Journal of Pharmaceutical Care
jpc.tums.ac.ir

The Effect of Morphine on the Incidence of Postoperative Nausea and Vomiting after Strabismus Surgery with Propofol

Mojtaba Rahimi Varposhti[1], Darioush Moradi Farsani[1*], Masoud Fouladgar[2]

[1] Department of Anesthesiology and Intensive Care, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
[2] MD student, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
Received: 2017-08-13, Revised: 2017-09-22, Accept: 2017-10-27, Published: 2017-12-01.

ARTICLE INFO

Article type:
Original article

Keywords:
Morphine
Postoperative Nausea and Vomiting
Strabismus

ABSTRACT

Background: Corrective strabismus surgery is associated with moderate pain and a very high incidence of postoperative nausea and vomiting (PONV). In our treatment centers Morphine is used a lot and it's associated with high incidence of PONV and we have few alternative analgesics. The aim of this study was to compare the incidence of postoperative emesis with intravenous morphine in patients undergoing corrective strabismus surgery with propofol anesthesia with the control group.

Methods: In a prospective, double-blind, randomized study, 126 patients who were candidates for strabismus surgery (either sex or any age) were randomly assigned to receive morphine or placebo. None of the patients received any premedication and a standardized anesthesia technique was used for all the patients. The incidence of PONV in patients within 24 hours after the surgery was compared.

Results: During 24 hours after strabismus surgery, 29 (46%) patients in the morphine group and 27 (42.9%) in the control group had nausea. The frequency of vomiting was 11 (17.5%) patients in morphine group and 9 (14.3%) in the control group. There was no significant difference between the two groups regarding nausea episodes (P=0.85) and vomiting episodes (P= 0.8).

Conclusion: According to the results of this study, morphine does not increase PONV after strabismus surgery.

J Pharm Care 2017; 5(3-4): 61-65.

► Please cite this paper as:
Rahimi Varposhti M, Moradi Farsani D, Fouladgar M. The Effect of Morphine on the Incidence of Postoperative Nausea and Vomiting after Strabismus Surgery with Propofol. J Pharm Care 2017; 5(3-4): 61-65.

Introduction

Strabismus is an alignment disorder of eye characterized by a vertical, horizontal, or torsional deviation of one eye compared to another. Although strabismus is commonly diagnosed in children, adults may also suffer strabismus due to various causes, including trauma, surgical procedures, thyroid disorders, and neurological disorders (1). Strabismus affects approximately 4% of the adult population. There are various therapeutic methods for strabismus treatment, including treatment of the underlying cause, weakening the opposing extra ocular muscles by means of botulinum toxin, and surgical treatment (2). The most common side-effects of the

* *Corresponding Author*: Dr Darioush Moradi Farsani
Address: Department of Anesthesiology and Intensive Care, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
Tel: +989133050830. Fax:+983136684510.
Email: dmoradi@med.mui.ac.ir

strabismus surgery are pain and postoperative nausea and vomiting (PONV) (3). Eye surgeries have a strong association with the incidence of PONV (4-8). However, this association is not at the same level for all types of eye surgeries: the incidence of PONV in intraocular or extra ocular surgeries in non-strabismus affected patients are half that in strabismus affected (9, 10). Vomiting is the most common complication after eye surgery and the incidence of PONV is between 40% and 88% of children aging less than two years old who underwent strabismus surgery (3, 5, 9, 10). The etiology of nausea and vomiting occurrence after strabismus surgery is not yet fully understood. Some hypotheses have been proposed to explain this mechanism, and most of them suggest factors such as stretching of the ocular muscles, visual changes resulting from strabismus surgery, pain, inhaled anesthetic drugs, and narcotic analgesics such as morphine as the causes of postoperative nausea and vomiting (7, 8, 10-12). Some studies show that anesthetic drug Propofol reduces the incidence of PONV compared to halothane, although this effect is reduced when Propofol is used with morphine (12). Opioids such as Morphine and Non-steroidal anti-inflammatory drugs (NSAID) are among the efficient drugs used to control postoperative pain (4). Morphine is one of the narcotic analgesic drugs used to control pain after surgery. Of course, the opioid application is associated with increased nausea and vomiting after surgery. The possible mechanisms for this complication of Morphine is the following: delayed evacuation of the gastric contents, the sensation of the vestibular center, and direct action at the chemoreceptor trigger zone. Other complications of using Morphine are excessive sedation and the risk of respiratory depression (13). Although, high incidence of PONV following Morphine application as an analgesic has been observed in the strabismus surgery operation (14), but, postoperative pain in these patients is severe, which in some cases, does not respond to any other drug except narcotics. Given the fact that in our treatment centers this drug is used a lot and we have few alternative analgesics in our country, the aim of this study was to compare the incidence of postoperative emesis with intravenous morphine in patients undergoing corrective strabismus surgery with propofol anesthesia with the control group.

