Rev Bras Anestesiol. 2020;xxx(xx):xxx–xxx

Sociedade Brasileira de Anestesiologia

Brazilian Journal of ANESTHESIOLOGY

Revista Brasileira de Anestesiologia

CLINICAL RESEARCH

Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial

Amir Ahmadzadeh Amiri [a], **Kasra Karvandian** [b,*], **Mohammad Ashouri** [c], **Mojgan Rahimi** [b], **Ali Ahmadzadeh Amiri** [a]

[a] *Tehran University of Medical Sciences, Imam Khomini Hospital Complex, Tehran, Iran*
[b] *Tehran University of Medical Sciences, Imam Khomeini Hospital Complex, Department of Anesthesiology, Tehran, Iran*
[c] *Tehran University of Medical Sciences, Imam Khomeini Hospital Complex, Department of General Surgery, Tehran, Iran*

Received 24 November 2019; accepted 20 April 2020

KEYWORDS
PONV;
General anesthesia;
Intravenous anesthesia;
Endotracheal anesthesia;
Laparotomy

Abstract
Background: Postoperative Nausea and Vomiting (PONV) is a multifactorial surgical complication with an unclear underlying cause. Anesthetic methods, patients' characteristics and the type of surgery are considered as factors affecting PONV. This study was designed to compare the effect of inhalational and intravenous anesthesia in abdominal surgery on the incidence and severity of PONV.
Methods: A single-blinded prospective randomized clinical trial on 105 patients aged 18 – 65 years was carried out. Patients were divided into two groups of Total Intravenous Anesthesia (TIVA) and inhalational anesthesia. The incidence and the severity of PONV were examined at 0, 2, 6, 12 and 24 hours after the surgery. The use of a rescue antiemetic was also evaluated.
Results: 50.9% of the patients in the inhalation group and 17.3% of the patients in the intravenous group developed PONV ($p < 0.001$). The incidence of vomiting was reported in 11.3% of the inhalational group and 3.8% of the TIVA group ($p = 0.15$). 24.5% of patients in the inhalation group and 9.6% of patients in the intravenous group needed an antiemetic medication ($p = 0.043$).
Conclusion: The incidence of postoperative nausea and vomiting and the need for administration of an antiemetic rescue drug and the severity of nausea in patients were significantly lower in the TIVA group.

* Corresponding author.
E-mail: karvandian@tums.ac.ir (K. Karvandian).

https://doi.org/10.1016/j.bjane.2020.08.004

Please cite this article in press as: Amiri AA, et al. Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.08.004

PALAVRAS-CHAVE
NVPO;
Anestesia geral;
Anestesia intravenosa;
Anestesia endotraqueal;
Laparotomia

Comparação entre anestesia intravenosa e inalatória na náusea e vômito pós-operatório de laparotomia: estudo clínico randomizado

Resumo:
Justificativa: Náusea e Vômito no Pós-Operatório (NVPO) é uma complicação multifatorial com etiologia não esclarecida. A técnica anestésica, as características dos pacientes e o tipo de cirurgia são considerados fatores que afetam a NVPO. O presente estudo foi desenhado para comparar o efeito da anestesia inalatória com anestesia intravenosa na incidência e gravidade de NVPO na cirurgia abdominal.
Método: Foi realizado estudo clínico mono-cego prospectivo randomizado com 105 pacientes com idades de 18 — 65 anos. Os pacientes foram divididos em dois grupos, Anestesia Total Intravenosa (TIVA) e anestesia inalatória. A incidência e gravidade de NVPO foram avaliadas em cinco momentos: 0, 2, 6, 12 e 24 horas pós-cirurgia. O uso de antiemético de resgate também foi avaliado.
Resultados: NVPO ocorreu em 50,9% dos pacientes no grupo inalatória e 17,3% dos pacientes no grupo TIVA ($p < 0,001$). A incidência de vômitos relatados foi 11,3% no grupo inalatória e 3,8% no grupo TIVA ($p = 0,15$). Necessitaram de medicação antiemética 24,5% dos pacientes no grupo inalatória e 9,6% dos pacientes no grupo TIVA ($p = 0.043$).
Conclusão: A incidência de náusea e vômito no pós-operatório, a necessidade de administração de droga antiemética de resgate e a gravidade da náusea foram significantemente mais baixas no grupo TIVA.

