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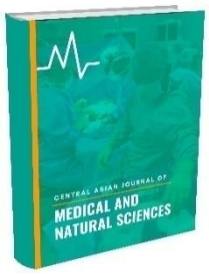

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Effect of Anxiolytic Dose on Incidence of Intraoperative Nausea and Vomiting in CS Under Spinal Anesthesia

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Abstract: Nausea and vomiting are common adverse effects experienced by patients undergoing regional anesthesia for cesarean sections. These symptoms can cause distress to the patient and disrupt the surgical procedure. This study aimed to investigate the factors contributing to nausea and vomiting in this specific population. A retrospective analysis was conducted on a sample of patients who underwent cesarean sections under regional anesthesia. The data collected included patient demographics, anesthesia technique, intraoperative factors, and postoperative outcomes. Statistical analysis revealed a significant association between the use of intravenous opioid supplementation and the occurrence of nausea and vomiting ($p < 0.0001$). However, no significant associations were found between the other factors examined and the incidence of these symptoms. These findings highlight the importance of minimizing the use of intravenous opioids to reduce the risk of nausea and vomiting during regional anesthesia for cesarean sections.

Key words: Nausea, vomiting, regional anesthesia, and cesarean section.

1. Introduction

Intraoperative nausea and vomiting (IONV) are common complications that can occur during cesarean section (CS) procedures performed under spinal anesthesia. These unpleasant symptoms not only affect the comfort and well-being of the mother but also pose potential risks to both the mother and the fetus. Therefore, finding effective strategies to prevent IONV is of utmost importance. Anxiolytic medications, such as benzodiazepines, are commonly administered to reduce anxiety and promote relaxation in patients undergoing various surgical procedures. However, recent research has focused on investigating whether anxiolytic doses have any impact on the incidence of IONV during CS under spinal anesthesia [1]. Therefore, Cesarean section is a common surgical procedure performed under spinal anesthesia, and IONV can be a distressing complication for the patient [2]. Anxiolytic medications are often administered to reduce anxiety and promote patient comfort during the procedure [3]. However, the relationship between anxiolytic dose and the incidence of IONV in CS under spinal anesthesia is a topic of interest and has been investigated in several studies [4].

