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Efficacy of prophylactic dexamethasone in prevention of postoperative nausea and vomiting

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Abstract *Objective:* Many trials have been conducted with regard to the relative benefits of prophylactic anti-emetic interventions given alone or in combination, yet the results remain unknown. This study reviewed the efficacy of a single prophylactic dose of dexamethasone on postoperative nausea or vomiting (PONV) after abdominal hysterectomy.

Methods: In a prospective study of 100 women undergoing total abdominal hysterectomy (TAH) under general anesthesia, the dexamethasone group (n = 50) received a single dose (8 mg) immediately after the operation, and the saline group (n = 50) received a dose of saline as a placebo, in addition to conventional management. The incidence of nausea, vomiting, the need for an anti-emetic and patient satisfaction with the management of PONV were evaluated during the first 24 postoperative hours.

Results: The overall frequency of nausea during the initial postoperative 24 in the dexamethasone and saline groups were 12% and 18%, respectively, and vomiting was 10% and 16%, respectively (P = 0.001). However, there was a lower need for a rescue anti-emetic drugs in the dexamethasone group (18% vs 24%), but it was not statistically significant (P = 0.06).

Conclusion: The results of this study indicate that a single prophylactic dose of dexamethasone after an operation can reduce postoperative nausea and vomiting.

1. Introduction

Postoperative nausea and vomiting (PONV) is an unpleasant and relatively common occurrence

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sequel of general anesthesia that may increase morbidity, prolong hospital stay and can lead to serious complications [1,2]. The overall incidence of PONV in adults is 20%—30%; the incidence rate in patients of high-risk groups can be as high as 70%—80% [3]. The incidence of postoperative nausea or vomiting depends on numerous non-anesthetic factors, including the type of surgery, duration of surgery, use of postoperative opioids, age, smoking, history of motion sickness and previous postoperative nausea history [4,5].

The etiology and consequences of PONV are complex when taking into consideration patients' medical- and surgery-related factors. A thorough understanding of these factors is necessary for the management of PONV [6]. The most common drugs used for the treatment of PONV include butyrophenones, benzamides, histamine receptor antagonists, muscarinic receptor antagonists, and 5-HT3 (5-hydroxy tryptamine 3) receptor antagonists. Non- pharmacologic treatment methods, such as acupuncture, electro-acupuncture, transcutaneous electrical nerve stimulation (TENS), and acupressure have also been studied for their efficacy in the prevention of PONV [7]. There are no completely effective anti-emetic agents for this condition, but recommendations for treatment strategies are separately available. The optimal strategy for prevention and management of PONV is still controversial. Even though many drugs have been studied for the prevention of PONV, prophylaxis is not very effective, may be costly, and has a potential risk of adverse drug reactions [8,9]. Tong J. Gan, et al. reported ''reducing baseline risk factors can significantly decrease the incidence of PONV. Strategies recommended to reduce baseline risk include: the avoidance of general anesthesia by the use of regional anesthesia; preferential use of propofol infusions; avoidance of nitrous oxide; avoidance of volatile anesthetics; minimization of peri-operative opioids and adequate hydration [10]''.

Dexamethasone is a high-potency, long-acting glucocorticoid with little mineralocorticoid effect, with a biologic half-life of 36—72 h that has been extensively used in the perioperative setting. Dexamethasone is a low-cost and effective anti-emetic drug, with minimal side effects after a single-dose administration [3]. Dexamethasone was first reported to be an effective anti-emetic regimen in patients receiving cancer chemotherapy [11]. Recently, studies showed that dexamethasone can be effective in preventing PONV in adults and children. Compared with other preventive medications, dexamethasone has equal or even better efficacy in reducing the incidence of PONV and has the advantages of low cost and longer effectiveness as well. Although the action mechanism of dexamethasone is hitherto not fully understood, animal studies have confirmed that the vomiting center in the brain stem plays a central role [12—14].

The purpose of this study was to evaluate the efficacy of a single prophylactic dose of dexamethasone treatment for reducing PONV in women undergoing general anesthesia for abdominal hysterectomy.