Introduction

Studies show that Postoperative Nausea and Vomiting (PONV) is the most frightening surgical complication causing unpleasant feelings and dissatisfaction in patients, even more than pain.[1–4] Although the exact cause of PONV is unclear, it seems to be a multifactorial complication.[5–9]

Laparoscopic surgery may sometimes be complicated or turned into open abdominal surgeries due to inadequate surgical aspects and interventions. In these cases, increscent of inhaled or intravenous anesthesia agents' reception, as well as body trauma and the risks of complications such as PONV increases in accordance with the increased duration of the operation. Patients' satisfaction has decreased because of such factors. The methods of anesthesia that decrease these harmful effects are necessary to apply within the open abdominal surgeries.

General anesthesia can be provided by using inhaled or intravenous anesthetics. Intravenous anesthesia with propofol and alfentanil is used increasingly in outpatient surgeries due to the proven effective impacts on recovery time, PONV and pain.[10,11] A meta-analysis showed that no adequate evidence is to be found for propofol and alfentanil's effect on decreased PONV.[12] In this study, propofol for intravenous anesthesia and isoflurane for inhaled anesthesia are used to evaluate and compare the effect of these two methods of anesthesia on the incidence and severity of PONV in patients undergoing laparotomic surgery.

Methods

After the approval by the Tehran University of Medical Sciences ethics committee (ethical approval ID: IR.TUMS.IKHC.REC.1397.076), this study was performed as a single-blinded prospective clinical trial. The study was conducted according to the declaration of Helsinki. All patients aged 18 — 65 years, with ASA class I and II, who underwent elective abdominal laparotomic surgery in Imam Khomeini Hospital Complex, Tehran, were included. The data was collected between August 2018 and May 2019. In the case of a history of motion sickness or PONV or unwillingness of the patient, the patients were excluded. The study process was clarified, and all patients provided written informed consent. This study has been registered at the clinical trial registry under the trial ID: IRCT20190904044685N1 (https://www.irct.ir/trial/41928).

According to a similar study,[13] the incidence of PONV was found to be 30% in the inhalational group. According to the parameters of $\alpha = 0.05$, $\beta = 0.11$, $P_1 = 0.3$, and $P_2 = 0.05$, and utilizing the standardized formula, the sample size of this study (considering the additional 10% to prevent sample loss) was calculated to be 50 patients in each group.

Randomization was performed on an individual level using 4 number blocks created in excel software. Allocation concealment has been carried out. The patient is blind to the type of anesthesia. The researcher and the anesthesiologist (PI) were not blinded to the group of study subjects. Thus, the study was conducted in a single-blinded manner. However, data collectors and data analysts have been blinded.

All patients entered the operating room and underwent standard monitoring. Midazolam 0.02 $mg.kg^{-1}$ and fentanyl 2 $\mu g.kg^{-1}$ were administered intravenously to all patients as premedication and general anesthesia was induced by intravenous thiopental sodium 5 $mg.kg^{-1}$, as the main anesthetic drug and atracurium 0.5 $mg.kg^{-1}$ was used as a neuromuscular relaxant. In the inhalation group, Isoflurane 1.5%—1.7% in combination with 1 mL fentanyl and 1 mL atracurium were

Please cite this article in press as: Amiri AA, et al. Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.08.004

