Journal of
Pain Management & Medicine

Research Article Open Access

Antiemetic Effects of Midazolam and Propofol during Spinal Anesthesia on Women Undergoing Elective Cesarean Sections

Zabetian H[2], Kalani N[2], Khalili A[1]*, Sahraei R[2] and Radmehr M[2]

[1]*Medical Ethics Research Center, Jahrom University of Medical Sciences, Jahrom, Iran*
[2]*Department of Anesthesiology, Jahrom University of Medical Sciences, Jahrom, Iran*
[3]*Departmet of Obstetrics & Gynecology, Jahrom University of Medical Science, Jahrom, Iran*

Abstract

Background and objective: Nowadays, Cesarean is the most common surgery among women, and anesthesia is an elective technique in these surgeries. Unfortunately, spinal anesthesia in Cesarean section is associated with high incidence of nausea and vomiting. The aim of this research is the comparison of the effects of propofol and midazolam on nausea and vomiting in pregnant women undergoing elective Cesarean section with spinal anesthesia.

Methodology: We conducted a double-blind clinical trial recruiting 42 patients aged 15 years to 35 years with ASA class I and II who were undergoing Cesarean section that divided into two groups. Both groups were treated with 7 ml/kg of Ringers solution. Patients had spinal anesthesia with 65 mg of 5% lidocaine and then 1.5 cc midazolam and 2 cc propofol were intravenously administered to patients in Group A and Group B, respectively. Also, after the baby was born, Apgar score was measured at 1 minute and 5 minutes after birth. The obtained data were analyzed using repeated measurement and chi-square tests in SPSS software. Level of significance was determined to be $p<0.05$.

Findings: Comparison of the antiemetic effects of propofol and midazolam in pregnant women after elective caesarean section showed that in all minutes, except in the thirtieth minute, nausea and vomiting were higher in the midazolam group and a significant difference was observed between two groups in this regard ($p=0.96$).

Results: Administration of propofol immediately after spinal anesthesia was more effective in reducing nausea and vomiting, compared to administration of midazolam.

Keywords: Midazolam; Propofol; Spinal anesthesia; Cesarean; Nausea and vomiting

Introduction

As general anesthesia for Cesarean section is associated with major complications and problems such as the inability for intubation and aspiration of gastric contents into the airways and increase mortality of mothers in pregnant women, to reduce these complications, local anesthesia has been used frequently in recent decades [1]. Benefits of local anesthesia for Cesarean section include decreasing risk of aspiration, reduced mortality related to difficult intubation, reduced surgery related bleeding, and decreasing need for taking medicines suppressing the central nervous and respiratory systems transferred through the placenta to the baby [2]. In spite of applying the necessary treatments, nausea and vomiting are still one of the most common complications of anesthesia which cause the patients undergo an unpleasant experience during surgery [3]. Hypotension is one of the factor that contributed to nausea and vomiting after spinal anesthesia (systolic pressure less than 80), anesthesia above the fifth thoracic vertebra, adding vasoconstrictors to local anesthesia [4] vagus stimulation, psychological factors, and stimulation during surgery such as push on the abdomen for fetus delivery, visceral manipulation [5,6]. Nausea and Vomiting during surgery is associated with the risk of viscera damage, increased duration of surgery, and the risk of aspiration, patient's stress, and disruption in surgery process [6]. Different medications are traditionally used for relieving this condition; the most common of them is metoclopramide. However, extrapyramidal effects of them have caused concerns and made physicians cautious in prescribing it [7,8]. Propofol is an intravenous anesthetic, which is involved in induction and continuity of anesthesia. Recently, antiemetic effects of this medication in low and sub-hypnotic doses has been reported and taken into account [5,8,9]. Midazolam (generally benzodiazepines) is the most common medication used in premedication before surgery [10]. The most important effect of these treatments includes sedative-hypnotic function and amnesic properties. In addition, benzodiazepines act as an anticonvulsant and are commonly used for treatment of seizure. At higher doses, these substances show anti-anxiety and muscle-relaxing effects. In addition to anti-anxiety effect, they are effective medication for reducing nausea and vomiting caused by surgery [11,12]. Due to the high frequency of Cesarean sections in Iran and the harmful effects of vomiting during and after this operation, the present study aims to compare the effects of propofol and midazolam on nausea and vomiting in pregnant women undergoing elective Cesarean section with spinal anesthesia in order to identify the most effective treatment to control nausea and vomiting.

