



Journal of Medical Sciences

ISSN 1682-4474

science
alert

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JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

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Effects of Dexamethasone on Early Postoperative Pain, Nausea and Vomiting and Recovery Time after Ambulatory Laparoscopic Surgery

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Corticosteroids can decrease pain and postoperative nausea and vomiting after surgery. Therefore, we conducted a double blinded placebo controlled study to evaluate the effect of preoperative administration of dexamethasone on early postoperative pain, nausea and vomiting and recovery process, after ambulatory laparoscopic surgery. One hundred women undergoing laparoscopy under general anesthesia for Assisted Reproductive Technologies (ART) were randomly assigned to receive either dexamethasone 8 mg IV, or an equal volume of saline before the start of surgery. Patients were premedicated with fentanyl 2 $\mu\text{g kg}^{-1}$ and midazolam 2 mg intravenously. Anesthesia was induced with propofol 2 mg kg^{-1} and then maintained by 100 $\mu\text{g kg}^{-1} \text{h}^{-1}$ propofol with oxygen. Tracheal intubation was facilitated by succinylcholine 1.5 mg kg^{-1} and atracurium was injected 0.03 mg kg^{-1} when it was necessary. All patients were fast-tracked directly from the operating room to the recovery area. The severity of postoperative pain in dexamethasone group was significantly less than saline group ($p = 0.011$). Ten patients (20%) in control and only one patient (2%) in dexamethasone group required additional IV analgesic ($p = 0.012$). Two (4%) patients in dexamethasone group and 21 (42%) in saline group had nausea and vomiting within 2 hour after surgery ($p = 0.014$). The ambulation time was not different but recovery time and home readiness time was significantly shorter in dexamethasone group ($p = 0.02$ and $p = 0.01$, respectively). Side effects related to the use of dexamethasone was not found. We concluded that administration of IV dexamethasone 8 mg before surgery, shortened the recovery time and time to home readiness; decreased postoperative pain, nausea and vomiting in patient population undergoing ambulatory laparoscopic surgery.

Key words: Dexamethasone, laparoscopy, pain, recovery time, nausea, vomiting

INTRODUCTION

Glucocorticoids are well known for their analgesic, anti-inflammatory, immune-modulating and anti-emetic effects, although the mechanisms by which glucocorticoids exert their action are far from clarified (Sapolsky *et al.*, 2000; Huang *et al.*, 2001).

Several randomized, clinical trials in many different major and minor surgical procedures have been conducted to examine the effects of a perioperative single-dose glucocorticoid administration on surgical outcome (Wang *et al.*, 2000; Holte and Kehlet, 2002; Bisgaard *et al.*, 2003; Paech *et al.*, 2007).

The overall results on postoperative outcome have either been positive in favor of the glucocorticoid group or without differences between study groups, with postoperative nausea and vomiting and pain as outcome parameters most significantly improved (Wang *et al.*, 2000; Coloma *et al.*, 2001; Laiq *et al.*, 2005; Feo *et al.*, 2006; Paech *et al.*, 2007).

Surgery for Assisted Reproductive Technologies (ART) has developed in many countries and performed on an ambulatory basis. Since the duration of surgery in these procedures is short, the main purpose of anesthesia for these operations, is shortening the recovery time by reducing the common complications such as nausea, vomiting and pain.

Therefore, we designed a placebo-controlled study to test the hypothesis that a single dose of 8 mg IV dexamethasone, would decrease postoperative pain, nausea and vomiting and facilitate early recovery after ambulatory laparoscopy in these group of patients.

MATERIALS AND METHODS

This randomized clinical trial was performed in Dr. Shariati Hospital of Tehran University of Medical Sciences from November 2006 to February 2007. The study protocol conformed to the ethical guidelines of the 1989 Declaration of Helsinki.

After Institutional Ethics committee approval, each patient's informed consent was obtained separately. One hundred ASA I and II women aged 20-45 years, who were scheduled for outpatient laparoscopic surgery under general anesthesia for Assisted Reproductive Technologies (ART) were included in this study. Patients with sensitivity to Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), gastrointestinal bleeding, known allergy to any study drug, those receiving chronic steroid therapy were excluded.