Methods

We obtained approval from the institutional review body for human research and written informed consent was obtained from all patients. Patients with chronic usage of anti-emetic drugs, any uncontrolled systemic diseases such as renal failure or any respiratory complication, sedative medication or drug addiction, and smoking and alcohol usage were excluded. Also In cases of any problems leading to alteration in anesthetic techniques, or if the patient refused to continue the participation in the study, the patient has been excluded.

Prior to the induction of anesthesia, all patients received 5 ccs/kg of an intravenous Ringer's lactate solution within 20 minutes to prevent hypotension during induction and maintenance of the anesthesia, and sufficient fluid therapy was performed according to the relevant standard protocols. In both of the groups, induction of anesthesia was performed in a completely identical method in the form of a total intravenous anesthesia (TIVA) as follows: Thiopental sodium 5 mg/kg, Atracurium 0.5 mg/kg, Midazolam 0.02 mg/kg and Fentanyl 1 μg/kg, all by intravenous injection. Maintenance of anesthesia was carried out by intravenous infusion of Propofol (150 μg/kg/min) with oxygen (3 liters/min). Patients were allocated randomly to two groups. Group 1 (Morphine) received morphine 0.15 mg/kg intravenously (i.v.) before the start of surgery; group 2 (control) received 5 cc of Normal saline i.v. before the start of surgery.

The postanaesthetic recovery unit (PARU) at our institution is divided into phases 1 and 2; initial recovery from anaesthesia occurs in phase 1, the average length of stay being approximately 1 h. Pain was assessed at 15-min intervals until discharge using a Visual analog scale (VAS) score (15) by a recovery room nurse blinded to the analgesic given. If additional analgesia was required as indicated by a score greater than 3 based on the VAS, Pethidine 0.4 mg/kg i.v. was administered. Time to first response to command and the incidence of nausea and vomiting were also noted. VAS score used to rate the severity of nausea (16).Vomiting was defined as the forceful expulsion of stomach contents. Persistent nausea and vomiting (greater than twice while in recovery) was treated with 0.1 mg/kg of Ondansetron i.v. Patients were discharged when our standard post anaesthesia care unit criteria had been met. The incidence of nausea and vomiting, severity of pain and hemodynamic parameters in both groups were recorded at 0-2, 2-6, and 6-24 hour after surgery.

The sample size in this study was considered based on the sample size formula, with 95% confidence interval estimation and 80% power factor of the test and according to the estimation of nausea and vomiting in both of the groups which were 50%, 63 subjects were calculated for each group.

Results were analyzed using the unpaired t test, chi-square test or Mann-Whitney U test, as appropriate. $P < 0.05$ was considered statistically significant. The statistical software used to analyze the data was SPSS version 20.

Results

63 patients in each group were included in the study, and none were excluded from the study within the study duration. There were no differences in patient characteristics between the two groups (Table 1). In

Table 1. Demographic data of the patients in both groups.

Variable		Morphine group (N=63)	Control group (N=63)	P -Value
Gender	Male	31 (%49.2)	35 (%55.6)	0.59
	Female	32 (%50.8)	28 (%24.4)	
Age (years)(mean±SD)		20.3±16.8	18.6±13.5	0.9
Surgery time	Morning	45 (%71.4)	48 (%76.2)	0.68
	Evening	18 (%28.6)	15 (%23.8)	

the Morphine group, 45 cases underwent surgery in the morning and 18 patients underwent surgery in the evening; and in the control group 48 individuals underwent surgery in the morning and 15 cases underwent surgery in the evening, and there was no significant difference in regards to the time of surgery (morning or evening) between the groups (Table 1).