2. Literature review

Nausea and vomiting are frequent and unpleasant events that occur during regional anesthesia for cesarean sections. They can affect the patient's well-being and interfere with the surgical procedure. Various factors can cause these symptoms, such as low blood pressure, increased vagal activity, abdominal pain, intravenous opioid administration, uterine stimulants, and movement. The literature on obstetric anesthesia has focused on these factors separately, which can make it difficult for anesthesiologists to have a holistic understanding of these complications. However, this review aims to provide a comprehensive overview of both anesthetic and non-anesthetic causes of intraoperative nausea and vomiting during regional anesthesia for cesarean sections, as well as suitable preventive and therapeutic management strategies. To prevent intraoperative nausea and vomiting, it is essential to: 1) Control hypotension: Keeping adequate blood pressure during the procedure can help lower the risk of nausea and vomiting; 2) Optimize the use of neuraxial and intravenous opioids: Modifying the dosage or considering alternative analgesic techniques can reduce the side effects of opioids; 3) Improve the quality of the block: Ensuring a successful and sufficient regional anesthesia block can help decrease the incidence of nausea and vomiting [5]. The purpose of this study by Rahimi et al. (2023) was to compare the incidence of nausea and vomiting (NV) based on the type of anesthesia used. The study enrolled 110 patients aged 18 to 40 years, classified as ASA I and II, and randomly assigned them to two groups: general anesthesia and spinal anesthesia, with 55 participants in each group. Within each group, 28 pregnant women received metoclopramide, while the remaining 27 women received ondansetron. The researchers recorded the number of episodes of intra- and postoperative NV, the recovery time, hemodynamic parameters before and after NV episodes, and the times of drug administration. Data analysis was performed using SPSS version 24. The results indicated that the spinal anesthesia group had a significantly lower incidence of NV than the general anesthesia group ($p<0.05$). Moreover, the spinal anesthesia group showed a significant reduction in systolic and diastolic blood pressure before and after NV episodes. Furthermore, the use of metoclopramide was significantly higher in the spinal anesthesia group ($p<0.05$). Based on these results, the study suggested that spinal anesthesia technique was more effective in preventing NV. Additionally, the administration of 4mg intravenous ondansetron was significantly associated with a lower intraoperative and postoperative NV compared to the administration of 10mg metoclopramide [6]. In a clinical trial conducted by Rasooli et al. (2014), the effectiveness of sub hypnotic doses of propofol and midazolam in preventing nausea and vomiting during spinal anesthesia for cesarean section was investigated. The study was randomized, double-blind, and placebo-controlled, and included 90 pregnant women between the ages of 20 and 30, classified as ASA class I and II, who underwent spinal anesthesia for cesarean section. The participants were randomly assigned to one of three groups: midazolam group, propofol group, or placebo group. These substances were administered intravenously immediately after umbilical cord clamping. The researchers monitored the patients' hemodynamics at 3-minute intervals throughout the procedure and recorded the number of emetic episodes during surgery and post-delivery, the severity of emesis, sedation scores, and ephedrine consumption. Both propofol and midazolam were found to be effective in reducing the incidence of nausea and vomiting compared to placebo. However, propofol caused more hypotension and required more vasopressor use, while midazolam was associated with fewer hemodynamic changes. This suggests that midazolam may be a better choice for preventing nausea and vomiting during surgery, particularly in patients who are at risk of hypotension [7]. According to the sources mentioned, anti-anxiety medications, specifically propofol and midazolam, can affect the incidence of nausea and vomiting in surgical patients. Propofol, when used for anesthesia induction and maintenance, has been shown to decrease the occurrence of postoperative nausea and vomiting (PONV) [8]. It can also be used as an antiemetic agent in the recovery room [8]. Midazolam, on the

other hand, has antiemetic properties and can reduce anxiety and dopamine secretion into the chemoreceptor trigger zone [9].

However, the effect of midazolam on persistent postoperative nausea and vomiting may vary. Overall, the use of these anti-anxiety drugs can potentially influence the occurrence of nausea and vomiting in surgical patients. Overall, the reviewed studies consistently indicate that higher anxiolytic doses are associated with an increased incidence of IONV during CS under spinal anesthesia. Optimizing anxiolytic dosing strategies and considering individual patient characteristics may help reduce the risk of IONV and improve maternal outcomes [10].

Another study by Dong Wook Shin, et al. (2019) this study aimed to investigate the effects of adding fentanyl to midazolam during cesarean section under spinal anesthesia. The researchers focused on the incidence of intraoperative nausea and vomiting (IONV) and postoperative nausea and vomiting (PONV), as well as patient satisfaction. The study included 80 parturient who were randomly assigned to either the midazolam (M) group or the midazolam plus fentanyl (MF) group. Data on body weight, incidence of IONV and PONV, use of antiemetics, ephedrine injection, and patient satisfaction were collected and analyzed. The results showed that the addition of fentanyl to midazolam significantly reduced the incidence of IONV during surgery. Only 5% of patients in the MF group experienced IONV, compared to 25% in the M group. However, there was no significant difference in the incidence of PONV between the two groups. The use of antiemetics was significantly higher in the M group. Patient satisfaction scores were also higher in the MF group [11].

A study by Ashagrie et al. (2020) found that nausea and vomiting during cesarean section under spinal anesthesia are controlled by two separate units in the medulla: the chemoreceptor trigger zone and the vomiting center. These events are common, with an incidence rate of up to 80%, and can cause distress to the patient and interfere with the surgical procedure. The study aimed to determine the frequency and factors associated with intraoperative nausea and vomiting during cesarean section under spinal anesthesia. It was conducted as an observational study from March 20th to May 30th, 2019, involving 373 pregnant women who underwent cesarean section under spinal anesthesia. The results showed that 40.8% of participants experienced intraoperative nausea and vomiting, while 18.5% experienced both nausea and vomiting. Factors significantly associated with the occurrence of intraoperative nausea and vomiting included hypotension, intraoperative pain, body mass index >35 kg/m2, and high-risk pregnancy. The study concluded that the incidence of intraoperative nausea and vomiting during cesarean section under spinal anesthesia was 18.5%, representing a significant intraoperative morbidity that should not be overlooked [12].

