Granisetron Versus Dexamethasone in Prophylaxis of Nausea and Vomiting After Laparoscopic Cholecystectomy

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Abstract

Background: Post-operative nausea and vomiting (PONV) is one of the common problems after laparoscopic cholecystectomy.

Objectives: The current study aimed to compare Dexamethasone effect with that of Granisetron in prevention of PONV.

Patients and Methods: In the current study 104 patients aged 20-60 with ASA class I or II who were candidates for laparoscopic cholecystectomy were included in the study. Patients were randomly divided into two groups of A and B. 15 minutes before anesthesia induction, in group A patients 3 mg Granisetron and in group B patients 8 mg Dexamethasone was intravenously injected. Then both groups underwent general anesthesia with similar medications. After operation the prevalence of nausea and vomiting was assessed at three time intervals (0-6 hours, 6-12 hours and 12-24 hours after consciousness).

SPSS software version 16 was employed to analyze data. T test, chi-square test and Fischer exact test were performed level of significance was \( P < 0.05 \).

Results: There was no significant difference between age, gender proportion, weight, height, and body mass index (BMI) of patients in the two groups. In Dexamethasone group, seven patients experienced nausea and three patients had vomiting, and in Granisetron group, five patients experienced nausea and three patients had vomiting after consciousness. Statistical analysis indicated no significant difference between the two groups in this regard.

Conclusions: Intravenous injection of 8 mg Dexamethasone or 3 mg Granisetron before anesthesia induction had similar effects in prophylaxis of nausea and vomiting after laparoscopic cholecystectomy.
1. Background
Laparoscopic cholecystectomy is a standard treatment for cholelithiasis. In laparoscopic methods, the tissue injury is less than open surgeries but still post-operative nausea and vomiting (PONV) are among common complications, and its prevalence has been reported in different studies about 44%-83% (1, 2). PONV can lead to sweating, tachycardia, abdominal pain, prolonged recovery duration, and increased risk of aspiration (3). The etiology of PONV is not still known well, but it is probably a multifactorial phenomenon (4, 5). Gas entrance into the abdominal cavity during laparoscopy can cause increased pressure of peritoneal cavity, which is known to lead to PONV (3). Prolonged entrance of CO2 leads to pneumoperitoneum, peritoneal distention, and diaphragmatic stimulation. Intra-abdominal manipulation is one of the causes of PONV (4, 5). Different medications have been evaluated in PONV prophylaxis and patient satisfaction after cholecystectomy (1-7). Previously, anti-cholinergics, anti-histamines and phenothiazines were used to prevent PONV (8); but low effect of these medications and their complications led to drug shifts. Recent studies have shown that serotonin receptor antagonists are more effective than previous medications in PONV prophylaxis (3, 9). It has been proved that Granisetron and Ondansetron are effective medications in this field (9) but by considering the high price of these drugs, suitable substitutes are required. It was tried to compare Dexamethasone effect on PONV prophylaxis with serotonin receptor antagonists in this study. Dexamethasone is a low price corticosteroid which has anti-inflammatory effects, and some studies have also evaluated its effect on nausea and vomiting prophylaxis after chemotherapy (4, 5).

2. Objectives
The current study aimed to evaluate Dexamethasone effect versus Granisetron in nausea and vomiting prophylaxis after laparoscopic cholecystectomy.

3. Patients and Methods
After ethical committee approval and registration in IRCT (IRCT138903033939N1), 110 patients aged 20-60 who were candidates for laparoscopic cholecystectomy were included in the study. Informed consent was obtained from patients before enrollment. The patients were in ASA1 or ASA2 class in physical condition according to the American Society of Anesthesiology classification. Exclusion criteria included pregnancy, body mass index (BMI) higher than 30, history of previous abdominal surgery, existence of underlying diseases, and opium, or steroid consumption during the week before the operation. The patients were allocated, by computer-generated random numbers, into two groups. The random allocation sequence was concealed in sealed opaque envelopes until a group was assigned. Fifteen minutes before anesthesia induction, 3 mg Granisetron was injected intravenously to group A and 8 mg Dexamethasone to group B patients. All patients underwent general anesthesia with the same medications for induction, sodium thiopental 5 mg/kg, Sufentanil 0.5 μg/kg and Atracurium 0.6 mg/kg for facilitation of tracheal intubation, during anesthesia patients were monitored by electrocardiography, pulse oximetry, noninvasive blood pressure and scenography. Anesthesia maintenance in both groups was achieved by Isufluran 1.5% and after 30 minutes from induction of anesthesia incremental doses of 5 μg sufentanil was administered every 15 minutes. During laparoscopy, intra-abdominal pressure was maintained at 12 mmHg. At the end of operation CO2 was carefully evacuated by manual compression of the abdomen with open trocars. Post-operative nausea and vomiting was assessed at three time intervals (0-6 hours, 6-12 hours, and 12-24 hours after consciousness). 10 mg of Metoclopramide was injected in case of PONV existence. SPSS software version 16 was employed to analyze data. In order to compare quantitative and qualitative data between the two groups’ Chi-square test (and Fisher’s exact test if required for frequencies less than five) was utilized for the qualitative variables and Student’s t-test for quantitative variables. In cases of non-adherence, and non-parametric, equivalent assessment was employed. The level of significance was $P < 0.05$.