Within the 24 hours after strabismus surgery, 29 patients (46%) in the Morphine group and 27 patients (%42.9) in the control group demonstrated nausea and there was no significant difference (P=0.85) in this regard. Within the 24 hours after strabismus surgery, 11 cases in the Morphine group (17.5%) and 9 patients in the control group (14.3%) suffered vomiting and no significant difference was observed (P=0.8). At 2 hours after surgery, 16 cases in the Morphine group (25.4%) and 13 (20.6%) of patients in the control group experienced nausea and no significant difference existed (P=0.67). At 2-6 hours after surgery, 22 patients in the Morphine group (34.9%) and 18 individuals in the control group (28.6%) were nauseous, which there was no significant difference in this regard (P=0.56). At 6-24 hours after surgery 9 patients in the Morphine group (14.3%) and 7 cases in the control group (11.1%) experienced nausea, and there was no significant difference between the groups (P=0.79). At 2 hours after surgery, 6 cases in the Morphine group (9.5%) and 4 patients in the control group (6.3%) experienced vomiting and there was no significant difference between the groups in this regard (P=0.74). At 2-6 hours after surgery 8 patients in the Morphine group (12.7%) and 8 cases in the control group (12.7%) suffered vomiting (P=1). Also, within 6-24 hours after surgery, 4 individuals in the Morphine group (6.3%) and 3 cases in the control group (4.8%) experienced vomiting, (P=1) (Table 2). Within 24 hours after the surgery, apnea, hypoxia or bradypnea was observed in none of the patients. Based on VAS score, the severity of nausea in the Morphine group at time intervals of 0-2, 2-6, and 6-24 hours was 1.33, 1.63 and 0.52, respectively. Based on VAS, the severity of nausea in the control group at time intervals of 0-2, 2-6, and 6-24 hours was 1.75, 1.60 and 0.44, respectively; Therefore, in these three time intervals, the severity of nausea between the groups revealed no significant difference (P=0.65 in the interval of 0-2 hours and P=0.95 in the interval of 2-6 hours and P=0.76 in the interval of 6-24 hours).

Within the first 2 hours after surgery, the mean heart

Table 2. Incidence of nausea and vomiting in the study groups.

Variable		Morphine group (N=63)	Control group (N=63)	P- Value
Nausea	0-24	29 (%46)	27 (%42.9)	0.85
	0-2	16 (%25.4)	13 (%20.6)	0.67
	2-6	22 (%34.9)	18 (%28.6)	0.56
	6-24	9 (%14.3)	7 (%11.1)	0.79
Vomiting	0-24	11 (%17.5)	9 (%14.3)	0.8
	0-2	6 (%9.5)	4 (%6.3)	0.74
	2-6	8 (%12.7)	8 (%12.7)	1.00
	6-24	4 (%6.3)	3 (%4.8)	1.00

Table 3. Hemodynamic parameters of the patients in the study groups.

Variable		Morphine group (N=63)	Control group (N=63)	P- Value
Heart rate (Mean±SD)	**0-2**	83.1±11.91	85.2±10.3	0.3
	2-6	84.9±8.9	85.2±10.3	0.39
	6-24	83.1±8.0	85.4±8.1	0.12
Mean arterial pressure (Mean±SD, mm Hg)	**0-2**	84.9±11.7	86.2±10.5	0.65
	2-6	85.1±11.4	86.9±10.1	0.34
	6-24	85.1±11.2	87.2±10.1	0.4
Saturation of oxygen (Mean±SD, %)	**0-2**	98.3±1.9	98.3±1.7	0.76
	2-6	98.1±1.9	97.8±1.8	0.32
	6-24	98.4±1.5	98.2±1.6	0.93
Respiratory rate (Mean±SD)	**0-2**	19.3±6.02	19.5±4.6	0.37
	2-6	19.8±5.9	20.5±4.4	0.93
	6-24	19.3±5.9	19.4±4.4	0.85

rate (HR) in the Morphine and the control groups was 83.1±11.9 and 85.2±10.3 per minute, Mean arterial Pressure (MAP) was 84.9±11.7 and 86.2±10.5 mmHg, saturation of oxygen (SPO2) was 98.3±1.9 and 98.3±1.7 and respiratory rate (RR) was 19.3±6.02 and 19.5±4.6 breaths per minute, respectively; so there were no significant differences between the groups in regards of HR, MAP, SPO2 and RR within the first two hours (P=0.3 for HR, P=0.65 for MAP, P=0.76 for SPO2 and P=0.37 for RR). Also, there were no statistical differences between the groups in regards to HR, MAP, SPO2 and RR within the other time periods of the study (Table 3).

