was 4 respectively. Demographic characteristics of all the patients were summarized in table-1 and in graph-1.

Table: I maternal demographic profile

CHARACTERISTICS	GROUP O (n=12)	GROUP G (n=11)
Age (years)	30.4±4.21	28.14±5.24
Weight(Kg)	72.10±11.5	69.58±10.28
Gravida	1.4	1.9
Previous caesarean section(%)	3	4

Graph: I Maternal demographic profile



A total 24 patients were studied for the incidence and severity of nausea and vomiting during Intra-operative and post-operative period with the time interval of 0-5 hours and 5-10 hours respectively was shown in table-2.

Table: II Incidence and severity of nausea-vomiting

Characteristics	Group O	Group G	Proportion difference
Intraoperative			
Nausea			
Incidence(%)	6	5	0.701
Severity	1	1	0.629
Vomiting			
Incidence(%)	2	2	0.768
Severity	1	0	0.790
Postoperative(0-5h)			
Nausea(%)			
Incidence(%)	2	2	0.795
Severity	0	0	0.690
Vomiting			
Incidence(%)	1	1	0.621

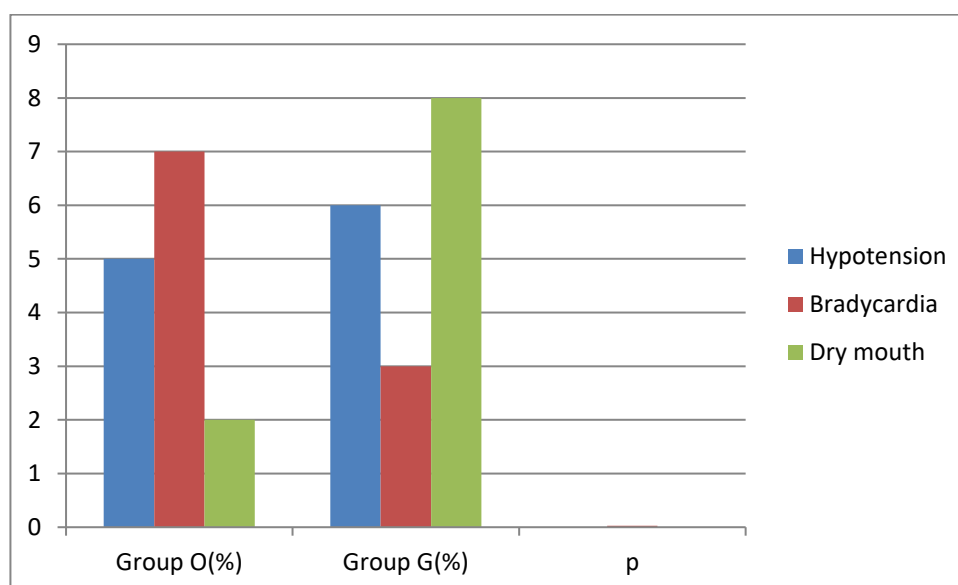
Severity	0	0	0.297
Postoperative(5-10h)			
Nausea			
Incidence(%)	4	2	
Severity	0	0	0.912
Vomiting			
Incidence(%)	2	0	
Severity	0	0	0.321

Furthermore it was observed that the incidence of vomiting was least in the patients of glycopyrrolate group. Hence, the result in glycopyrrolate group was found statistically less in ondansetron group. The most common laboratory findings were hypotension, bradycardia and dry mouth. Demographic characteristics were summarized in table-3 and graph-2.

Table: III Incidence of side-effects

Characteristics	Group O(%)	Group G(%)	Proportion difference
Hypotension	5	6	
Bradycardia	7	3	0.03
Dry mouth	2	8	0

Graph: II Difference between group-O and group-G



DISCUSSION:

Out of 24 patients 3 patients are dropped, one from each group of Ondansetron and Glycopyrrolate from the study to know the effect of partial spinal anesthesia and general anesthesia¹³. After the delivery of baby in one of the patient of glycopyrrolate, supplemented spinal anesthesia was injected with ketamine. The significant efficacy of bradycardia¹⁴ was less in group-G than in group-O. Hence it proves that glycopyrrolate decreases the incidence of bradycardia by 30% and increases the incidence of dry mouth by 52%. The proportion difference between the two drugs in hypotension patients had found to be no changed¹⁵.

The time interval between the two groups during postoperative pain scores and additional analgesic requirements has shown no significant results. Anticholinergics are shown to possess anti emetic properties. Atropine¹⁶ which is a tertiary amine unlike the glycopyrrolate contains quaternary ammonium. So, atropine is free to show its side effects in fetus, as it resists passage across placental barrier when administered to the mother. The action of anticholinergic inhibits the action of muscarinic receptors by decreasing its volume and free acidity of

gastric secretion by decreasing pharyngeal, tracheal and bronchial secretion. On the other hand ondansetron causes delayed ventricular prolongation without knowing fetal safety and associated cost issues.

The results confer to the results by Abouleish et al¹⁷. and Ure et al¹⁸. that showed ondansetron and glycopyrrolate was superior to placebo. However, Abouleish et al reported a high incidence of nausea and vomiting with Ondansetron, due to the difference in time of administration of the studied drug, as they administered the drug after the delivery of fetus.

On the other hand the incidence of hypotension is higher as they are contributed to emesis when compared with the present study. The significant anti emetic effect of glycopyrrolate was shown by Biswas et al¹⁹. when compared to dexamethasone and metoclopramide. The decrease in the study of nausea and vomiting was demonstrated by Yentis et al. A comparative study by Sahoo et al²⁰. which showed the decreased incidence of ondansetron in parturients in comparison to placebo due 5-HT antagonist blocking Bezold Zarisch reflex via 5-HT₃ receptor located in intracardiac vagal nerve endings. Kar et al. study reported decreased incidence of dry mouth due to proper preloading of parturient before intrathecal block when compared to the present findings of study which is higher in glycopyrrolate group.

CONCLUSION:

In conclusion the findings support the anti-emetic effect of glycopyrrolate to ondansetron during intra operative and post-operative patients undergoing cesarean section was increased due to the incidence of dry mouth. The combination of intravenous dexamethasone and intrathecal atropine has additive anti emetic effect after spinal anesthesia for cesarean delivery. The administration of glycopyrrolate intravenously before spinal anesthesia in cesarean section affects the control of prevention of nausea and vomiting and could be advantageous for both the mother and baby. So glycopyrrolate could be better than dexamethasone and metoclopramide.

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