WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 3, 245-254. Research Article ISSN 2277– 7105

THE EFFICACY OF DEXAMETHASONE AND PROPOFOL IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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Article Received on
08 Jan. 2019,

Revised on 29 Jan. 2019,
Accepted on 18 Feb. 2019

DOI: 10.20959/wjpr20193-14344

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) are one of the most common complaints following anesthesia and surgery. This study was designed to evaluate the efficacy of dexamethasone, propofol to prevent PONV in patients undergoing laparoscopic cholecystectomy. **Methods:** 119 patients were included in this randomized, **Results:** Dexamethasone was more effective in preventing PONV than propfol.

KEYWORDS: laparoscopic cholecystectomy, postoperative nausea and vomiting, dexamethasone.

INTRODUCTION

Postoperative nausea and vomiting (PONV) are one of the most common complaints following anesthesia and surgery. The overall incidence of PONV has been estimated to 30% depending on surgical, patient and postoperative factors. The patients undergoing laparoscopic cholecystectomy are especially prone to PONV, with the reported incidence of 53%-72%.[1]

In an attempt to decrease such a high incidence, many antiemetics have been studied. However, because of the multifactorial origin of PONV, none of the currently available antiemetics is fully effective in all patients. At present, when antiemetics of different

pharmacological classes are available, it is possible to combine them and provide better control of PONV without producing additional side effects.[2]

Dexamethasone has been used as an antiemetic for more than 20 years in patients receiving chemotherapy, with limited side effects, and has also been reported to decrease PONV when added to the antiemetic regimen. Recently, a combination of ondansetron and dexamethasone has been shown to be a highly effective prophylactic measure in patients undergoing laparoscopic cholecystectomy. However, the higher cost of ondansetron has been a significant factor limiting its routine prophylactic use.[3]

Postoperative nausea and vomiting (PONV) are distressing and frequent adverse events of anesthesia and surgery, with a relatively high incidence following laparoscopic cholecyatectomy (LC). When no prophylactic antiemetic is given, the reported incidence of PONV is 46–72% in patients undergoing LC. These symptoms predispose to aspiration of gastric contents, wound dehiscence, psychological distress, and delayed recovery and discharge times. Patients who experience PONV consume more resources and require additional health care professional time than do those in whom these complications are avoided.[4] Pharmacological approaches, including anticholinergics, antihistamines, phenothiazines, butyrophenones, benzamides, corticosteroides, and serotonin receptor antagonists, have been investigated in the prevention and treatment of PONV, with various results.[5] Among them, serotonin receptor antagonists (e.g., ondansetron) are the most effective antiemetics in patients undergoing various types of surgery. Previously, Hemly demonstrated that ondansetron was more effective than traditional antiemetics, droperidol, and metoclopramide, for the prophylaxis against PONV following LC.[6] However, several investigations have criticized the use of prophylactic antiemetic therapy with serotonin receptor antagonists, because of their high cost.[7]

Postoperative nausea and vomiting are one of the most important causes of patients' discomfort. The incidence of PONV after surgery is in the range of 20–30% but it may be up to 50–70% after laparoscopic surgeries.[8] Various patients related to risk factors such as female sex, nonsmoking status, history of PONV, and motion sickness have been identified as risk factors for PONV. Several anaesthesia related factors such as the use of opioid and nitrous oxide and duration of general anaesthesia have been implicated as risk factors of PONV. Prevention of PONV after laparoscopic surgeries is a challenge to the perioperative physicians as it is distressing for the patients and more and more such surgeries are

performed on a day care basis. So, an effective prophylactic regimen is highly desirable for early home discharge.

Among the drugs that are being used for PONV prophylaxis, 5HT3 antagonists, such as ondansetron, granisetron, palonosetron, and ramosetron, and dexamethasone are the two most commonly used nowadays. However, no drug has been found to provide complete PONV prophylaxis. A number of studies have compared ondansetron with dexamethasone for PONV prophylaxis after laparoscopic surgeries. These studies are not unanimous in reporting their results and there is no consensus on which drug is better in PONV prophylaxis. However, in most of the studies, the number of patients that received study drug is relatively small in a number ranging from 20 to 100 and that may be one of the reasons why statistical significance could not be found. Hence, we planned this meta-analysis of randomized control trials where ondansetron has been compared with dexamethasone for PONV prophylaxis in patients undergoing laparoscopic surgeries.

