



Pharmacological efficacy and safety of ondansetron for managing gynecological laparoscopic postoperative nausea and vomiting

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ABSTRACT

Postoperative nausea, retching and vomiting are among the most common postoperative complaints and key causes of morbidity after general, regional, or local anesthesia and surgery. To study the clinical effect of ondansetron on patients with gynecologic laparoscopic operation. We performed a comparative-analysis of published, randomized, controlled trials to determine the relative efficacy and safety of ondansetron for prevention and treatment of postoperative nausea and vomiting. The results demonstrated that the prophylactic administration of ondansetron was more effective in preventing postoperative vomiting, but the drug were compared with placebo. The overall risk of adverse effects was not different.

Key words: Ondansetron; Gynecological Laparoscopic Operation; Nausea and Vomiting; Comparative Study

INTRODUCTION

In recent years, laparoscopic surgery also called keyhole surgery or minimally invasive surgery (MIS), is a surgical technique [1]. Medically, versus an open procedure, laparoscopic surgery have remarkably advantages of less pain, reduced hemorrhaging and smaller incision, which reduces pain and shortens postoperative recovery time, as well as resulting in less post-operative scarring and so on [2-3]. Therefore, laparoscopic surgery has been widely carried out in clinical gynecological laparoscopic operation. Laparoscopic surgery, refers only to operations within the abdomen or pelvic cavity, which belongs to the field of endoscopy. A laparoscope contains a fibre optic system to illuminate the operative site, a lens system to view the operative site that is usually connected to a video camera (videoscopic procedures using a laparoscope or endoscope) and a channel to allow access for intervention using long, thin instruments. Through small incisions a surgeon can introduce additional instruments through side ports. Rather than a 20 cm cut as in traditional cholecystectomy, two or five cuts of 5-15 mm will be sufficient to perform a laparoscopic removal of a gallbladder. The abdomen is usually insufflated with carbon dioxide gas to create a working and viewing space [4].

On the other hand, compared with non-laparoscopic surgery, the high incidence of postoperative nausea and vomiting (PONV) become the patients' most unbearable complaints, which increases the patient's pain and affects the quality of life of patients [5]. PONV is the most frequent unpleasant postoperative complication affecting about a third of the surgery patients, and a variety of factors may account for it, especially the higher incidence of gynecological laparoscopic surgery. It usually occurs within 24h after surgery.

The PONV prevention and management have attracted high attentions of the clinical anesthesiologist, and 5-hydroxytryptamine (5-HT₃) receptor antagonists have been shown to play a better role in the prevention of PONV

[6]. Ahead of clinical experiments, we performed a literature search of English references using both the MEDLINE database and a manual search. Double-blinded, randomized, controlled trials comparing the efficiency of the prophylactic administration of ondansetron, droperidol and metoclopramide therapy during general anesthesia were included. Our research aims to illustrate the clinical effect of prevention and treatment of PONV of representative 5-HT₃ receptor antagonist ondansetron after gynecological laparoscopic surgery.

EXPERIMENTAL SECTION

Materials and General Information

From December 2011 to December 2013, 200 patients who had gynecological laparoscopic surgery at Baoji Central Hospital were selected for the clinical study. All the patients had no surgical contraindications, aged from 18 to 56 years, possessed the average age of (31.6 ± 8.5) years and graded ASA I-II. Among them were 83 cases of ovarian cyst, 64 cases of uterine fibroids and 53 cases of ectopic pregnancy. All patients had no symptoms of nausea and vomiting before surgery, and they had not taken any antiemetic drugs one week before surgery. The exclusion criteria can be listed as follows, patients with long-term use of hormones, patients with drug allergies, patients with the history of motion sickness and smoking, patients with gastrointestinal or brain diseases that can cause nausea and vomiting. There were 42 cases of ovarian cysts, 32 cases of uterine fibroids and 26 cases of ectopic pregnancy among 100 patients in the control group whose age was 19-56 years, the average age was (32.1 ± 7.3) years and average body weight was (54.6 ± 10.3) kg. The other 100 patients in the observation group whose age was 18-56 years, average age was (31.9 ± 8.1) , and average weight was (55.2 ± 11.6) kg, there were 41 cases of ovarian cysts, 32 cases of uterine myoma, and 27 cases of ectopic pregnancy. The patients of two groups compared with age, weight, type of illness, type of surgery, anesthetics and other general information, the difference was not statistically significant ($P > 0.05$) and of comparability.

Treatment Methods

The 200 patients were randomly divided into two groups of whom had laparoscopic surgery under general anesthesia. The observation group was injected intravenous ondansetron 8mg, 0.5h before the end of the laparoscopic surgery. Meanwhile, the control group was adapted sodium chloride injection 4ml before the end of operation without utilization of antiemetic drug. After 24 hours of laparoscopic surgery. Frequency and degree of patient's nausea and vomiting were observed and recorded individually. If the patients continued vomiting for more than 10 minutes or even serious, they should be injected ondansetron immediately for treatment, and were recorded in the two group's ADR at different times.

Curative effect evaluation were taken under the evaluation criteria of PONV shown in table 1, and was divided into 5 grades. Level 0 mean no nausea and vomiting, level 1 indicated mild nausea, no vomiting, level 2 was the intense nausea and 1~2 times of vomiting, level 3 was gravis nausea and 3~5 times of vomiting, moreover, level 4 was frequent nausea and 5 or more times of vomiting.

