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Original Article

Comparing the Effects of Midazolam and Ondansetron in Postoperative Nausea and Vomiting

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Abstract

Background: Nausea and vomiting after a cesarean section (CS) are among the common side effects that cause dissatisfaction among doctors. The aim of this study was to compare the effects of intravenous midazolam and ondansetron on the reduction of nausea and vomiting after spinal anesthesia in CS.

Methods: This double-blind clinical trial study was conducted on CS candidates who underwent spinal anesthesia (N = 80). After spinal anesthesia, the patients were randomly divided into two groups. Midazolam was administered to one group and ondansetron to the other group. The severity of nausea, the severity of vomiting, and the degree of satisfaction were recorded during surgery and recovery.

Results: No significant difference was observed between the two groups in terms of the severity of nausea and vomiting. In addition, the results demonstrated that the level of satisfaction in the midazolam group was higher than that in the ondansetron group, but this difference was not statistically significant ($P < 0.05$).

Conclusion: The results of this study showed that midazolam can reduce nausea and vomiting. On the other hand, the results confirmed that both ondansetron and midazolam can have the same effects on reducing nausea and vomiting.

Keywords: Midazolam, Ondansetron, Nausea and vomiting, Regional anesthesia

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Introduction

Many surgeries are performed every year for different therapeutic, diagnostic, and restorative purposes. One of these common surgeries is the cesarean section (CS) (1).

In abdominal surgeries such as CS, postoperative pain, nausea, and vomiting are the most common postoperative complications. This complication is found in more than 66% of patients who underwent spinal CS, and it is the main concern of 40–70% of patients undergoing surgery (2).

Nausea is expressed as nausea and the desire to vomit by the patient, and vomiting is defined as expelling the contents of the stomach from the mouth by force or belching (3,4). Postoperative nausea and vomiting (PONV) is one of the most common and important clinical complications that occurs after surgery and anesthesia. Therefore, PONV is considered an important cause of postoperative discomfort. The occurrence of nausea and vomiting leads to physical and psychological complications (3).

Nausea and vomiting can cause many problems for the patient after surgery. Problems such as patient dissatisfaction, the long stay of the patient in the post-anesthesia care unit, and, in rare cases, the cause of lung aspiration can be due to nausea and vomiting after surgery (5). Nowadays, drugs such as antihistamines, antidopaminergics, anticholinergics, phenothiazines, steroids, and even acupuncture are used to reduce nausea and vomiting after surgery (6).

Considering the extensive side effects of these drugs, today it is preferred to use serotonin antagonists, which are highly effective against nausea and vomiting, and their side effects are less than those of other common drugs for reducing nausea and vomiting after surgery (7).

Ondansetron is used to prevent and treat nausea and vomiting during and after surgery. It is a typical example of 5-HT3 antagonists, which are highly important in preventing nausea and vomiting caused by surgery and chemotherapy. It exerts its antiemetic effect by inhibiting peripheral and 5-HT3 receptors in the vomiting center and chemoreceptor activation zone, but exerts its effect mainly by inhibiting peripheral 5-HT3 receptors and vagal

afferent nerves (8).

Midazolam is an anti-anxiety drug from the anticonvulsant and muscle relaxant group with central action, which is part of the short-acting benzodiazepine group of drugs. This drug causes relaxation and forgetfulness by weakening the central nervous system (9), and studies show that midazolam and other benzodiazepines can reduce PONV in addition to reducing anxiety (10).

Based on research, midazolam produces its anti-nausea and vomiting effects by reducing dopaminergic activity, reducing 5-hydroxytryptamine, reducing gamma-aminobutyric acid activity, inhibiting dopamine secretion, and reducing adenosine absorption (11).

Choosing the right medicine to prevent nausea and vomiting during surgery is a serious challenge. Particularly when these drugs are used in pregnant women during spinal anesthesia, in this category of patients, in addition to preventing nausea and vomiting, drug side effects for the mother and baby are also an important issue. Spinal anesthesia is a suitable anesthesia method in which the injection of anesthetic drugs into the spinal canal causes analgesia in the lower limbs and part of the abdomen of the patient. This method is suitable for surgical analgesia in pregnant women because the patient receives less medication (3).

Therefore, there is a need for alternative drugs to treat nausea and vomiting, considering the side effects of metoclopramide and the relatively high cost of ondansetron. In addition, there may be situations where ondansetron and metoclopramide are unavailable or the patient does not respond to treatment or is sensitive to them. This study aimed to identify better options to replace these drugs so that patients receive the best medical services by receiving fewer drugs and spending less money.