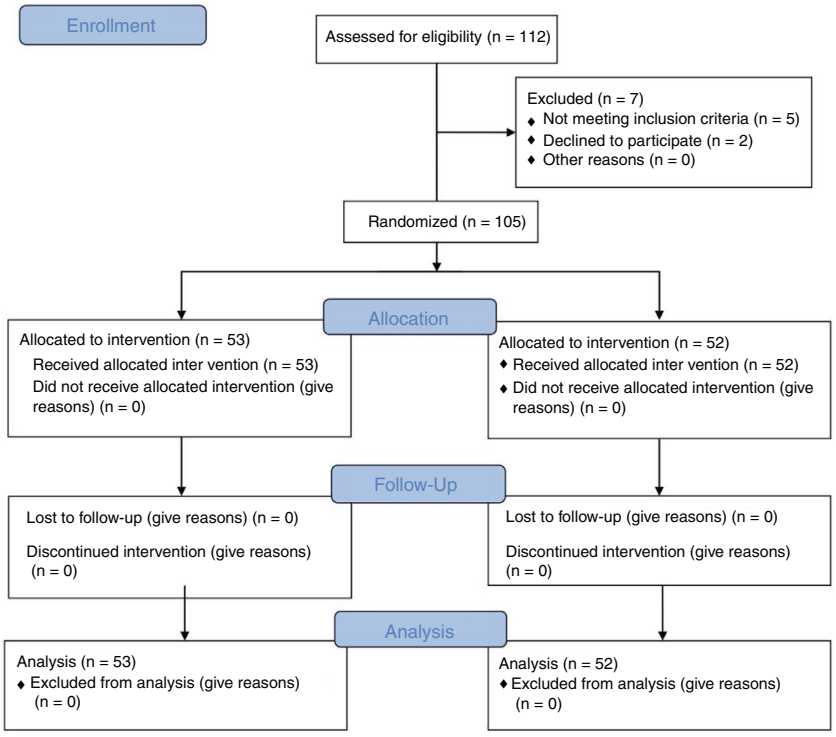

Fig. 1 Study enrollment flow diagram (CONSORT).

used every 45 – 60 min during the operation. In the intravenous group, 50 mL of propofol 1% was combined with 1 – 2 mL of remifentanil and was intravenously infused at the speed of 15 – 20 mL.h^{-1}. Depending on the patients' needs and duration of the surgery, the dosage was altered by ±5 mL.

The incidence of PONV during the first 24 hours after surgery was evaluated as the main outcome. The incidence and severity of patients' nausea and vomiting were recorded in the recovery room (zero hour), 2, 6, 12 and 24 hours after the surgery by both verbal and visual methods using the VAS. The VAS scores the severity of PONV, as 0 meaning no nausea and vomiting and 10 meaning the most severe nausea and vomiting the patient has ever experienced. The questionnaire by which the patients' data were recorded was adopted [14], translated and modified based on our study's aim and goals. However, the incidence of the complications was controlled by intravenous administration of antiemetic drugs based on the patients' need through a single dose of 4 mg ondansetron. No additional adverse effects related to anesthetic interventions were observed by the end of the study.

The data are shown as mean and Standard Deviation (SD), or median and range. Demographic and perioperative data were compared using the Student's *t*-test. The comparison between the groups was performed using the paired and unpaired *t*-test. Incidences were calculated using Fisher's exact test, scoring systems were analyzed using the Wilcoxon's rank-sum test. All data had been checked for a normal distribution using the Kolmogorov-Smirnov test. A p-value of less than 0.05 was considered as the level of statistical significance. Statistical analyses were calculated using SPSS version 21. (SPSS Inc., Chicago, Illinois)

Results

A total of 112 patients met the inclusion criteria to be enrolled in the study. Due to 3 patients having had a previous history of PONV, 2 patients with a positive history of drug reaction and two patients not wanting to continue their participation, a total of 7 patients were excluded from the study. Eventually, a total of 105 patients enrolled in our study. The Inhalational group consisted of 53 (50.47%) patients who received inhalational anesthesia, while the TIVA group consisted of 52 (49.53%) who received total intravenous anesthesia. The study's flow diagram (CONSORT) is presented in Fig. 1.

The number of patients who showed symptoms of nausea or vomiting before surgery was not significantly different between the two groups, with a total of 9 patients in the Inhalational group (16.3%) along with 11 patients in the TIVA group (22%) ($p = 0.11$). The details of the demographic characteristics of the study groups can be viewed in Table 1.

Twenty-seven patients (50.9%) in the inhalational group and 9 patients in the TIVA group developed PONV. This observed difference between the study groups was statistically significant ($p < 0.001$). The total incidence of PONV in our study population was 36 out of 105 patients (34.3%). A significant difference was also observed in the incidence of nausea without vomiting between the two groups ($p = 0.002$). The necessity for antiemetic rescue drug admission was also different between the two groups. Thirteen patients in the inhalational group (24.5%) needed medical intervention to control the vomiting, while 5 patients in the TIVA group (9.6%) needed antiemetic medication ($p = 0.043$). The incidence of nausea, vomiting, PONV, and antiemetic prescription can be found in detail in Table 2.