BACKGROUND

Laparoscopic cholecystectomy

Laparoscopic gallbladder surgery is a procedure to take out your gallbladder. During this procedure, the surgeon makes 4 small incisions (cuts) in your abdomen (belly). A harmless gas is pumped into your abdomen so that the doctor can better see your organs. A long tube with a tiny camera at the end (a laparoscope) is put through one of the incisions. The camera sends a video of the inside of the abdomen to a computer screen. This allows your doctor to see and take out the gallbladder using other small surgical tools. The entire procedure usually lasts less than 2 hours.

Omar et al have compared single incision versus 3-port laparoscopic cholecystectomy in patients with symptomatic gallstones. Our congratulations to the authors for a well-designed study with thoughtprovoking learning outcomes, especially for developing countries with high-volume centers in terms of a number of laparoscopic cholecystectomies performed. They compared the clinical outcome of single incision (both single incision laparoscopic cholecystectomy [SILC] port and 3-port techniques combined) with three port laparoscopic cholecystectomy.[9]

Only a few studies previously have compared single incision laparoscopic colecystectomy with 3-port laparoscopic cholecystectomy in a prospective, randomized manner. The authors

conclude that SILC is a safe and acceptable technique when performed by experienced surgeons. Certain observations, however, may need to be answered before acceptance of this conclusion. First, combining the 2 techniques of SILC using SILC port and 3 port in a single group has the potential to affect the results, because nowhere it is mentioned how many (the number) of these 2 techniques were used in the study (in both techniques there can be differences in ergonomics, interferences with operative workflow, achieving the critical view of safety, 4 and intraoperative and postoperative outcomes). The authors have included comparison of the success rate (P = .01), intraoperative conversion rate (P < .01), and readmission rates (P =.06) of the procedures in the patient outcomes table (Table II), but they need to explain if this is the primary or secondary outcome measure, because the conclusion statement of feasibility of SILC depends on these results. Also, a statement on the timing of follow-up in the postoperative period also should be mentioned (e.g., 1 week/1 month/ 1 year). In the intraoperative outcomes, complications related to gastrointestinal injury (stomach, duodenum, and small or large bowel) should have been included. There is no mention of the number of patients requiring an abdominal drain and the indications for drain placement, although they mentioned that drains were placed through the umbilical incision in SILC group and the right subcostal incision in the three-port laparoscopic cholecystectomy group. Such drains may have a bearing on postoperative complications (an umbilical hernia, wound infection, etc.).

The authors state they had no difficulty in patients with a body mass index >35 or the presence of acute cholecystitis with regards to SILC, but nowhere do they mention the number of such patients in the 2 groups. One of the noteworthy points mentioned by the authors is that the surgeon performing SILC was relatively low on the learning curve, and there might be a high chance of intragroup variability in the need of an additional trocar placement (4 cases in the first 10 cases) and the mean operating time (first 10 cases was 103 minutes and last 10 cases was 47 minutes), but this is in contradiction to the conclusion, which states that SILC should be performed by experienced surgeons. These points make us think that after achieving substantial experience in SILC, the results might be a better reflection of post procedural outcomes. Hence, patients should have been included only after the surgeon completed the learning curve.[10]

METHODS

We studied 126 patients (51 men and 75 nonpregnant women) in the hospital of alkark, aged 25–68 years, and undergoing LC. Indications for LC in this clinical trial were symptomatic cholelithiasis, chronic cholecystitsts, and cholecycystic polyp. Exclusion criteria were antiemetics given 24 hours before surgery; gastrointestinal diseases; a history of motion sickness and/or previous PONV; pregnancy or menstruation; and laparoscopy replaced by laparotomy.

Patients were receiving, propofol 0.5 mg/kg, or propofol 0.5 mg/kg combined with dexamethasone 8 mg at the end of the surgical procedure. The doses of propofol and dexamethasone chose in this study were taken from previous reports by Song et al. and Smith et al.