Based on the VAS, the severity of pain in the Morphine group at time intervals of 0-2, 2-6, and 6-24 hours was 4.58, 4.38 and 5.15, respectively. Based on the VAS, the severity of pain in the control group at time intervals of 0-2, 2-6, and 6-24 hours was 7.22 and 6.73 and 5.98 respectively. Therefore, according to the VAS, there was a significant difference between the groups in regards of severity of pain at time intervals of 0-2 and 2-6 (P = 0.002 at time interval of 0-2 and P=0.007 at time interval of 2-6), but no significant difference between the groups at time intervals of 6-24 (P=0.36).

Discussion

During the 24 hours period after the surgery, the incidence of nausea and also the incidence of vomiting in the Morphine group was more than the control group, but no significant differences were observed. Of the three time intervals in which patients were studied, the incidence of nausea and vomiting in both of the groups at the time intervals of 2-6 hours was more than two other intervals, and this incidence at the time intervals of 6-24 hours was less than other two intervals. In all three intervals, the incidence of nausea and vomiting was greater in the Morphine group than in the control group, but no significant difference was present. These findings suggest that probably prescription of Morphine may not significantly increase the incidence of nausea and vomiting after surgery. Evaluation of the patients' vital signs after strabismus surgery in both of the groups revealed no significant difference. Also, through investigating 126 patients in regards to the possible side effects of Morphine administration, no cases of hypoxia, bradypnea, and apnea were found. Totally, mentioned findings suggest that administration of 0.15 mg/kg of Morphine and with full intravenous anesthesia with Propofol did not probably have a significant side effect.

There was no significant difference in the severity of nausea according to the VAS score between the groups in any of the three time intervals of the study, but contrary to the expectations, this rate was slightly higher in the control group than in the Morphine group. The reason for this issue is unclear and maybe the presence of more pain in this group can partly justify this finding. Among these three time intervals, the highest nausea severity in both groups was at the time interval of 2-6 hours, and the lowest rate was at the time interval of 6-24 hours, which could suggest that probably the highest severity of nausea is present in the primary hours after the surgery, that this rate did not reveal significant difference between the Morphine and the control group. Assessing the severity

of pain based on VAS score, in both study groups, the highest rates were at the time interval of 0-2 hours, and this rate was significantly lower in the Morphine group at the time interval of 0-2 and 2-6 hours than the control group, but there was no significant difference in regards of the time interval of 6-24 hours which could suggest that the administration of Morphine as an analgesic drug plays an effective role in controlling postoperative pain after strabismus surgery in the first few hours after the surgery operation. Up to the time of conducting this investigation, it is the first independent study for comparing the effect of Morphine with a control group in patients undergoing strabismus surgery with intravenous anesthesia method in our center. Also, this study is in line with various investigations which evaluated the effects of different causes of nausea and vomiting after strabismus surgery. Wennström et al., (17) compared the effect of Voltaren with Morphine on the incidence of nausea and vomiting after strabismus surgery in pediatric patients. They studied two groups of children (N=25) who were underwent strabismus surgery; one group received injected Diclofenac (Voltaren) and the other group had Morphine as the analgesic drugs. In the Voltaren group, 3 individuals (12 %) and in the Morphine group, 18 cases (72%) experienced nausea and vomiting after surgery and both of the drugs had a good analgesic effect but there was no significant difference in terms of pain control between the groups. In another study, Munro et al., (14) evaluated postoperative nausea and vomiting in two groups of children involving 21 cases in each, which one group received a dose of 0.75 mg/kg of Ketorolac and the other had 0.1 mg/kg of Morphine as analgesic drugs. The incidence of nausea and vomiting after surgery was 19% and 71%, respectively, which was significantly higher in the Morphine group (this was not in accordance with our results), and no significant difference was observed in regards of recovery room hospitalization duration and severity of pain. Of course, other studies have been conducted for evaluating the effects of other factors on postoperative nausea and vomiting. For example, results of the previously published article by the author of the current study revealed that administration of ondansetron and midazolam significantly reduced the incidence of PONV compared to the Metoclopramide and the group (18).