Please cite this article in press as: Amiri AA, et al. Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.08.004

Table 1 Demographic characteristics of study groups.

Groups variables		Inhalation (n = 53)	TIVA (n = 52)
Age (years)		46.4 (12.31)	46.65 (13.28)
Gender	Male	28 (52.8)	27 (51.9)
	Female	25 (47.2)	25 (48.1)
BMI (kg. m^{-2})		26.28 (3.74)	25.28 (4.27)
ASA	I	34 (64.2)	34 (65.4)
	II	19 (35.8)	18 (34.6)
N/V before surgery		9 (16.3)	11 (22)
Surgical history		23 (43.4)	29 (55.8)
Tobacco addiction		14 (26.4)	15 (28.8)

TIVA, Total Intravenous Anesthesia; n, Number; BMI, Body Mass Index; ASA, American Society of Anesthesiologists; N/V, Nausea or Vomiting. Data are Mean (SD) or count (proportion).

Table 2 Incidence of PONV.

Complications	Inhalation (n = 53)	TIVA (n = 52)	Total (n = 105)	p-value
Nausea	21 (39.6)	7 (13.5)	28 (26.7)	0.002
Vomiting	6 (11.3)	2 (3.8)	8 (7.6)	0.15
PONV	27 (50.9)	9 (17.3)	36 (34.3)	<0.001
Antiemetic	13 (24.5)	5 (9.6)	18 (17.1)	0.043

PONV, Postoperative Nausea and Vomiting; TIVA, Total Intravenous Anesthesia; n: Number. Data are count (proportion).

Table 3 Incidence and severity of PONV divided by time points.

Time / Groups	0h	2h	6h	12h	24h	p-value	
						Within group	Between groups
PONV							
Inhalation (n = 53)	21 (39.6)	19 (35.8)	10 (18.9)	4 (7.5)	9 (17)	< 0.001	0.07
TIVA (n = 52)	7 (13.5)	5 (9.6)	3 (5.8)	2 (3.8)	1 (1.9)	0.002	
VAS							
Inhalation (n = 53)	1.7 (2.46)	1.72 (2.7)	0.76 (1.77)	0.34 (0.3)	0.49 (1.27)	< 0.001	0.03
TIVA (n = 52)	0.52 (1.6)	0.46 (1.58)	0.31 (1.46)	0.15 (0.98)	0.04 (0.28)	< 0.001	

PONV, Postoperative Nausea and Vomiting; n, Number; TIVA, Total Intravenous Anesthesia; VAS, Visual Analogue Scale. Data are Mean (SD) or count (proportion).

In our study, the mean severity of nausea based on the VAS was significantly less in the intravenous group in comparison with the inhalation group, at all the observed checkpoints, from 0 to 24 hours after surgery ($p = 0.03$). However, the difference was statistically only marginally significant regarding the incidence of PONV in the 5 studied checkpoints ($p = 0.07$) (Table 3).

Changes in the severity of PONV in the 5 studied checkpoints can be observed in Fig. 2 divided by study groups.

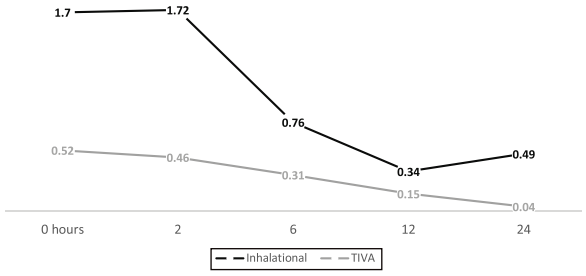

Fig. 2 Changes in severity of PONV at 5 studied checkpoints in two groups of study. PONV, Postoperative Nausea and Vomiting; VAS, Visual Analogue Scale; TIVA, Total Intravenous Anesthesia.

Discussion

The incidence of PONV has been variable between 10% to 63% in different studies and on different populations and different types of surgical procedures.[1–7,15–18] In the study of Rohm et al.[19] the incidence of PONV was 0% in the intravenous group and 33.35% in the inhalation group. Only eight percent of patients in the inhalation group needed antiemetic medication. In the study of Kim et al.,[20] the incidence of PONV was 14.6% in the intravenous group and 51.3% in the inhalation group. The amount of antiemetic medication administration was also reported by 4.2% in the intravenous group and 25.6% in the inhalation group. The results of both studies are in line with the current study, which show that the incidence of PONV is significantly less

Please cite this article in press as: Amiri AA, et al. Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.08.004

in the patients undergoing intravenous anesthesia in comparison with inhalational anesthesia.