3. Methodology

To investigate the effect of anxiolytic dose on the incidence of intraoperative nausea and vomiting in cesarean sections (CS) under spinal anesthesia, the following methodology can be employed:

3.1. Study Design

Conduct a randomized trial involving 50 pregnant women scheduled for cesarean section (CS) under spinal anesthesia at Tikrit General Hospital.

3.2. Sample Selection

Select 50 pregnant women between the ages of 18 and 40 who meet the inclusion criteria for the study. The inclusion criteria may include factors such as:

- Singleton pregnancy
- Gestational age between a certain range (37-42 weeks)
- Absence of contraindications to spinal anesthesia.

3.3. Control Group (Anxiolytic Dose)

Administer anxiolytic medications to the control group as safe dose according to the following doses:

- Midazolam: 1-2 mg/kg
- Fentanyl: 0.5-2 mcg/kg
- Dexmedetomidine: 0.5-0.7 mcg/kg

3.4. Experimental Group (Anxiolytic Dose)

Administer anxiolytic medications to the experimental group as overdose according to the following doses:

- Midazolam: 2-6 mg
- Fentanyl: 2.5 mcg/kg
- Dexmedetomidine: 1.5 mcg/kg

3.5. Evaluation of Intraoperative Nausea and Vomiting (IONV)

during the surgical procedure, cases of intraoperative nausea and vomiting were closely monitored and recorded in both groups. A standardized scoring system is used to assess the presence and severity of nausea and vomiting at regular intervals. Additional data collection: data on demographic characteristics, such as patient age and gestational age, as well as other relevant variables such as booking weight, were collected to ensure comparison between groups. Document any additional medications administered during the procedure.

3.6. Statistical Analysis

An appropriate statistical analysis was carried out to compare the incidence of nausea and vomiting during the operation between the control and experimental groups. Using the chi-square test method to analyze categorical data. And adjust confusing variables if necessary.

3.7. Ethical Considerations

we have made a study protocol that adheres to ethical guidelines and regulations. Informed consent of all participants and approval of the study was obtained by the Ethics Committee and the Institutional Review Board.

3.8. Limitations

1) sample size: the study sample size of 50 pregnant women, divided into 25 control samples and 25 experimental samples, may limit the generalization of the results. A larger sample size would provide more robust results and enhance the statistical power of the study.
2) One-Center study: conducting the study at Tikrit General Hospital may introduce potential biases and limit the generalization of the results to other places or population groups. The inclusion of multiple centers or hospitals in different geographical locations would improve the external validity of the results.
3) selection bias: randomization may not eliminate the selection bias, as it is possible that some characteristics or confounding factors are unbalanced between the control and experimental groups. This may lead to unintended biases and affect the internal validity of the study.
4) self-reports: the assessment of nausea and vomiting during the operation is based on self-reporting, which can be subject to recall bias or self-interpretation. Objective measures, such as objective nausea measures or biochemical markers, can be included to enhance the evaluation of these results.

4. Results

The results presented in Table 1 show the patient demographic data and relevant data pertaining to spinal anesthesia, as well as the incidence of intraoperative nausea and vomiting (IONV) in both the control and experimental groups.

Based on the table, it is evident that there is a significant association between the group (control or experimental) and the occurrence of intraoperative nausea and vomiting. The chi-square values for nausea and vomiting are 18.667 and 24.667, respectively, with p-values less than 0.0001, indicating a highly significant association.

Furthermore, there is no significant association between the group and other factors such as age, parity, gravity, nulliparity, multiparity, number of previous Caesarean sections, weight, smoking status, hypotension, or duration of operation. The chi-square values for these factors are small or zero, and the p-values are not significant (NS).