Not addressing the other causes involved in nausea and vomiting, moderate sample size, and short-term follow-up time can be noted as limitations of our study.

In this study, although administration of Morphine compared with the control group negligibly increased nausea and vomiting after the strabismus surgery, this difference was not significant. Morphine has been effective in the control of postoperative pain after strabismus surgery and also has not significantly altered the vital signs of patients after surgery and there were no complications such as hypotension, tachycardia, decreased respiratory rate and SPO2 loss with this drug. Given the fact that in our treatment centers Morphine is used a lot and we have few alternative analgesics in our country, we advise it as an effective analgesic medication without significant side effects for relieving postoperative pain after strabismus surgery.

References

1. Gunton KB, Wasserman BN, DeBenedictis C. Strabismus. Prim Care. 2015;42(3):393-407.
2. Kushner BJ. The benefits, risks, and efficacy of strabismus surgery in adults. Optom Vis Sci 2014;91(5):e102-9.
3. Wan MJ, Hunter DG. Complications of strabismus surgery: incidence and risk factors. Semin Ophthalmol 2014;29(5-6):421-8.
4. Coppens M, Versichelen L, Mortier E. Treatment of postoperative pain after ophthalmic surgery. Bull Soc Belge Ophtalmol 2002;(285):27-32.
5. Lesin M, Sundov ZD, Jukic M, Puljak L. Postoperative pain in complex ophthalmic surgical procedures: comparing practice with guidelines. Pain Med 2014;15(6):1036-426.
6. Kaufman S, Martin-Sheridan D. Postoperative nausea and vomiting after strabismus surgery: mechanisms, treatment, and implications for practice. CRNA 1996;7(3):139-43.
7. Tramèr M, Moore A, McQuay H. Prevention of vomiting after paediatric strabismus surgery: a systematic review using the numbers-needed-to-treat method. Br J Anaesth 1995;75(5):556-61..
8. Wolf R, Morinello E, Kestler G, et al. PONV after strabismus surgery: Risk adapted prophylaxis?. Anaesthesist 2016;65(7):507-13.
9. Williams N, Strunin A, Heriot W. Pain and vomiting after vitreoretinal surgery: a potential role for local anaesthesia. Anaesth Intensive Care 1995;23(4):444-8.
10. Allen LE, Sudesh S, Sandramouli S, Cooper G, McFarlane D, Willshaw HE. The association between the oculocardiac reflex and post-operative vomiting in children undergoing strabismus surgery. Eye (Lond). 1998;12 (Pt 2):193-6.
11. Rose J, Watcha M. Postoperative nausea and vomiting in paediatric patients. British journal of anaesthesia. 1999;83(1):104-17.
12. Weir PM, Munro HM, Reynolds PI, Lewis IH, Wilton N. Propofol infusion and the incidence of emesis in pediatric outpatient strabismus surgery. Anesthesia and analgesia. 1993;76(4):760-4.
13. Trang T, Al-Hasani R, Salvemini D, Salter MW, Gutstein H, Cahill CM. Pain and Poppies: The Good, the Bad, and the Ugly of Opioid Analgesics. J Neurosci 2015;35(41):13879-88.
14. Munro H, Riegger L, Reynolds P, Wilton N, Lewis I. Comparison of the analgesic and emetic properties of ketorolac and morphine for paediatric outpatient strabismus surgery. Br J Anaesth 1994;72(6):624-8.
15. Rauh KH, Andersen RS, Rosenberg J. Visual analogue scale for measuring post-operative pain. Ugeskr Laeger 2013;175(24):1712-6.
16. Meek R, Kelly AM, Hu XF. Use of the visual analog scale to rate and monitor severity of nausea in the emergency department. Acad Emerg Med 2009;16(12):1304-1310.
17. Wennström B, Reinsfelt B. Rectally administered diclofenac (Voltaren) reduces vomiting compared with opioid (morphine) after strabismus surgery in children. Acta Anaesthesiol Scand 2002;46(4):430-4.
18. Moradi Farsani D, Alikiaei B, Hoseinzadeh F. Comparison of Ondansetrone, Metoclopramide and Midazolam for Preventing PONV Prophylaxis after Strabismus Surgery. J Arak Uni Med Sci 2017;20(2): 67-77.