However, Visser et al.[21] reported in their study that the difference between intravenous and inhalational anesthesia in terms of the incidence of PONV and the need for antiemetic medication isn't significant. Since the PONV is a multifactorial complication and depends on the patients' condition, anesthesia, and the surgery, some levels of difference are expected in the reported incidences rates. A comparison between different groups and different studies should be performed while taking equal conditions into account to reduce confounding and bios causative factors. Although numerous are studies in line with the results of our study, due to limited similar studies conducted within the searched keywords, a significant comparison regarding the accuracy of the results would not yet be a viable option.

In the study of Akkurt et al.[10] as well as the study of Gashi et al.,[22] along with this study, the level of PONV severity (based on VAS) up to 24 hours after surgery was significantly less in the patients undergoing intravenous anesthesia in comparison with inhalation. In contrast, Kim et al.[20] reported a not statistically significant difference between the two methods of anesthesia, despite the lower VAS range in patients undergoing intravenous anesthesia. Differences in the characteristics of the statistical population including population size, demographic factors, and the type of surgery – which are different from the present study – maybe the causative agent in the difference observed in the significance of PONV severity in a different statistical population.

Summarizing the above-mentioned studies and the obtained results in the current study, the effect of different methods of anesthesia on the incidence of postoperative nausea and vomiting and the need for readministration of antiemetic rescue drug, the severity of nausea in patients, and the frequency of opioid analgesic administration, are highly dependent on the patients' condition, type of surgery, type and duration of anesthesia and so on. Given the irreversible effects of this complication in patients, especially after neurosurgery and open abdominal surgery, it is important to determine the appropriate method and its application forms, to provide the basal requirement to conduct further studies in the future, and also to apply to different statistical societies with different conditions.

We would like to address a potential limitation to our study. In this study, we compared the incidence and severity of PONV in elective abdominal laparotomic surgeries. Given the fact that the incidence or severity of PONV may be affected by the type of surgery as well as the type of anesthesia, the results may have been to some extent biased by not taking the underlying disease and the exact type of surgery into consideration. To that end, we would suggest that further studies evaluating postoperative nausea and vomiting with regards to the underlying disease would result in more precise outcomes.

Conclusion

In conclusion, we observed the successful effect of propofol used in TIVA in comparison with isoflurane used in inhalational method of anesthesia in decreasing the occurrence and severity of PONV in laparotomic abdominal surgeries, resulting in reduced need for antiemetic rescue medication. Lower levels of PONV also leads to better quality of postoperative satisfaction both in the patients and medical team and further limits more complications. We recommend taking advantage of this method of anesthesia especially in patients with higher risk of developing PONV in order to better control the postoperative recovery period.

Key messages

Intravenous anesthesia using propofol demonstrated a statistically significant reduction in the occurrence, severity, and the need for antiemetic rescue medication of postoperative nausea and vomiting after elective laparotomic abdominal surgery, in comparison with inhalational anesthesia.

Funding

This project was financially granted by Tehran University of Medical Sciences.

RCT registry

This study has been registered at Iranian Registry of Clinical Trials under the ID: IRCT20190904044685N1.

Conflicts of interest

The author declares no conflicts of interest.

Acknowledgments

The authors whose names are listed would like to thank the staff of Imam Khomeini Hospital Complex statistics center for their support and assistance in data gathering and analysis.

References

1. Iqbal IM, Spencer R. Postoperative nausea and vomiting. Anesth Int Care Med. 2012;13:613–6.
2. Maitra S, Som A, Baidya DK, et al. Comparison of ondansetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries: a meta-analysis of randomized controlled trials. Anesthesiol Res Pract. 2016;2016:7089454.
3. Bakri MH, Ismail EA, Ibrahim A. Comparison of dexmedetomidine and dexamethasone for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Korean J Anesthesiol. 2015;68:254–60.
4. Golembiewski J, Tokumaru S. Pharmacological prophylaxis and management of adult postoperative/postdischarge nausea and vomiting. J Perianesth Nurs. 2006;21:385–97.
5. Sayed JA, Riad MAF, Ali MOM. Comparison of dexamethasone or intravenous fluids or a combination of both on postoperative nausea, vomiting, and pain in pediatric strabismus surgery. J Clin Anesth. 2016;34:136–42.