On arrival in the operating room, standard anesthesia monitors were placed. Patients preoxygenated with oxygen

(5 L min⁻¹) by mask with a port for monitoring expired CO₂ levels. All patients were premedicated with midazolam 2 mg IV (Amp 5 mg mL⁻¹, MIDAZOLEX®5, EXIIR-IRAN) and fentanyl 2 µg kg⁻¹ (Amp 10 mL, Fentanyl-Janssen™, Belgium). Patients were subsequently administered either 2 mL saline (Control group) or 8 mg dexamethasone (Amp 8 mg 2 mL, DEXACID®, Rasht-Iran) intravenously (Dexamethasone group). Randomization was based on computer-generated codes that were concealed until interactions were assigned.

The coded syringes were prepared by an independent anesthetist in equal volume (2 mL) and shape, there fore both the anesthesiologist and the patient was blinded to the group assignment.

Anesthesia was induced with propofol 2 mg kg⁻¹ (Amp 20 mL, Dongkook Pharm. Co, LTD) and then maintained by 100 µg kg⁻¹ h⁻¹ propofol with oxygen.

Tracheal intubation was facilitated by succinylcholine 1.5 mg kg⁻¹ (Vial 500 mg, BIOLOGICI ITALIA LAB™-ITALY) and atracurium was injected 0.03 mg kg⁻¹ (Amp 10 mg mL⁻¹ Mayne Pharma Plc™, UK) when it was necessary. At the end of the operation, the propofol infusion was discontinued and after reverse of muscle relaxant, trachea was extubated and patients were moved from the operating table to the transport stretcher before transfer to the step-down (Phase II) recovery unit. Duration of surgery and anesthesia, severity of postoperative pain, presence of Post Operative Nausea and Vomiting (PONV) were recorded. Surgery time was determined from skin incision to completion of the procedure and anesthesia time was calculated from the start of the propofol injection to tracheal extubation. Before leaving the operating room, fast-track eligibility (score > 9) was assessed using a standardized criteria unit by a blinded observer (Feeley and Macario, 2005; Chung *et al.*, 1995). Pain scores were recorded using a 10 cm linear Visual Analog Scale (VAS), with 0 corresponding to no pain and 10 to the worst imaginable pain.

The requirements for additional intravenous opioid analgesics were also recorded in the Phase II recovery unit. Recovery times from extubation to oral intake (i.e., time until the patient was able to tolerate oral intake), ambulation (i.e., time until the patient walked unassisted) and home readiness (i.e., time until the patient was judged to be fit for discharge home) were assessed at 15 min intervals in Phase II recovery by a blinded observer. Home readiness required that the patient be awake, alert, with stable vital signs on sitting and standing, not experiencing side effects and be able to ambulate without assistance.

Statistical analysis: A sample size of 50 patients in each group will be sufficient to detect a 30% difference of in the incidence of postoperative nausea and vomiting and/or pain between the study groups assuming power of 95% and a significant level of 0.05. Statistical analysis was performed With SPSS package version 11.5. Data were analyzed by independent sample t-test, chi-square or fisher exact test when appropriate. $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The patients' characteristics (e.g., age, weight) and the durations of anesthesia and surgery were similar between the two groups (Table 1).

All patients achieved a fast-track score > 9 (post anesthesia recovery score) before leaving the operating room.

The severity of postoperative pain in dexamethasone group was significantly less than saline group ($p = 0.011$). Ten patients (20%) in control group and only one patient (2%) in dexamethasone group required additional IV analgesic that was statistically significant ($p = 0.012$) (Table 2).

The ambulation time was not different but recovery time and home readiness time was significantly shorter in dexamethasone group ($p = 0.02$ and $p = 0.01$, respectively) (Table 2).

We used the total incidence of nausea and vomiting to present PONV, in the operating room before transferring to recovery (phase I) and during stay in recovery (phase II) (zero to two hours postoperatively). Two (4%) patients in dexamethasone group and 21 (42%) in saline group had nausea and vomiting after surgery ($p = 0.014$).