Methods

Research Methods and Study Population Information

The present double-blind clinical trial was conducted at Hamedan Fatemieh hospital under the supervision of Hamedan University of Medical Sciences. All patients participating in this study (80 people) were pregnant women aged 14-40 who were candidates for CS. The samples were selected based on the existing method and then divided into two groups receiving midazolam (group A) and ondansetron (group B) using a random table (12).

Interventions

At the stage of entering the operating room, a history was taken of the patients, and every patient meeting the exclusion criteria was removed by the researcher.

The exclusion criteria included high-risk pregnancy, preeclampsia, a history of an underlying disease such as motion sickness, diabetes, a history of nausea and vomiting in the past 24 hours, digestive diseases such as esophageal-gastric reflux, hiatal hernia, and liver diseases. The other criteria were delayed gastric emptying, following the reduction of stomach movements following surgeries such as vagotomy and partial gastrectomy, gastric outlet obstruction, muscular dystrophy, obesity especially body mass over 40 years old, brain lesions, migraine, and drug sensitivity. The remaining exclusion criteria included severe anxiety (which causes the release of catecholamines and a decrease in the pH of the stomach and an increase in the volume of gastric fluids), a history of drug addiction, a history of neurological and mental diseases, and patients who are prohibited from spinal anesthesia.

Patients were under complete monitoring after being placed on the surgical bed; monitoring included the measurement of arterial blood pressure, heart rate, and arterial oxygen saturation. Then, the patients received 500 cc of intravenous crystalloid serum and were subjected to spinal anesthesia with spinal needle No. 25 in the sitting position using the Midline method from the L5-L4 or S1-L5 space.

About 10 mg of bupivacaine 0.5% plus sufentanil 2.5 µg were injected into their subarachnoid space by an anesthesiologist.

At this stage, the patient's position was supine and supported by an oxygen mask. The surgery started after the anesthesiologist confirmed the anesthesia level of the patient. After the babies were born, the patients were randomly divided into two groups.

Group A received midazolam (20 µg by weight), and group B received ondansetron (4 mg) intravenously. The injection drug syringe was prepared in advance by the researcher and provided to the anesthesiologist. The anesthesiologist did not know the type of injection drug.

10 mg of ephedrine was prescribed to treat patients whose blood pressure decreased by more than 20%. Also, 0/5 mg atropine was prescribed to patients whose heart rate decreased by more than 20%. About 2 L of crystalloid fluid was injected during the procedure for all patients. The number of times of nausea and vomiting and the amount of ephedrine and atropine used, along with the patient's vital signs, were checked and recorded in the checklist. After the surgery, the patients were transferred to the recovery room.

Data Collection

In the applied checklist, the patient's vital signs were recorded according to the control standard of patients under spinal anesthesia every 2 minutes in the first 6 minutes of receiving anesthesia, then every 5–15 minutes after anesthesia, and every 10 minutes until the end)13). The recovering patients were also subjected to cardiorespiratory monitoring, and the questionnaire information was completed by recovery nurses upon arrival, 10, 20, and 30 minutes after entering recovery.

The level of satisfaction of the patients was checked based on the visual analogue scale criterion, which includes a 10-cm-long horizontal bar, and the patient showed his nausea to the questioner on the zero to the maximum axis. Scores of 1–3, 4–7, and 8–10 indicate mild, moderate, and

severe nausea, respectively (14).

Patients' nausea and vomiting were measured using the nausea vomiting scale during recovery (Table 1). Metoclopramide (10 mg) was injected when the disease had a score of 2 (Table 1) or more (15).

Statistical Analysis

After completing the data collection stage, descriptive analysis was used to review the information. An independent t-test was employed for each group, and a t-test was utilized for the normal distribution of data. Finally, SPSS software (version 16) was used for statistical evaluations ($P < 0.05$).

Results

Demographic data showed that most of the examined patients were between 25 and 30 years old (55%). No significant difference was observed in the two studied groups in terms of demographic characteristics ($P > 0.05$, Table 2).

According to the vital signs of the patients, the mean systolic blood pressure and diastolic blood pressure, mean arterial blood pressure, arterial blood oxygen saturation, and heart rate, there was no significant difference between the midazolam and ondansetron groups ($P > 0.05$).

Based on the findings (Table 3), no significant difference was found in nausea and vomiting before and after spinal anesthesia or recovery in the midazolam and ondansetron groups ($P > 0.05$). Although the average level of satisfaction in the midazolam group was higher than that in the ondansetron group (Figure 1), this finding was not statistically significant ($P > 0.05$, Table 4).