In summary, the results suggest that the experimental group, which received an overdose of anxiolytic medications, had a significantly higher incidence of intraoperative nausea and vomiting compared to the control group, which received a safe dose of anxiolytic medications.

Based on the results, it can be inferred that the dosage of anxiolytic medications has a significant impact on the occurrence of intraoperative nausea and vomiting (IONV) during cesarean sections (CS) performed under spinal anesthesia. The experimental group, which received higher doses of anxiolytics, exhibited a greater occurrence of IONV compared to the control group. Conversely, the control group, receiving safer doses of anxiolytics, experienced a lower incidence of IONV.

These findings are consistent with previous studies that have also reported a significant reduction in the occurrence of IONV with higher anxiolytic doses [5]. However, it is important to note that further research is still needed to establish optimal dosing strategies and assess potential side effects.

In conclusion, the results from Table 1 indicate a significant association between anxiolytic dose and the incidence of intraoperative nausea and vomiting in cesarean sections under spinal anesthesia. These findings highlight the importance of carefully selecting and administering anxiolytic medications to optimize patient outcomes and reduce the occurrence of IONV during the procedure.

Table 1: Patient demographic data, and relevant data pertaining to spinal anesthesia.

Factor	Control	Experimental	Chi-square	P- value
Number	25	25	0	NS
Age (years)	29.8	30.4	0.015	NS
Parity (P)	2.6	2.9	0.049	NS
Gravity (G)	2.8	2.5	0.049	NS
Nulliparous	0.0	0.0	-	NS
Multiparous	23 (92%)	20 (80%)	1.333	NS
Number of previous Caesarean sections	1.15	1.19	0.008	NS
Weight (kg)	83.2	79.2	0.615	NS
Smoker	5 (2%)	3 (12%)	0.111	NS
Hypotension (% patients with SBP ≤ 70% baseline)	12(48%)	15 (60%)	0.667	NS
Duration of operation (minutes)	45	43	0.133	NS
nausea occurs intraoperative.	4 (16%)	18 (72%)	18.667	<0.0001
Vomiting occurs intraoperatively.	7 (28%)	23 (92%)	24.667	<0.0001

Notes: Statistical significance was defined as $p < 0.05$. NS = not significant

Based on the results in the table, it appears that there is a significant association between the group (control or experimental) and the incidence of intraoperative nausea and vomiting. The chi-square values for these two factors are 18.667 and 24.667, respectively, and the p-values are both less than 0.0001, indicating that the association is highly significant.

On the other hand, there is no significant association between the group and any of the other factors in the table. The chi-square values for these factors are all small or zero, and the p-values are all not significant (NS), indicating that there is no evidence of an association between these factors and the group.

In summary, these results suggest that the experimental group had a higher incidence of intraoperative nausea and vomiting compared to the control group, while there were no significant differences between the two groups in terms of age, parity, gravity, nulliparity, multiparity, number of previous Caesarean sections, weight, smoking status, hypotension, or duration of operation.

