

The Prophylaxis and Treatment with Ondansetron for Postoperative Nausea and Vomiting

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Abstract

Objective: Postoperative nausea and vomiting (PONV) is the common complication of patients undergoing laparoscopic cholecystectomy (LC). Aim of this study is to determine the efficacy of ondansetron for PONV after LC and exploring the most effective time of using it.

Methods: The clinic data of 120 patients with chronic cholecystitis (selected randomly from all the patients undergone LC at the Second Affiliated Hospital of Chongqing Medical University between 2012 and 2014) were analyzed retrospectively. The data were divided into three groups: the preoperative group (n=40), postoperative group (n=40) and control group (n=40). The preoperative group received 8 mg of ondansetron intravenously 30 minutes prior to the induction of anesthesia while the postoperative group received 8 mg of ondansetron intravenously when anaesthesia recovery, the control group received no antiemetic. The incidence of PONV and the adverse effects during the postoperative periods (48 hrs) were recorded in the data. If the PONV happened, the patients received 8mg of ondansetron intravenous again.

Results: Significant differences were found between the preoperative group and postoperative group (preoperative: 27.5% vs. postoperative group: 10%) and the preoperative group and control group (preoperative: 27.5% vs. control group: 50%). To the PONV case, using ondansetron intravenous again about 88% got control. No clinically important adverse effects were noted.

Conclusion: Administration of ondansetron is effective in the prevention and cure of PONV for LC. Late administration (anaesthesia recovery) is significantly more effective.

Keywords: Laparoscopic cholecystectomy; Ondansetron; Postoperative nausea and vomiting

Introduction

Nausea and vomiting are common complications after surgery operation; some statistics shows that the frequency of nausea and vomiting after operation in hospital surgery patients is 20%-37% [1-4]. PONV is due to the anesthesia and operation for patients with gastrointestinal stimulation. Because of CO₂ could take gastrointestinal tracts, so PONV more occurs after LC. PONV is one of the most common complications of the patients after LC.

PONV could cause patients vomit aspiration, could affect sputum expectoration and cause pneumonia, may affect the recovery of intestinal function, could cause wounds pain acutely even because of the increasing of abdominal pressure, the wounds bursting.

Prevention and treatment of PONV help to decrease psychological distress, and advance exhaust and recovery time [2-4].

At present, dexamethasone and metoclopramide are the main drugs for PONV, but the effect not very well. Ondansetron, a selective blocking agent of the serotonin 5-hydroxytryptamine type 3 (5-HT₃), the half-life of Ondansetron is 3 hrs, the apparent volume of distribution is 140 L and the plasma protein binding rate is 70-80%. Ondansetron is a highly effective antiemetic that has been used for both the prophylaxis and treatment of PONV [5,6]. However, the most effective time for using of ondansetron for the patients after LC has not been established clearly. Aim of this study is to determine the efficacy of ondansetron for PONV after LC and the most effective time of using it.

Materials and Methods

Patients and grouping

The retrospective study selected 120 patients randomly from all the patients undergone LC at the Second Affiliated Hospital of Chongqing Medical University between 2012 and 2014. Exclusion criteria were

history of motion sickness or previous PONV, gastrointestinal disorders, use of antiemetic medication within 24 h before the surgery and smoking habit. All the 120 patients are 60 male patients and 60 female patients, the oldest is 70 years old and the youngest is 20 years old, and the average is 45 years old. All the 120 patients were divided into three groups: the preoperative group (n=40), postoperative group (n=40) and control group (n=40). The information of patients is in Table 1.

Drugs and drug delivery

All patients received standard anesthesia in the operation room. Patients were monitored during anesthesia by heart beat rate, continuous electrocardiogram, noninvasive blood pressure and peripheral blood oxygen saturation. Anesthesia was induced with fentanyl 0.005 mg/kg, propofol 0.5-2 mg/kg. Anesthesia was maintained with sevoflurane and fentanyl.

The preoperative group received 8 mg of ondansetron intravenously 30 minutes prior to the induction of anesthesia while the postoperative group received 8mg of ondansetron intravenously when anaesthesia recovery, the control group received no antiemetic. The incidence of PONV and the adverse effects during the postoperative periods (48 hrs)

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were recorded in the data.

monitoring index

The incidence of PONV and the adverse effects during the postoperative periods (48 hrs) were recorded in the data. If the PONV happened, the patients received 8 mg of ondansetron intravenously again. Observe the adverse reactions in 48 hrs, such as headache, dizziness, excessive sedation, extrapyramidal reactions and so on.

Data analysis and processing

The statistical software program Statistical Package for Social Science (version 17.0; SPSS) was used to perform the analysis. Comparisons were assessed by the chi-square test. Differences between groups were declared to be statistically significant at $p < 0.05$.

Result

The histopathological diagnosis was all chronic cholecystitis. The incidence of PONV in the three groups could be found in Table 2. Compared the preoperative group with the control group, $\chi^2=4.27$, $P < 0.05$, the postoperative group with the preoperative group, $\chi^2=4.02$, $P < 0.05$, and the postoperative group with the control group, $\chi^2=15.24$, $P < 0.05$. The differences between the three groups are all statistical significant.

In the all 120 patients who received LC, there were 35 patients affected by PONV. All the 35 patients were given 8mg of ondansetron intravenously. The incidence of PONV in patients in each group after therapeutic use could be found in Table 3.

No clinically important adverse events were found in the data.