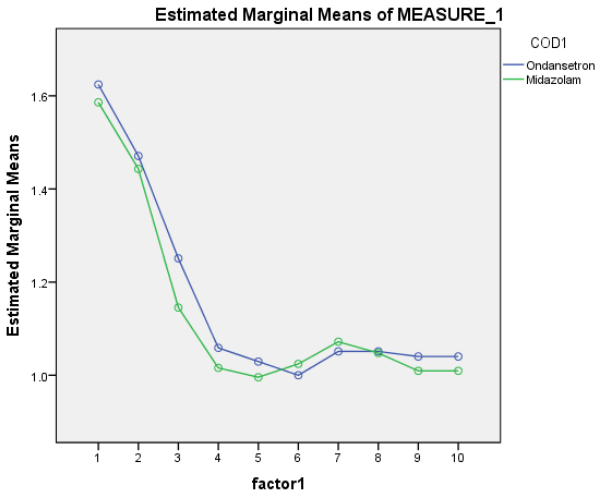

Figure 1. Patients' Satisfaction

Table 1. Score of Nausea and Vomiting

	Score
No nausea and no vomiting	0
Nausea without vomiting	1
Nausea and vomiting	2
Vomiting more than twice a minute	3

Discussion

Spinal anesthesia is one of the most common methods It can be used to control patients However, emergency surgery candidates do not fast It should be noted that this method can be dangerous It causes nausea and vomiting in patients, and following nausea and vomiting, it can increase the patient's dissatisfaction and requires a long stay of the patient in the post-anesthesia care unit, and in rare cases, it causes pulmonary aspiration. Prevention and control of this complication should be received special attention (16).

Nausea and vomiting are highly common in abdominal surgeries. Therefore, people who undergo CS are at risk of nausea and vomiting both because of the type of surgery and the type of anesthesia (17).

The findings of this comparative study regarding the effects of intravenous midazolam and ondansetron on the rate of nausea and vomiting after spinal anesthesia in CS revealed that both ondansetron and midazolam had the same effects on reducing nausea and vomiting in patients, which is consistent with the findings of Honarmand et al. However, in the study by Honarmand et al, it was found that using the combination of ondansetron and midazolam can be more effective than injecting each of these drugs separately (18).

In the study of Greene and Habib conducted with the aim of using midazolam to prevent anxiety before surgery and nausea and vomiting after surgery, the results showed that midazolam can reduce nausea and vomiting after surgery (19), which is in line with the results of the present study.

Considering that nausea and vomiting are among the annoying side effects of anesthesia, especially spinal anesthesia, which can affect many patients, especially those

Table 2. Average Age of Patients

Medicines	Age		
	Average	*df*	*P* Value
Midazolam	30.50	79	0.05
Ondansetron	29.37	77.44	0.061

Table 3. Average Nausea and Vomiting in Two Drugs, Ondansetron and Midazolam

Review Time	Average Nausea and Vomiting	
	Midazolam	Ondansetron
Before anesthesia	1.980	1.004
After anesthesia	1.552	1.333
Recovery	1.142	1.041
P value	0.007	0.005

Table 4. Average Patient Satisfaction

Medicines	Satisfaction		
	Average	*df*	*P* Value
Midazolam	3.15	78	0.081
Ondansetron	3.50	72.334	0.081

who undergo abdominal surgery, it is highly important to use the right medicine to control this complication. According to the findings of the present study, midazolam could also help prevent this complication. Considering that this drug is effective in controlling nausea and vomiting in patients' anxiety, it can be used to prevent complications after anesthesia.

Limitations of the Study

In this study, the number of examined patients was limited due to the investigation of a treatment center.

Conclusion

Both midazolam and ondansetron could reduce nausea and vomiting after surgery with almost the same effects. Due to the lower price of midazolam, its sedative effect, and its fewer side effects, this drug can be a suitable choice for controlling nausea and vomiting after the patient's operation in cases of ondansetron sensitivity or its unavailability.

Suggestions for Further Research

It is suggested that this study be re-examined with abdominal surgery patients. Because in this type of surgery, the possibility of complications such as nausea and vomiting is high, and the definitive results of this research can help reduce the consumption of unnecessary drugs.

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Authors' Contribution

Conceptualization: Nasim Alipor.
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Competing Interests

None declared.

Ethical Approval

The research protocols were under the supervision of the Ethics Committee of Hamadan University of Medical Sciences (Ethical No. 9603091549). All participants were informed about the research process and entered into this research with informed consent. At any time, none of the participants wished to continue cooperation and could withdraw from the study.

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