Identical syringes (covered with red tape) containing each drug were prepared by personnel not involved in the study. No patients received preanesthetic medication. Anesthesia was induced with propofol 2 mg/kg IV and fentanyl 1 lg/kg IV, and vecuronium 0.1 mg/kg IV was used to facilitate tracheal intubation. After tracheal intubation, anesthesia was maintained with sevoflurane 1.0–3.0% (inspired concentration) and air in oxygen. Additional analgesia during surgical procedure was achieved with fentanyl 50–100 lg. Ventilation was mechanically controlled and adjusted to maintain PETCO2 at 35–40 mmHg throughout surgery, as measured by an anesthetic/respiratory gas analyzer. Muscle relaxation was achieved with vecuronium, as required. A nasogastric tube was inserted, and suction was applied to empty the stomach of air and other contents. Before tracheal extubation, the nasogastric tube was again suctioned and then removed. For reversal muscle relaxation, atropine 0.02 mg/kg and neostigmine 0.04 mg/ kg were administered IV, and the trachea was extubated when the patient was awoken. The awakening time was defined as the period from the discontinuation of anesthesia to eye opening on command. For postoperative analgesia, the wound was infiltrated with 10 ml of ropivacaine 1.0% and 10 ml of lidocaine 1.0%, which was the routine technique in our institution. Pentazocin 15 mg was given intramuscularly when patients requested another analgesic regimen.

Postoperatively, all episodes of emetic symptoms (nausea, retching, and vomiting) during the first 24 hours after anesthesia were recorded by a researcher (MN) blinded to the treatment assignment. Nausea was defined as subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as the labored, spasmodic, rhythmic

contractions of the respiratory muscles without the expulsion of gastric contents; vomiting was defined as the forceful expulsion of gastric contents from the mouth. Patients with more than one symptom were categorized as having experienced the most severe symptom (vomiting[retching[nausea). The researcher interviewed patients and recorded the details of any adverse effects throughout the study, as well as any spontaneous complaints.

Before beginning the study, a power analysis indicated that at least 40 patients in each group would be required to detect a decrease in the incidence of PONV of 30% with a power of 0.8 (a = 0.05). Statistical analyses of data among the groups were performed analysis of variance (ANOVA) (continuous variables), Student's t-test (continuous variables), the chi-squared test (discrete variables.

RESULTS

Thus, 119 patients were enrolled, and 40 patients were assigned to each treatment group. Patient characteristics and information on surgery and anesthesia are summarized. The treatment groups were comparable in terms of patient demographics. Waking time was different among the groups (P = 0.667: propofol, P = 0.000: dexamethasone, the incidence of patients experiencing PONV during the first 24 hours after anesthesia was 33% with propofol (P = 0.003), 15% with dexamethasone (P = 0.001), The efficacy of propofol combined with dexamethasone was superior to that of propofol alone (P = 0.029). No clinically important adverse events due to the study drugs, including extrapyramidal signs caused by traditional antiemetics (e.g., droperidol, metoclopramide), were observed in any of the groups. No patients reported disturbed normal daily activity.

Table1.

	propofol	**dexamethasone**	**P value**
Waking time (min)	9-4	9-1	0,000
Nausea	33%	19%	0,000
Retching	9%	1%	0,000
Vomiting	22%	15%	0,000

This study compared the efficacy of dexamethasone and propofol with either antiemetic alone in patients undergoing laparoscopic cholecystectomy. Although laparoscopic cholecystectomy decreased surgical morbidity and has become an accepted procedure for the treatment of cholelithiasis, the high incidence of PONV remains a major clinical problem.[11]

The etiology of PONV after laparoscopic surgery performed under general anesthesia is not fully understood, but is probably multifactorial. Several factors, including age, sex, smoking, history of motion sickness, intraoperative use of fentanyl and isoflurane, residual pneumoperitoneum after CO2 insufflation, whereas those with a history of motion sickness and smoking were excluded from the study. Therefore, the difference in the incidence of PONV among the groups could be attributed to the variation in the antiemetic drugs administered.[12]

As mentioned before, dexamethasone is a corticostereoid with an anti-inflammatory effect that provides postoperative analgesia, prevents nausea and vomiting in patients receiving highly emetogenic cancer chemotherapy, and reduces postoperative nausea and vomiting.