Table 1: Demographic data, surgery and anesthesia time in the study groups

Parameters	Control(n = 50)	Dexamethasone (n = 50)
Age (years)*	35±10	36±9
Weight (kg)*	75±16	80±11
ASA (I/II)†	36/14	38/12
Surgery time (min)*	30±14	33±10
Anesthesia time (min)*	45±16	46±14

*: Values are expressed as means±sd †: ASA = American Society of Anesthesiologists

Table 2: Postoperative Pain; Nausea and vomiting; Recovery, Ambulation and home readiness times and additional Analgesics Requirements in study groups

Parameters	Control (n = 50)	Dexamethasone (n = 50)
VAS Pain score (0-10)†	7(2-9)	3(0-4)*
PONV†† (n, %)	21(42%)	2(4%)
Recovery time (min)	68±4	60±2*
Ambulation time (min)	73±15	70±14
Home readiness (min)	120±23	95±32*
Analgesic requirement (n, %)	10(20%)	1(2%)*

†: Data are presented as median (Range); *: $p < 0.05$ compared to control group; ††: Post operative nausea and vomiting

Side effects related to the use of dexamethasone was not found.

Although surgery for assisted reproductive technologies performed on an ambulatory basis and duration of surgery in these procedures is short, common complications such as nausea, vomiting and pain can delay recovery and increase discharge time. In a placebo controlled study we showed that administration of 8 mg dexamethasone intravenously before surgery, decreased postoperative pain, nausea and vomiting, shortened the recovery and time to home readiness in these patient population.

We found that two (4%) patients in dexamethasone group compared with 21(42%) patients in saline group had nausea and vomiting within 2 h after surgery ($p = 0.014$). In a study by Wang *et al.* (2000) for evaluating the effect of 10 mg dexamethasone in ninety women undergoing laparoscopic tubal ligation, 27% of patients in dexamethasone group compared with 63% in saline group reported nausea and vomiting within 4 h after surgery ($p < 0.01$) that was correlated with present study.

Laiq *et al.* (2005) evaluated the efficacy of 8 mg intravenous dexamethasone for preventing PONV in hundred women undergoing gynecological laparoscopic surgery. They found that 26% of patients in the dexamethasone group in comparison with 54% of patients in the saline group reported PONV ($p < 0.01$) that was similar to present study.

In another study, by Coloma *et al.* (2001) the effect of 4 mg IV dexamethasone compared with saline in eighty patients undergoing ambulatory anorectal surgery. They found that incidences of postoperative pain and PONV were small in both groups but the time to home readiness was significantly shorter in the dexamethasone group.

In present study the severity of postoperative pain in dexamethasone group was significantly less than saline group, These differences, may be due to their lower dose of dexamethasone and also different type of surgery.

Feo *et al.* (2006) studied the effect of 8 mg dexamethasone in 101 patients undergoing laparoscopic cholecystectomy. They reported that Seven patients (14%) in the treatment group had nausea and vomiting compared with 24 (46%) in the control group ($p = 0.001$), but no difference in postoperative pain scores and analgesic requirements was detected between groups. This difference in postoperative pain with present study, may be due to their different method and drugs were used for induction and maintenance of anesthesia.

In most studies the commonly used dose for preventing PONV and postoperative pain were 8-10 mg (Wang *et al.*, 2000; Bisgaard *et al.*, 2003; Laiq *et al.*, 2005; Feo *et al.*, 2006).

We chose the dose of 8 mg which had the best results and the least side effects according to previous studies. Dose-response studies, however, will be necessary in the future to determine the optimal dose of dexamethasone for prevention PONV and postoperative pain in patients undergoing ambulatory laparoscopic surgeries for ART.

Long-term corticosteroid therapy may have significant morbidity. However, side effects from brief (24-48 h), even high dose corticosteroid treatment have been rare. Although a single dose of dexamethasone is considered safe, further study is indicated.

In conclusion, we found that 8 mg dexamethasone significantly reduced the incidence of postoperative pain, PONV and shortened the recovery process in women undergoing laparoscopic surgery.

ACKNOWLEDGMENTS

Author would like to special thanks to anesthesia staff for gathering patient's information and data. This study was supported by a grant from Tehran University of Medical Sciences.

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