4. Results
Out of 110 patients assessed for eligibility, 104 patients were enrolled into the study, out of which 53 patients were placed in Dexamethasone group and 51 patients in Granisetron group. Mean age in Dexamethasone group was 43.6 ± 6.1 years whereas 41.2 ± 8.2 in Granisetron group. Data analysis indicated no significant difference in mean age between the two groups (Table 1). There was

| Table 1. Patient’s Characteristics | Dexamethasone Group (n = 53) | Granisetron Group (n = 51) | P value |
|----------------------------------|-----------------------------|---------------------------|---------|
| Age, y                           | 43.6 ± 6.1                  | 41.2 ± 8.2                | 0.322   |
| Sex, Male                        | 12                          | 14                        | 0.571   |
| BMI, kg/m²                       | 26.3 ± 4.4                  | 27.2 ± 5.1                | 0.419   |
| Operation time, min              | 48 ± 15                     | 54 ± 18                   | 0.237   |
| Anesthesia time, min             | 59 ± 17                     | 63 ± 20                   | 0.338   |

Abbreviation: BMI, body mass index.
also no significant difference in gender, BMI and opera-
tion characteristics between the two groups (Table 1).
In the first 24 hours after operation, seven patients in
Dexamethasone group experienced nausea and three pa-
tients had vomiting , in Granisetron group, five patients
experienced nausea and two had vomiting. Data analysis
indicated no significant difference in nausea and vom-
iting prevalence between the two groups (Table 2). Only
one case in Dexamethasone group reported headache.
In Granisetron group, one case of vertigo and one case of
headache were reported. Statistical analysis indicated no
significant difference between the two groups in this re-
gard (P value: 0.614).

5. Discussion
The current study showed that intravenous injection of
8 mg Dexamethasone, or 3 mg Granisetron have similar
effects on PONV prophylaxis in laparoscopic cholecystec-
tomy. These results of the current study indicated that
Dexamethasone is a suitable substitute for Granisetron.
Fukami et al. showed that Dexamethasone injection
before laparoscopic cholecystectomy leads to signifi-
cant reduction of nausea, vomiting and post-operative
pain. Fukami’s study was a clinical trial performed on
80 patients (10). In another clinical trial performed by
Binachin et al. Dexamethasone had significant effect on
PONV reduction after laparoscopic cholecystectomy but
it had no effect on pain reduction and admission dura-
tion (11). In similar studies which were performed by
Feo et al. (4) and Bisgard et al. (6), Dexamethasone effect
on PONV reduction after laparoscopic cholecystectomy
were confirmed. Karanicolas’ meta-analysis showed that dexa-
methasone leads to PONV reduction in comparison with
placebo after laparoscopic cholecystectomy (12). Biswas
et al. showed that combination of Granisetron and Dexas-
methasone is more effective than Granisetron alone on
PONV prophylaxis after laparoscopic cholecystectomy in
a clinical trial performed on 120 patients (13). Erhan et
al. evaluated Dexamethasone, Granisetron and Ondanset-
ron effects on PONV after laparoscopic cholecystectomy
in comparison with placebo. They showed that injec-
tion of 8 mg Dexamethasone is more effective than 3 mg
Granisetron or 4 mg Ondansetron in PONV prophylaxis
but the differences were not statistically significant (14).
Dexamethasone mechanisms in PONV prophylaxis are not
known well. Elhakim et al. expressed that Dexamethasone
can act as a serotonin receptor inhibitor in gastrointesti-
nal tract (1). Another study showed that Dexamethasone
leads to reduction of parasympathetic impulses to the
brain by decreasing tissue inflammation around surgery
site (7). Studies show that Vagus afferents in gastrointes-
tinal mucosa have 5-HT3 receptors which cause nausea
and vomiting. Serotonin selective receptor antagonists
(like Granisetron and Ondansetron) usually affect pe-
ripheral serotonin receptors in intestinal vagus afferents
(15). There were several limitations to this study. First,
because of ethical concerns, the placebo control group
was kept out. Second, patients were observed for only 24
h postoperatively because most patients who underwent
LC without complications were discharged a day after
operation. Third, the patients with underlying diseases
were excluded, so the results of the study should not be
generalized to other patients with severe underlying dis-
ases. Further studies should consider these limitations.
In conclusion, the results indicated that Dexamethasone
and Granisetron injection before anesthesia induction
have similar effects on nausea and vomiting prophylaxis
after laparoscopic cholecystectomy.

Acknowledgments
We thank surgery residents, especially Dr. Shahram Mo-
radi, and Anesthesia nurses, Mrs. Faranak Soufipour and
Mrs. Nahid Nazari for their help and kind cooperation.

Authors’ Contribution
The work presented here was carried out in collabora-
tion between both authors.

Financial Disclosure
None declared.

Funding/Support
None declared.

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vention of postoperative nausea and vomiting in patients un-

Table 2. Intervention Outcomes

|                      | Dexamethasone Group (n = 53), No. (%) | Granisetron Group (n = 51), No. (%) | P value |
|----------------------|--------------------------------------|-------------------------------------|---------|
| Nausea               | 7 (13)                               | 5 (10)                              | 0.587   |
| Vomiting             | 3 (6)                                | 2 (4)                               | 0.999   |
| Metoclopramide use   | 3 (6)                                | 2 (4)                               | 0.999   |
| Side effects         | 1 (2)                                | 2 (4)                               | 0.614   |

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