2. Methods

This prospective, double-blind, placebo-controlled study was designed and conducted on 100 women undergoing abdominal hysterectomy for various indications. All patients were referred to Shahid Sadoughi hospital in Yazd from June 2009 to September 2010. The adopted protocol was approved by the hospital research and ethics committee (Institutional Review Board) in accordance with the Helsinki declaration. All women were interviewed individually by the researcher. Written informed consent was obtained from all the patients.

Sample size estimations were based on the results of a previous study, and assuming an α level of 0.05 and β error of 0.8, 44 patients were needed per group to detect a 10 point difference on a 0—100 visual analog nausea scale score. To account for possible loss to follow-up, it was decided to include 50 patients per trial arm.

Women were excluded from the study if they had a known allergy/hypersensitivity to dexamethasone, nausea or vomiting within 24 h before their operation, had received an anti-emetic within 48 h before surgery, or had any gastrointestinal disorders (*e.g.*, esophagitis, gastritis). Before entry into the study, patients provided detailed medical histories and demographic information.

All surgeries were performed under general anesthesia. In this hospital, general anesthesia was comprised of pre-medication of 2 mg midazolam intravenous (IV) and induction anesthesia fentanyl 2 μg/kg + propofol 2 mg/kg IV with ventilation of N2O - O2 (50—50) and infusion of propofol 100—200 mg/kg/min as maintenance anesthesia.

At the end of the surgery, the patients were randomly allocated to either the administration of a single dose of dexamethasone 8 mg IV (50 women) or saline 2 mL IV (50 women) as a placebo, in addition to conventional management. Randomization was performed with a computer-driven random

number sequence and sealed in opaque envelopes. Prior to each operation, the set was prepared with identical syringes containing dexamethasone or saline for injection with the purpose of maintaining blindness in the study.

Following surgery, all women were transferred to the post-anesthesia care unit (PACU) and stayed there for around 2 h. Lactated Ringer (1000–2000 mL) was used as fluid maintenance. Morphine 5 mg IV was used as pain rescue medication during PACU stay and mefenamic acid 500 mg PO Q4H hours was given as part of the standard post-operative pain procedures. Postoperatively, patients were NPO for 12 h and were observed for 24 h. At the discretion of the attending surgeon, feeding was started on the first post-operative day with clear liquid and solid food was started after bowel function was established. During the observation period, arterial blood pressure (BP), heart rate (HR), and respiratory rate (RR) were monitored every 4 h except when patients were sleeping. All were given routine prophylactic antibiotics.

The frequencies of nausea and vomiting, the intensity of nausea, and the proportions of patients who requested rescue anti-emetic were recorded. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. Vomiting was defined as the forceful expulsion of gastric contents from the mouth. Also retching was recorded as an episode of vomiting. Nausea was scored by using a linear scale from 0 to 10, with 0 representing no nausea and 10 representing nausea ''as bad as it can be.'' Rescue medication for severe nausea (nausea for more than 30 min or at the patient's request to treat intolerable nausea) and vomiting (more than one emetic episode in 15 min) were treated according to the hospital's routine (metoclopramide 10 mg IV PRN every 8 h). The treatment was repeated if necessary. The postoperative nausea, vomiting and medications required were evaluated and recorded by a second-year resident and were collected every 4 h during the first 24 h after surgery. The duration of hospital stay and the incidence of side effects were recorded as well.

Patients were asked to rate their level of satisfaction by using a scale from 0 to 10.

Analysis of data was performed with the SPSS 15.5 software. Statistical methods included Student's *t*-test, Fisher exact test and χ^2 test; *p*-values less than 0.05 were considered as significant.

3. Results

One hundred women completed the study: 50 women received a single dose (8 mg) of dexamethasone and 50 women received saline as a placebo in addition to conventional management. Table 1 shows that there was no difference in the demographic and medical characteristics of both studied groups. As a result of the study design, the two study groups were also identical for indication of hysterectomy.

Table 2 presents the frequencies of post-operative nausea and vomiting. As shown in Table 2, patients who received dexamethasone differed from those who received saline alone in total frequency of nausea and vomiting (22% vs 34%, $P = 0.004$) and in percentage of patients requiring a rescue anti-emetic during the 24 h following surgery, but it was not statistically significant (18% vs 24%, $P = 0.06$).

Patient satisfaction with dexamethasone was higher than saline. Hospital stay was similar in both groups, and adverse reactions were not seen in any group.