Methodology

This double-blind clinical trial with the code IRCT2014031717039N1, after approval by the Research Council of Jahrom University of Medical Sciences and the Ethics Committee, was carried out on 42 patients aged 15 years to 35 years with ASA class I and II (A) who were undergoing cesarean section that both groups are elective schedule and also none of them had emergency indications (most of them were previous section and rest of them had requested section). The

***Corresponding author**: Khalili A, Department of Obstetrics & Gynecology, Jahrom University of Medical Science, Jahrom, Iran, E-mail: azadehkhalili80@yahoo.com

Received July 27, 2016; **Accepted** August 31, 2016; **Published** September 19, 2016

Citation: Zabetian H, Kalani N, Khalili A, Sahraei R, Radmehr M (2016) Antiemetic Effects of Midazolam and Propofol during Spinal Anesthesia on Women Undergoing Elective Cesarean Sections. J Pain Manage Med 2: 116.

statistical population included American Society of Anesthesiologists pregnant women referred to Shahid Motahari University of Jahrom and had an elective Cesarean section spinal anesthesia. The 42 pregnant women were selected as the sample using simple random sampling method and then were randomly divided into two groups of 21 (midazolam and propofol. Exclusion criteria were; history of mental and physical illnesses, receiving any painkiller medications or anti-depression, hypnotic, and psychotropic medications, overweight women more than 100 kg, using any drugs or alcohol. ICU care after surgery, allergic history of propofol or midazolam, additional treatment requires and bad conditions during surgery, high level anesthesia and decrease patient's breathing, class 3 or class 4 of anesthesia (according to American Society of Anesthesiologists), and hemodynamic disorders. Before entrance to the operation room, patients did not receive any medication. At the start of study, the patients recognized about the research, reasons, and possible complications and then they endorsed a written consent, then patient prepare for operation and installation of electrocardiography leads on chest, oximetry pulse, and sphygmomanometer cuffs on arms, blood pressure and heart rate of patients were recorded from the monitor. Both groups were received 7 ml/kg/min of Ringer's solution to increase preload and preventing spinal related hypotension. Before administration of the two desired medications (midazolam or propofol), the first blood pressure, and heart rate of the patients were recorded and then spinal anesthesia was applied with 65 mg of 5% lidocaine. In the next step, 1.5 cc midazolam and 2 cc propofol were intravenously administered to patients in Group A and Group B, respectively. At 1, 3, 5, 10, 15, 30, and 60 minutes after spinal anesthesia, nausea and vomiting grade (based on the number of vomiting and the number nausea sensation), blood pressure, heart rate, and respiratory rate were measured and recorded. Also, after the baby was born, Apgar score was measured at 1 minute and 5 minutes after birth. In case of lowered blood pressure during surgery, ephedrine was used. At the end of surgery, patients were kept at least one hour at recovery unit. The patients and the follow-up examiner were not aware of the type of administered medications (midazolam or propofol) (Table 1).

Statistical analysis

Independent samples tests was used for comparison effect of midazolam and propofol to preventing nausea and vomiting during caesarean section. Confidence interval was considered 95% and significance assigned to p-value <0.05. All statistical analyses were performed using the statistical package for Social Sciences version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

In this study, 42 pregnant women were equally divided into two groups of A (treated with midazolam) and B (treated with propofol).

In this part, the difference between two experimental groups in separate minutes will be studied and shown in bar-charts and graphs:

Age		
15-20	5	11.9
21-25	16	38
26-30	15	35.7
31-35	6	14.4
Weight		
50-65	9	21.4
66-80	25	59.6
80-95	8	19

Table 1: Demographic criteria

To study the relationship between nausea and vomiting in two groups in the first minute, in the midazolam group, 2 subjects (9.5%) had vomiting and 2 subjects had nausea, while these figure in the propofol group were zero. This revealed two significant difference between the experimental groups (p=0.036) (r=0.32) (Table 2).