The recommended dose in the prevention of PONV is 8-10 mg. Therefore, in our study a dose of dexamethasone was chosen. The mechanism of the antiemetic action of dexamethasone and the precise site of action remains unclear. A previous study has suggested that dexamethasone may antagonize prostangladin or release endorphins, resulting in mood elevation, a sense of well-being, and stimulate appetite.[13] Dexamethasone was found to be effective when used alone in the prevention of PONV in several studies.

DISSECTION

The principal finding of our meta-analysis is that dexamethasone is associated with a wave of less postoperative nausea in the first 4–6 hours after laparoscopic surgeries. Postoperative vomiting and nausea at 24 hours are similar with either drug. Need for rescue antiemetic is similar with both drugs. A most important strength of our analysis is that we have not found any significant amount of heterogeneity in any analysis.

Postoperative nausea and vomiting are a common compilation after laparoscopic surgeries and may be even more distressing than postoperative pain. PONV may even delay the discharge of the patients.[14] The incidence of PONV after laparoscopic cholecystectomy may be as high as 63% when no antiemetic prophylaxis is used. Dexamethasone is the two most commonly used drugs in clinical practice for PONV prophylaxis. Individual clinical studies have found that dexamethasone is effective antiemetic prophylaxis at a dose of 5–8 mg.[15]

Individual RCTs have found that dexamethasone is effective in PONV prophylaxis after laparoscopic surgeries. However, the small sample size was the most important limitation of

the RCTs that justifies the importance of a meta-analysis. Interestingly we have found that dexamethasone decreases the incidence of early PONV after laparoscopic surgeries and none of the previous studies has reported similar findings. Alghanem et al reported that ondansetron is less effective in preventing nausea in the 0–4 h period after surgery. However, their result did not reach statistical significance probably because of the small sample size.[16]

On the contrary Gautam et al found that dexamethasone is less effective in preventing early vomiting. However, we have not found such a finding in our analysis. The longer onset of action of dexamethasone may result in relative less effectiveness in preventing early PONV. Subramaniam et al. found that ondansetron is more effective in preventing early PONV and dexamethasone are more effective in preventing late PONV after strabismus surgery.[17]

These findings have not been reflected in our analysis because we believe that PONV after laparoscopic surgeries is caused by many factors such as abdominal insufflation; those may not be fully controlled by any single prophylactic drug.

Use of single dose dexamethasone is free from significant side effects including delayed wound healing. Moreover, it may decrease postoperative pain after laparoscopic cholecystectomy. Use of PONV prophylaxis is routine in clinical practice due to the high incidence of PONV in patients who did not receive any prophylaxis. Cost of care is also an important issue in today's healthcare system. As dexamethasone is significantly cheaper than ondansetron, the former one may be a better choice for PONV prophylaxis after laparoscopic surgeries.

CONCLUSION

Postoperative nausea and vomiting (PONV) are one of the most distressing and common side effects of anesthetics and may cause severe discomfort among patients. In addition, PONV can lead to delayed post-anesthesia admission and higher medical costs.

The incidence of PONV in patients has been reported to be from 20 to 70% after various types of surgeries, when no prophylactic antiemetic is provided.

PONV can cause severe discomfort amongst patients and is probably related to several factors, which include age, sex, operation type, and anesthesia-related factors. Other factors, including obesity, a history of motion sickness and/or a history of previous postoperative emesis, and also preoperative volume loading may have an important role in PONV. The

optimal strategy for preventing PONV remains contentious. Global prophylaxis for PONV is generally not recommended, although it has been demonstrated to be cost-effective in high-risk patients. PONV occurs frequently in patients undergoing lower abdominal surgeries. With respect to anesthetic agents, nitrous oxide (N2O) and volatile anesthetics increase the occurrence of PONV, but Propofol is known to have an antiemetic effect.

The data on the efficacy of specific antiemetics and their combination are still lacking, so definitive conclusions are difficult to make at present. On the other hand, while the efficacy of Propofol is presently not clear.

Dexamethasone is superior to ondansetron in preventing postoperative nausea after 4–6 h of laparoscopic surgeries. Both the drugs are of equal efficacy in preventing postoperative vomiting up to 24 h after surgery. However, results should be interpreted with caution due to clinical heterogeneity in the included studies.

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