4. Discussion

The results of this study showed that dexamethasone was effective in reducing the occurrence of PONV after abdominal hysterectomy. The overall incidence of PONV within the first 24 h after surgery was 22% in the group who used dexamethasone and 34% in the saline group.

These findings are in accordance with recent studies that showed dexamethasone can be effective in preventing PONV in adults and children. Compared with other preventive medications, dexamethasone has equal or even better efficacy in reducing the incidence of PONV and has the advantages of low cost and longer effectiveness as well [12–16].

Tzeng et al. reported that the administration of low dose dexamethasone (5 mg) was more effective than metoclopramide or saline in the prevention of post-operative nausea and vomiting associated with epidural morphine for post-operative analgesia [14]. Their study was about dexamethasone's effect on reducing nausea and vomiting in conjunction with morphine and epidural analgesia; they found that low dose dexamethasone was more effective than metoclopramide for PONV for post-operative analgesia. On the other hand, Liu and colleagues demonstrated that dexamethasone alone at doses of 5 mg and 2.5 mg are as effective as 10 mg in reducing the incidence of PONV after gynecologic surgery [17]. Although, El hakim et al. believed that 8 mg is the minimum dose of dexamethasone that effectively prevents PONV [14].

Table 1 Patient demographics and operation characteristics.

Characteristics		Dexamethasone group (n = 50)	Saline group (n = 50)	P value
Age (year) (Mean ± SD)		44 ± 5.6	43 ± 5.1	0.2
BMI (Mean ± SD)		23 ± 3.1	24 ± 4.5	0.08
Indication of Hysterectomy	AUB [N(%)]	36 (72)	33 (66)	0.07
	Others [N(%)]	14 (28)	17 (34)	
Duration of operation (minute) (Mean ± SD)		87 ± 12	89 ± 10	0.09
Duration of hospital stay (day) (Median)		3	3	—

Table 2 Incidence of nausea and vomiting and requiring a rescue anti-emetic during 24 h after surgery.

	Dexamethasone group (n = 50)	Saline group (n = 50)	P value
0—2 h after surgery [N (%)]			
Nausea	0 (0)	1 (2)	0.009
Vomiting	0 (0)	0 (0)	—
2—6 h after surgery [N (%)]			
Nausea	2 (4)	3 (6)	0.005
Vomiting	1 (2)	2 (4)	0.006
6—12 h after surgery [N (%)]			
Nausea	3 (6)	2 (4)	0.01
Vomiting	1 (2)	2 (4)	0.007
12—24 h after surgery [N (%)]			
Nausea	1 (2)	3 (6)	0.001
Vomiting	3 (6)	4 (8)	0.004
Totally	11 (22)	17 (34)	0.004
Requiring rescue anti-emetic	9 (18)	12 (24)	0.06

Henzi et al. also showed that a single prophylactic dose of dexamethasone is anti-emetic compared with a placebo, but the best late prophylaxis (after 24 h) of PONV is achieved by a combining dexamethasone with ondansetron or granisetron [18].

Dexamethasone is a glucocorticoid that produces a strong anti-emetic effect and, with its strong anti-inflammatory action, has been shown to decrease post-operative pain. This is the reason for patient satisfaction. In the present study, patient satisfaction with dexamethasone was higher than saline.

In the present study, no side effects related to the use of dexamethasone and saline were noted. Long-term corticosteroid therapy may have significant morbidity, such as an increased risk of infection, delayed wound healing, glucose intolerance, and adrenal suppression. However, side effects from brief (24 h) corticosteroid treatment have been rare [2].

Cost is an ever-increasing concern in today's healthcare system [8]. Dexamethasone is a relatively inexpensive drug in Iran. Dexamethasone 8 mg costs $0.38 US, whereas commonly used anti-emetic metoclopramide 10 mg cost $0.49 US.

Further studies with more patients and longer follow-up are indicated to show side effects of dexamethasone. Also, further studies with different doses of dexamethasone must be accomplished to obtain the minimum dose of dexamethasone that is effective in preventing PONV.

5. Conclusion

Results suggest that prophylactic administration of dexamethasone 8 mg can reduce the post-operative frequency of PONV in women undergoing abdominal total hysterectomy.

Conflict of interest

There is no conflict of interest.

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