In the third minute, 6 subjects in the midazolam group had vomiting (28.6%) and one subject in the propofol group had nausea (4.8%), which shows a significant difference between these two groups (p=0.053) (r=0.30). In the fifth minute, in the midazolam group, 2 subjects (9.5%) had vomiting and one subject (4.8%) had nausea, while in the propofol group only one subject (4.8%) had vomiting. This suggests a significant relationship between the experimental groups (p=0.29) (r=0.16). In the tenth minute, in the midazolam group one subject (4.8%) had vomiting and one subject (4.8%) had nausea, while these figures in the propofol was zero. This indicates a significant relationship between the experimental groups (p=0.15) (r=0.22). In the fifteenth minute, 2 subjects (9.5%) in the midazolam group had no vomiting, while no subject in the propofol group had vomiting or nausea. This shows a significant relationship between two studied groups (p=0.15) (r=0.22) (Table 3).

In the thirtieth minute, one subject (4.8%) in the midazolam group had nausea and 2 subjects (9.5%) in the propofol group had vomiting. Indicating a significant relationship between these two groups (p=0.59) (r=0.028). In the sixtieth minute, in the midazolam group, one subject had vomiting and one subject had nausea, while in the propofol group only one subject had vomiting. This suggests a significant difference between these two groups (p=0.96) (r=0.008) (Table 4).

Repeated measurement (analysis of variance with repeated measures) was used for studying the trend of changes in blood pressure (systolic) in two experimental groups at 1, 3, 5, 10, 15, 30, and 60

	n/v			
	Nausea	**Vomiting**	**No**	**Total**
Group A Midazolam	2	2	17	21
	9.50%	9.50%	81.00%	100.00%
Group B Propofol	0	0	21	21
	0.00%	0.00%	100.00%	100.00%

Table 2: Comparison of nausea and vomiting between midazolam and propofol groups in the first minute.

	n/v minute 15		
	Vomiting	**No**	**Total**
Group A Midazolam	2	19	21
	9.50%	90.50%	100.00%
	100.00%	47.50%	50.00%
Group B Propofol	0	21	21
	0.00%	100.00%	100.00%

Table 3: Comparison of nausea and vomiting between midazolam and propofol groups in the fifteenth minute.

	n/v 60 minute			
	Nausea	**Vomiting**	**No**	**Total**
Group A midazolam	1	1	19	21
	4.80%	4.80%	90.50%	100.00%
Group B propofol	0	1	19	21
	0.00%	4.80%	90.50%	100.00%

Table 4: Comparison of nausea and vomiting between midazolam and propofol groups in the sixtieth minute.

minutes. According to the results of this test, blood pressure changes in above-mentioned minutes show a significant difference in each group (p=0.001) but no significant difference was found between two groups in this regard (p=0.42).

To study the trend of changes in blood pressure (diastolic) in the two groups at 1, 3, 5, 10, 15, 30, and 60 minutes, by using analysis of variance, it was found that there is a significant difference between above-mentioned minutes in terms of mean and standard deviation values of diastolic blood pressure in each group (p=0.001). While no significant difference was observed between two groups (p=0.37).

Changes in heart rate in both groups were analyzed using analysis of variance with repeated measures. According to the mean and standard deviation values, it can be concluded that heart rate changes in each group show a significant difference between the studied points (from 1 to 60 minutes) (p=0.001), but no significant difference was found between two groups (p=0.37). Analysis of variance with repeated measures was also applied for evaluation of trend of change in O_2 saturation in the studied groups. The results of this test showed that there is no significant difference between the studied points (from 1 to 60 minutes) in terms of O_2 saturation changes (p=0.64), and also there is no significant difference between midazolam and propofol groups in this regard (p=0.63). The difference of respiratory rate changes between two groups was studied using analysis of variance. Mean and standard deviation values show that there is no significant difference between various studied minutes in each group in terms of respiratory rate changes (p=0.40) and also no significant difference was observed between two groups in this regard (p=0.37).