Statistical Methods

Table 1. Criteria of the clinical efficacy evaluation

Levels	Judging criteria
Level 0	no nausea, vomiting
Level 1	mild nausea, no vomiting
Level 2	moderate nausea, vomiting, 1~2
Level 3	severe nausea, vomiting, 3~5
Level 4	frequent nausea, vomiting > 5 times

IBM SPSS Statistics 18.0-statistical software was selected to entry, analysis and handle the original data, ($\bar{x} \pm s$) was chosen to express measurement data, χ^2 to test the enumeration data, the statistical data were compared between the two groups and experimented in t-test. $P < 0.05$ indicated a statistically significant difference.

RESULTS

As shown in table 2, two sets of data had a significant difference and were statistically significant. Patients in the observation group of level 2 or above (including level 2) accounted for 3%, which was significantly less than the control group 27%. The data was statistically significant ($P < 0.05$). The result illustrated that ondansetron had better preventive effect in gynecological laparoscopic operation for postoperative nausea and vomiting phenomenon. If PONV occurs more serious symptoms, the control group injected up to 2 times to relieve the symptoms of PONV in patients and the observation group injected 1 time to relieve. It demonstrated that ondansetron had a better therapeutic effect on postoperative nausea and vomiting after laparoscopic surgery.

Table 2. Comparison of the incidence of nausea and vomiting in two groups

Groups	PONV					Antiemetic drug injections
	Level 0	Level 1	Level 2	Level 3	Level 4	
Control group	32	42	15	6	3	2
Observer group	81	13	2	0	1	1

Table 2 displayed that level 0 of the observation group that PONV phenomenon did not occur in patients accounted for 82%, significantly better than the control group 31%; PONV incidence was 18%, obviously less than the control group 69%, indicating the effect of preventing PONV in the observation group better than the control group.

Table 3. The adverse reactions in two groups

Groups	2h after surgery	8h after surgery	16h after surgery	20h after surgery	24h after surgery
Control group	0	0	0	1	0
Observer Group	0	0	0	0	1

The results in Table 3 illustrated that the side effects of observer group versus the control group after injected ondansetron, specifically, the observation group had occurred only one case of adverse effects, which certificated that the application of ondansetron had high security. The observation group occurred one case adverse reactions after 20h and the control group occurred one case of adverse reactions after 24h. The main adverse reaction is the sense of dizziness, that may be due to the process of surgical operation or other factors. The overall risk of adverse effects was not different.

DISCUSSION

Clinically, gynecological laparoscopic cholecystectomy is the most common laparoscopic procedure performed owing to decreased scars, rapid postoperative recovery. The first publication on diagnostic laparoscopy by Raoul Palmer appeared in the early 1950s, followed by the publication of Frangenheim and Semm. Hans Lindermann and Kurt Semm practised CO₂ hysteroscopy during the mid-1970s [7]. In laparoscopic surgery, 5–10 mm diameter instruments (graspers, scissors, clip applier) can be introduced by the surgeon into the abdomen through trocars (hollow tubes with a seal to keep the CO₂ from leaking) [8]. Over one million cholecystectomies are performed in the U.S. annually, with over 96% of those being performed laparoscopically [9].

On average the incidence of nausea or vomiting after general anesthesia ranges between 25 and 30% [10]. In recent years, laparoscopic surgery use endotracheal intubation as anesthesia, and extubation may stimulate the throat to cause nausea and vomiting, meanwhile the use of morphine and other opioids in anesthesia also have strong emetic activity [11-13]. In addition, there are other reasons leading to PONV by external reflection and central effect, resulting in laparoscopic surgery PONV incidence as high as 70% -80%. Nausea and vomiting can be extremely distressing for patients and is therefore one of their major concerns. Nausea and vomiting have been associated with major complications such as pulmonary aspiration of gastric content, wound dehiscence and might endanger surgical outcomes after certain procedures, and delays postoperative recovery time [14], provoking distress of patients. Consequently, it is particularly important to prevent PONV.

PONV is composed of a variety of factors stimulation of peripheral reflex, PONV stimulates the outer periphery of the reflector by a variety of factors, and then sends a nerve impulse caused by adverse reactions due to central nervous system. In this process, the release of 5-hydroxytryptamine (5-HT₃) plays a decisive role. The introduction of the highly selective 5HT₃ receptor antagonist, ondansetron, in the early 1990s was a significant breakthrough. It can antagonize the central nervous system and 5-HT receptors of the outer periphery of the vagus nerve endings, and can play potent antiemetic [15-16]. Types of surgery and anesthesia drugs used by patients in this study were same and excluded patients with previous history of PONV. Despite the many studies, however, the evidence base to support rational antiemetic treatment remains patchy. Recent research has led to better understanding of some older drugs and has demonstrated that combinations of drugs are often useful.

CONCLUSION

In this clinical-study, we focused on the occurrence of PONV after ondansetron gynecological laparoscopic operation, the effect is satisfactory. There are 82% of 100 patients in the observation group having no PONV symptoms, and the incidence (18%) is much lower than the control group. Two sets of data are statistically significant ($P < 0.05$). Intravenous ondansetron did not have an impact on circulatory function, and did not have other significant adverse reactions

In summary, we demonstrated that the prophylactic administration of ondansetron was more effective in preventing postoperative vomiting, but the drug were compared with placebo. The overall risk of adverse effects was not different. Clinical judgement is therefore required to determine the relative risks and benefits of prophylactic antiemetic therapy in an individual patient. Formal cost-effectiveness analysis and further clinical research are necessary before developing formal guidelines for drug use.

Acknowledgements

This work was supported by Natural Science Research Fund of Shaanxi Province (2014JQ4154), Scientific Research Foundation of Shaanxi University of Science and Technology (BJ13-20), National Natural Science Foundation of China (Nos.11275164, 30960006 and 31100040), Programs for Science and Technology Development of Shaanxi Province, China (No. 2012K08-05) and Foundation of Shannxi Educational Committee (No.2013JK0727).

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