Please cite this article in press as: Amiri AA, et al. Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.08.004

6. Sekhavat L, Davar R, Behdad S. Efficacy of prophylactic dexamethasone in the prevention of postoperative nausea and vomiting. J Epidemiol Glob Health. 2015;5:175–9.
7. Couture DJ, Maye JP, O'Brien D, et al. Therapeutic modalities for the prophylactic management of postoperative nausea and vomiting. J Perianesth Nurs. 2006;21:398–403.
8. Mamaril ME, Windle PE, Burkard JF. Prevention and management of postoperative nausea and vomiting: a look at complementary techniques. J Perianesth Nurs. 2006;21:404–10.
9. Pleuvry BJ. Physiology and pharmacology of nausea and vomiting. Anesth Inten Care Med. 2006;7:473–7.
10. Akkurt BCO, Temiz M, Inanoglu K, et al. Comparison of Recovery Characteristics, Postoperative Nausea, and Vomiting, and Gastrointestinal Motility with Total Intravenous Anesthesia with Propofol versus Inhalation Anesthesia with Desflurane for Laparoscopic Cholecystectomy: A Randomized Controlled Study. Curr Ther Res Clin Exp. 2009;70:94–103.
11. Paech MJ, Lee BH, Evans SF. The effect of anesthetic technique on postoperative nausea and vomiting after day-case gynecological laparoscopy. Anaesth Inten Care. 2002;30:153–9.
12. Walldén J, Thörn SE, Lövqvist A, et al. The effect of anesthetic technique on early postoperative gastric emptying: Comparison of propofol-remifentanil and opioid-free sevoflurane anesthesia. J Anesth. 2006;20:261–7.
13. Naghibi K, Kashefi P, Azarnoush H, et al. Prevention of postoperative nausea and vomiting with a subhypnotic dose of Propofol in patients undergoing lower abdominal surgery: A prospective, randomized, double-blind study. Adv Biomed Res. 2015;11:35.
14. Kim TH, Choi BM, Chin JH, et al. The reliability and validity of the rhodes index of nausea, vomiting and retching in postoperative nausea and vomiting. Korean J Anesthesiol. 2007;52:59–65.
15. Bergese SD, Puente EG, Antor MA, et al. A prospective, randomized, double-blinded, double-dummy pilot study to assess the preemptive effect of triple therapy with aprepitant, dexamethasone, and promethazine versus ondansetron, dexamethasone and promethazine on reducing the incidence of postoperative nausea and vomiting experienced by patients undergoing craniotomy under general anesthesia. Front Med (Lausanne). 2016;5:29.
16. Olutoye O, Watcha MF. Management of postoperative vomiting in pediatric patients. Int Anesthesiol Clin. 2003;41:99–117.
17. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. Drugs. 2000;59:213–43.
18. Hans P, Bonhomme V. Why we still use intravenous drugs as the basic regimen for neurosurgical anaesthesia. Curr Opin Anaesthesiol. 2006;19:498–503.
19. Rohm KD, Piper SN, Suttner S, et al. Early recovery, cognitive function and costs of a desflurane inhalational vs. a total intravenous anaesthesia regimen in long-term surgery. Acta Anaesthesiol Scand. 2006;50:14–8.
20. Kim GH, Ahn HJ, Kim GHS, et al. Postoperative nausea and vomiting after endoscopic thyroidectomy: total intravenous vs. balanced anesthesia. Korean J Anesthesiol. 2011;60:416–21.
21. Visser K, Hassink EA, Bonsel GJ, et al. Randomized Controlled Trial of Total Intravenous Anesthesia with Propofol versus Inhalation Anesthesia with Isoflurane–Nitrous Oxide. Anesthesiology. 2001;95:616–26.
22. Gecaj-Gashi A, Hashimi M, Sada F, et al. Propofol vs isoflurane anesthesia-incidence of PONV in patients at maxillofacial surgery. Adv Med Sci. 2010;55:308–12.

Please cite this article in press as: Amiri AA, et al. Comparison of post-operative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.08.004