Discussion

Nausea and vomiting due to surgery and anesthesia are among the most common complications. The reported incidence of PONV after LC varies from 50 to 70% [7-10]. There are many researches for prevention and cure PONV, such as using gabapentin, dexamethasone, perphenazine and so on, they all have efficacy and some side-effects more or less [11-13]. This study we explored the most effective time of using Ondansetron hydrochloride for PONV after LC.

Ondansetron hydrochloride is a highly selective 5 - HT 3 receptor

antagonist. It functions so by antagonizing peripheral and central neurons of 5 - hydroxytryptamine receptor, thus blocking intestinal 5 - HT release and blocking the 5 - HT 3 receptor induced vagal afferent nerve excitability caused gag reflex, to the purpose of antiemetic [14]. It is a potent antiemetic with high selectivity effect, without other antiemetic drugs' side effects such as extrapyramidal reactions, sedation. The half-life of Ondansetron is 3 hrs, and the apparent volume of distribution is 140 L and the plasma protein binding rate is 70-80%.

In our department, in more than 600 cases of LC surgery, about 40% of patients had varying degrees of nausea and vomiting. Therefore, clinicians should pay attention to effective prevention and treatment of PONV, to relieve the suffering of patients after LC.

The reasons of LC postoperative nausea and vomiting are not entirely clear, but most investigations have proposed the following factors: patient characteristics, surgical procedure, anesthetic technique, and postoperative care [1,2,15,16]. The surgical procedure, anesthetic technique and postoperative care are the same for all patients who received surgery in our hospital. Therefore, in order to make the study more persuasive, we tried to make the patients we selected have the similar characteristics. For the patient characteristics, such as genders, history of motion sickness, previous PONV, nonsmoking status, and use of postoperative opioids were proposed as predictors [17,18]. So, besides the randomness of the selection, we added exclusion criteria in the study. The patients with history of motion sickness, previous PONV, gastrointestinal disorders, previous use of antiemetic medication within 24 hrs before the surgery, or smoking habit were excluded. The male to female ratio is 1:1.

We use ondansetron hydrochloride to prevent and treat PONV after LC. About the dosage, there have been many studies, ranging from 1 to 16 mg. Some authors considering 4 mg is enough effective dose [2,19,20], whereas others have found 8 mg to be the minimum effective dose [21-23]. In our study, we selected the cases of 8 mg dose in order to make the difference between preoperative group and postoperative group more persuasive.

The results show that with intravenous injection of 8 mg ondansetron 30 minutes before the surgery, the incidence of nausea, vomiting reactions was 27.5%, significantly lower than 50% of the control group; when inject 8 mg ondansetron intravenously approximately at

	Gender (male/female)	Age ($\bar{X} \pm S$)	Weight (kg, $\bar{X} \pm S$)	Height (cm, $\bar{X} \pm S$)	Operation time (min, $\bar{X} \pm S$)	Anesthesia time (min, $\bar{X} \pm S$)
Preoperative group	20/20	45.2 \pm 13.7	62.5 \pm 10.3	162.1 \pm 8.7	40.1 \pm 16.3	85.4 \pm 22.4
Postoperative group	20/20	43.7 \pm 14.5	63.4 \pm 11.7	165.2 \pm 9.3	39.9 \pm 15.8	83.2 \pm 21.8
Control group	20/20	46.1 \pm 14.1	63.1 \pm 12.6	162.8 \pm 7.2	39.6 \pm 16.7	82.7 \pm 20.6

Table 1: The information of patients.

	Num. of cases	Cases of PONV	Incidence(%)
Preoperative group	40	11	27.5
Postoperative group	40	4	10
Control group	40	20	50

Table 2: Incidence of PONV in patients of each group after prophylactic antiemetic.

	Num of cases	Cases of PONV	Incidence(%)
Preoperative group	11	1	9
Postoperative group	4	0	0
Control group	20	3	15

Table 3: Incidence of PONV in patients in each group after therapeutic use.

end of surgery, the incidence was 10%, significantly lower than that of preoperative group and control group. It shows that ondansetron can be effective in preventing PONV and the proper time is injected at the end of the surgery. Meanwhile, of all the 120 patients, 35 patients affected by PONV received ondansetron 8 mg intravenously, and 31 of them got symptom-free, and the remaining 4 patients had varying degrees of ease. It shows that ondansetron can also be effective in treating PONV.

The most effective timing of ondansetron administration has been an issue in several reports. Some reports had no significant difference [24]. Other reports, on the other hand, did not have take all the risk factors in control and the surgery procedure for the study was not LC [6]. Our study indicated that PONV occurred in 27.5% of the patients who received ondansetron just before the induction of anesthesia of LC, but when given at the end of surgery, the incidence decreased to 10%. The difference was significant and the risk factors were all taken in control. The reasons could be that ondansetron could reach plasma peak concentration within 10 minutes by intravenous administration, and it has many metabolic pathways, and hydrochloride *in vivo* elimination half-life is 3 hrs. In LC, the time of anesthesia is about 84 minutes, so its antiemetic benefit may be lost in long operation time. So after the operation, the drug concentration has been reduced, and could not perform the anticipated antiemetic function effectively. At that moment, another time of intravenous ondansetron use could be increase the drug concentration *in vivo* in patients, and then we can effectively achieve the antiemetic purposes.

Our study had a potential limitation. It was a retrospective study which is not as persuasive as a prospective study. However, we had to do it like this in order to take all the risk factors in control.

Conclusion

Administration of ondansetron is effective in the prevention and cure of PONV for LC. Late administration (anaesthesia recovery), compared to preoperative administration (within 30 min before surgery), is significantly more effective in the prevention of PONV for LC.

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