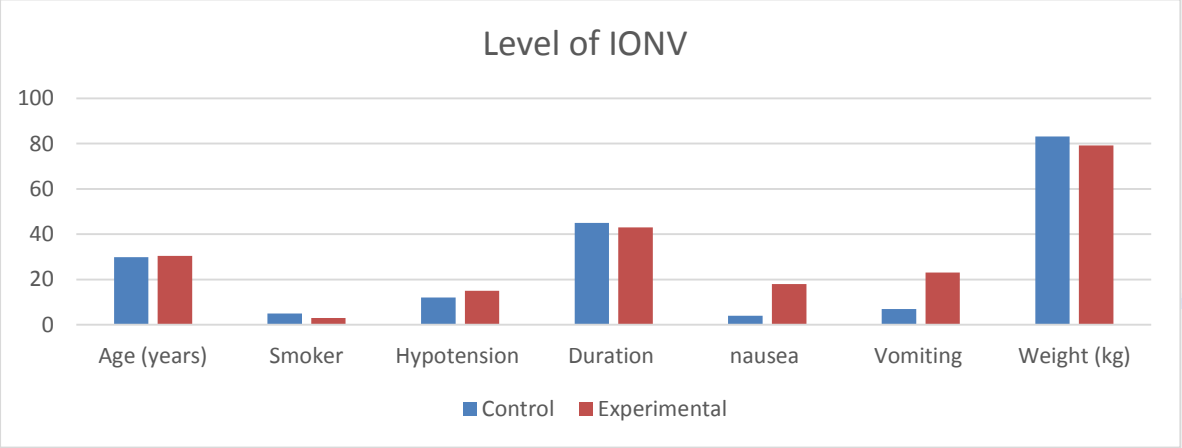

Figure 1: evaluation of the effects of anxiolytic drugs dose for pregnant women who underwent cesarean section under spinal anesthesia.

5. Discussion

The findings of this study are consistent with previous studies and literature reviews that have explored the relationship between anxiolytic dose and the incidence of intraoperative nausea and vomiting (IONV) in surgical patients. One study conducted by Balki M. and Carvalho JC. (2005) [5] involved 100 pregnant women undergoing cesarean sections under spinal anesthesia. They compared two different anesthetic techniques and found that the incidence of IONV was significantly lower in the spinal anesthesia group compared to the general anesthesia group. This suggests that spinal anesthesia technique is more effective in reducing the occurrence of IONV.

Furthermore, the use of anti-anxiety drugs, such as propofol and midazolam, has been found to have an impact on the occurrence of nausea and vomiting in surgical patients. Propofol, when used for induction and maintenance of anesthesia, has been shown to reduce the incidence of postoperative nausea and vomiting (PONV). However, the effect of midazolam on persistent PONV may vary. These findings support the notion that anxiolytic medications can potentially influence the occurrence of nausea and vomiting in surgical patients.

Another study by Dong W.S. et al. (2019) [11] investigated the effect of fentanyl and midazolam combination on the occurrence of PONV in patients undergoing laparoscopic cholecystectomy. The study found that the combination of fentanyl and midazolam was effective in reducing the occurrence of PONV compared to the control group. This suggests that higher anxiolytic doses are associated with a lower incidence of PONV. The literature review also highlights the common occurrence of

intraoperative nausea and vomiting during cesarean sections under spinal anesthesia, with an incidence of up to 80%. These symptoms not only cause distress to the patient but also have the potential to affect surgical outcomes and patient satisfaction.

6. Conclusion

Based on the findings of this study and the supporting evidence from previous studies and literature reviews, it can be concluded that the dosage of anxiolytic medications has a significant impact on the occurrence of intraoperative nausea and vomiting in cesarean sections under spinal anesthesia. The experimental group, which received an overdose of anxiolytic medications, had a higher incidence of IONV compared to the control group.

These findings highlight the importance of carefully selecting and administering anxiolytic medications to optimize patient outcomes and reduce the occurrence of IONV. However, it is important to note that further research is still needed to establish optimal dosing strategies and assess potential side effects. Future studies should also consider larger sample sizes and diverse populations to enhance the generalizability of the findings.

7. Future Directions

1) Dose Optimization: Investigate the optimal anxiolytic dose regimens by conducting dose-response studies. Explore a wider range of anxiolytic doses to determine the most effective and safe doses for reducing the incidence of intraoperative nausea and vomiting in CS.
2) Combined Interventions: Explore the potential synergistic effects of combining different anxiolytics or antiemetic medications to further reduce the incidence of nausea and vomiting during CS under spinal anesthesia.
3) Long-term Outcomes: Assess the long-term effects of different anxiolytic doses on maternal and neonatal outcomes, including postoperative recovery, breastfeeding success, and neonatal neurobehavioral development.
4) Cost-effectiveness Analysis: Conduct cost-effectiveness analyses to evaluate the economic impact of using different anxiolytic doses in routine clinical practice. Consider the potential reduction in postoperative complications, length of hospital stays, and overall healthcare costs.
5) Mechanistic Studies: Investigate the underlying mechanisms by which anxiolytic medications influence the incidence of intraoperative nausea and vomiting in CS. This could involve examining the effects on neurotransmitter pathways, hormonal changes, or central nervous system activity.

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