The following figure shows Apgar difference in babies in both groups which was studied using analysis of variance with repeated measures. Mean and standard deviation values show that there is no significant difference between check points (1, 3, 5, 10, 15, 30, and 60 minutes) (p=0.08) and also no significant difference was found between the studied groups in this regard (p=0.33) (Figure 1).

Discussion

In this research, 42 pregnant women undergoing elective Cesarean section with spinal anesthesia in Shahid Motahari Hospital of Jahrom were studied. Comparison of the antiemetic effects of midazolam and propofol in pregnant women after Cesarean section showed that at all minutes, except the thirtieth minute, nausea and vomiting were higher in the midazolam group and a significant difference was observed between two groups in this regard. Similar studies have been reported from previous studies. Khezri et al. [13], in a study, showed that 0.5 mg/kg of propofol is more effective than metoclopramide in prevention of nausea and vomiting after Cesarean section. Fujii and Numazaki [8] also showed that low dose of propofol is more effective than metoclopramide in reduction of nausea and vomiting after tonsillectomy in children. In addition, the results of a study conducted by Pierre et al. [14] corroborate the beneficial effect of low doses of propofol in the prevention of vomiting after surgeries. In a study conducted by Numazaki and Fujii [9] on women who underwent spinal anesthesia for Cesarean section, no significant difference was found in antiemetic effects of propofol, droperidol, and metoclopramide, although propofol showed better performance in controlling severe nausea in patients. The results of the present study are consistent with the findings of most previous studies. The results of a study conducted by Ahsan et al. [15], indicated that vomiting and nausea were significantly lower in patients treated with propofol then in those treated with sodium thiopental. In the study, conducted by Sade et al. [16] on prevention of vomiting and nausea after surgery by administration of sub-hypnotic doses of propofol (20 mg bolus and 1 mg/kg/h infusion), midazolam (1 mg bolus and 2 mg/kg/h infusion), and saline (2 cc IV). It was shown that the patients treated with propofol and midazolam had less vomiting and nausea than those treated with normal saline. However, no significant difference was found between efficiency of propofol and midazolam. Tarhan et al. [17] showed that antiemetic effects of midazolam and propofol are similar and there is no significant difference between them in this regard. Most previous studies have concurred on the point that propofol leads to reduced vomiting and nausea caused by surgery. In the present study, a significant reduction occurred in vomiting and nausea after Cesarean section in pregnant women in the propofol group. Since vomiting and nausea frequently occurs in the recovery room after Cesarean section, administration of propofol reduce this condition.

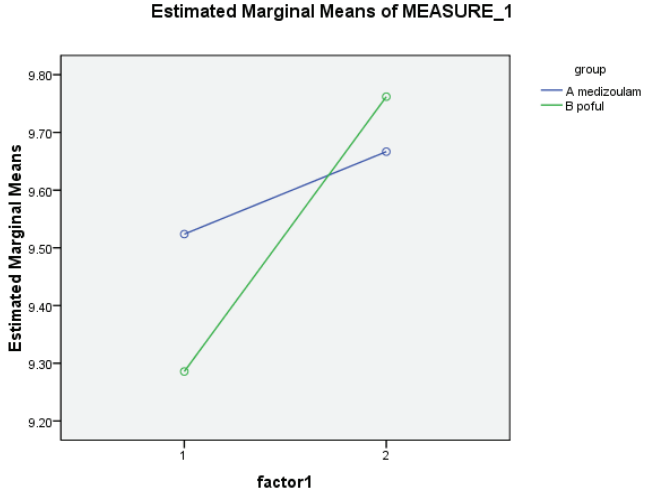

Figure 1: Comparison of trend of changes in babies Apgar in at 1 minute and 5 minutes after birth in the midazolam and propofol groups.

Conclusion

Propofol administration immediately after spinal anesthesia was more effective in reduction of vomiting and nausea compared to midazolam. Therefore, it is recommended that 20 mg (2 cc) propofol to be administered to pregnant women after Cesarean section in order to reduce vomiting and nausea in these patients. In addition, further studies are recommended to be conducted on more subjects in order to achieve a more accurate statistical evaluation.

References

1. Miller RD, Cucchiara RF (2000) Anesthesia, 5th ed. Philadelphia: Churchill Livingstone, USA. pp: 1512-1520.
2. Moller RD, Eriksson LI, Fleischer LA, Wiener-Kronish JP, Young WL (2010) Miller's Anesthesia, 6th ed. Philadelphia: Churchill Livingstone, USA. pp: 2046-2058.
3. Gan TJ (2006) Risk factors for postoperative nausea and vomiting. Anesth Analg 102: 1884-1898.
4. Borgeat A, Ekatodramis G, Schenker CA (2003) Postoperative nausea and vomiting in regional anesthesia: a review. Anesthesiology 98: 530-547.
5. Garcia-Migvel FJ, Montao E, Martin-Vicente V, Fuentes AL, Alsina FJ, et al. (2000) Prophylaxis Against Intraoperative Nausea and Vomiting during Spinal Anesthesia for Cesarean Section. Int J Anesth 4: N2.
6. Balki M, Carval JC (2005) Intra operative nausea and vomiting during cesarean section under regional anesthesia. Int J Obstet Anesth 14: 230-241.
7. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, et al. (2002) Volatile

anaesthetics may be the main cause of easly but not delayed post-operative vomiting. Br J Anaesth 88: 659-668.

8. Fujii Y, Numazaki M (2002) Dose-Range Effects of Propofol for Reducing Emetic Symptoms during Cesarean Delivery. Obstetr Gynecol 99: 75-79.

9. Numazaki M, Fujii Y (2000) Subhypnotic dose of Propofol for the prevention of nausea and vomiting during spinal anesthesia for cesarean section. Anaesth Intensive Care 28: 262-265.

10. Grottke O, Muller J, Dietrich PJ, Krause TH, Wappler F (2003) Comparison of premedication with clonidine and midazolam combined with TCI for orthopaedic shoulder surgery. Anasthesiol Intensivmed Notfallmed Schmerzther 38: 772-780.

11. Unlugenc H, Guler T, Gunes Y, Isik G (2004) Comparative study of the antiemetic efficacy of ondansetron, propofol and midazolam in the early postoperative period. Eur J Anaesthesiol 21: 60-65.

12. Bauer KP, Dom PM, Ramirez AM, O'Flaherty JE (2002) Preoperative Intravenous Midazolam: Patient Satisfaction and Other Perioperative Outcomes. Anesthesiology 96: A32.

13. Khezri MB, Reshad F, Javadi A (2009) Comparison of Metoclopramide and low dose Propofol for prophylaxis of nausea & vomiting after cesarean section. J Birjand Univ Med Sci 16: 5-8.

14. Pierre M, Kessebohm K, Schmid M, Kundt HJ, Hering W (2002) Recovery from anaesthesia and incidence and intensity of postoperative nausea and vomiting following a total intravenous anaesthesia (TIVA) with S-(+)-ketamine/propofol compared to alfentanil/propofol. Der Anaesthesist 51: 973-979.

15. Ahsan B, Vahedi MS, Zabihi S, Ardalan M (2008) Comparison of the effects of propofol versus thiopental induced anesthesia on postoperative nausea and vomiting. Sci J Kurdistan Univ Med Sci 12: 1-7.

16. Sade SS, Tanha FD, Sadeghi S (2010) Prevention of postoperative nausea and vomiting by administration sub hypnotic doses of propofol and midazolam during spinal anesthesia for cesarean section. J Family Reprod Health 4: 175-178.

17. Tarhan O, Canbay O, Celebi N, Uzun S, Sahin A, et al. (2007) Subhypnotic doses of midazolam prevent nausea and vomiting during spinal anesthesia for cesarean section. Minerva Medica 73: 629-633.