

Original Article

Effective analgesic dose of dexamethasone after painless abortion

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Abstract: Background and purpose: Dexamethasone is known to produce analgesic effects, but the optimal analgesic dosage of dexamethasone remains unclear, especially in patients without postoperative use of other analgesics. The purpose of this study was to explore the effective analgesic dose of dexamethasone in day surgery patients undergoing painless abortion. Methods: 287 patients undergoing painless abortion were randomly assigned to one of four groups: control group receiving saline and dexamethasone groups receiving 0.1, 0.15, or 0.2 mg/kg dexamethasone. Drugs were intravenously injected 30 min before induction of anesthesia. All patients underwent the same anesthesia procedure using propofol and remifentanyl. The visual analogue scale (VAS) scores and occurrence of nausea, vomiting and drug-induced side effects were recorded at 1, 2 and 24 h after operation. Results: There were no significant differences in patient's clinical characteristics, surgical features and frequency of occurrence of nausea and vomiting among the four groups ($P > 0.05$). The VAS scores at rest and during coughing at 2 h after operation (time of discharge from the hospital) were significantly lower in patients receiving 0.2 mg/kg dexamethasone compared with control patients ($P < 0.05$). Conclusion: Intravenous injection of 0.2 mg/kg dexamethasone before induction of anesthesia can significantly reduce the VAS scores at 2 h after painless abortion.

Keywords: Dexamethasone, abortion, analgesia, nausea, vomiting

Introduction

Dexamethasone is commonly used for the prevention of postoperative nausea and vomiting (PONV), and has been widely used for hospitalized surgery patients and day surgery patients because of its low cost. However, the analgesic effects of dexamethasone and the optimal analgesic dosage of dexamethasone remain controversial. It has been reported that the analgesic dosage of dexamethasone ranges from 6 mg to 80 mg [1-4]. However, these studies investigated the analgesic effect of dexamethasone on hospitalized patients with postoperative use of analgesics. There are no reports on the analgesic effect of dexamethasone in patients (such as day surgery patients) without postoperative use of analgesics. In the present study, we performed a randomized, double-blind, placebo-controlled study to investigate the effective analgesic dose of dexamethasone in day surgery patients undergoing painless abortion.

Methods

The Medical Ethics Committee of the Beijing YouAn Hospital approved this study, and all patients provided informed consent prior to inclusion in the study. This study included 287 patients who underwent painless abortion. Inclusion criteria were as follows: 1) age 18-36 years; 2) American Society of Anesthesiology (ASA) physical status I or II; 3) body mass index (BMI) $< 30 \text{ kg/m}^2$; and 4) nonsmoker. Exclusion criteria included: 1) severe heart, lung, liver or kidney function insufficiency; 2) a history of diabetes and gastrointestinal ulcer; 3) a history of chronic pain; 4) contraindicated or allergic to dexamethasone; and 4) administration of analgesic 24 h before anesthesia.

Patient assignment was randomized and double-blind. Using a computer-generated random number table, patients were assigned into four groups as follows: control group receiving 3 ml saline, and dexamethasone groups receiving

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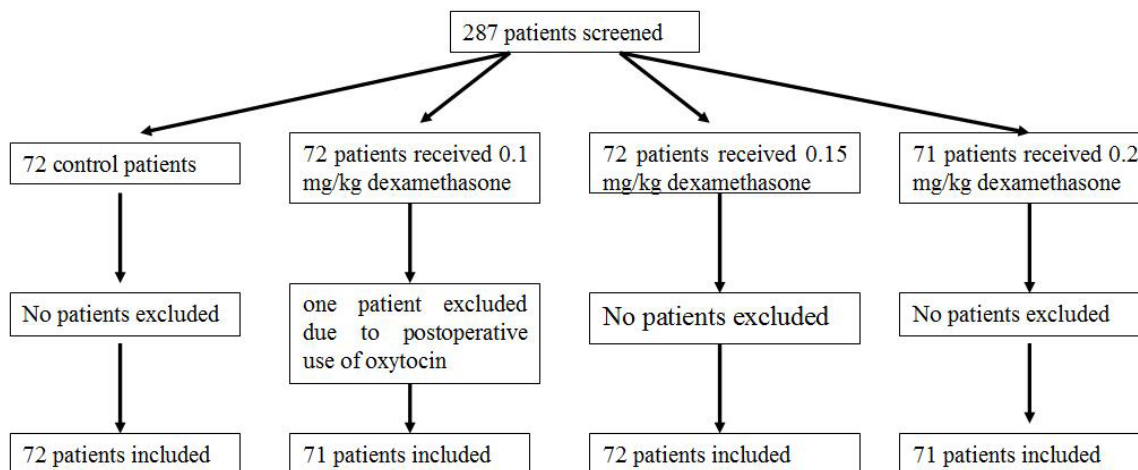


Figure 1. Patient flow chart with exclusion reasons.

Table 1. Clinical characteristics of patients and operation features in the four groups

	Control group (n = 72)	Group D1 (n = 71)	Group D2 (n = 72)	Group D3 (n = 71)
Age	26 (3)	27 (3)	28 (4)	27 (3)
BMI	22 (3)	22 (2)	23 (3)	23 (2)
PONV or motion sickness	11 (15)	13 (18)	17 (24)	15 (21)
ASA I/II	56/16	58/13	59/13	54/17
Anesthesia time (min)	13 (1.6)	12 (1.7)	13 (1.7)	13 (1.6)
Operation time (min)	6 (2.3)	6 (1.9)	5 (2.4)	6 (2.3)
Use of ephedrine (n)	9 (13)	11 (16)	17 (24)	15 (21)
Use of atropine (n)	14 (19)	18 (25)	10 (14)	12 (17)
Dosage of remifentanil (μg)	40 (4.6)	39 (4.6)	39 (4.9)	38 (4.6)
Dosage of propofol (mg)	188 (25)	176 (24)	183 (22)	178 (18)

Data are presented as n (%) or mean (standard deviation); BMI, body mass index, PONV, postoperative nausea and vomiting.

0.1, 0.15, or 0.2 mg/kg dexamethasone dissolved in 3 ml saline (Groups D1, D2 and D3, respectively). All drugs were prepared by a nurse blinded to the experimental conditions and were randomly assigned to each group by using a computer-generated random number table.

All patients were deprived of food for 6 h and water for 4 h prior to surgery. Open venous access was established in patients before they entered the operation room. All patients received drugs intravenously 30 min before operation. No other preoperative drugs were administered. The patients' electrocardiography (ECG), heart rate (HR), nontraumatic blood

pressure (BP), and peripheral blood oxygen saturation (SpO_2) were routinely monitored with a Philips MP70 electrocardiogram (Philips, the Netherlands) in the operating room. Patients were placed in the supine position. The elbow was fixed, and venous access was established in the left median cubital vein.

All patients underwent the same anesthesia procedure after disinfection and draping. Anesthesia was induced through an intravenous injection of remifentanil (0.25 $\mu\text{g}/\text{kg}$) at an injection rate of 0.125 $\mu\text{g}/\text{kg}/\text{min}$, followed by intravenous infusion of remifentanil at an infusion rate of 0.05 $\mu\text{g}/\text{kg}/\text{min}$. Propofol was infused at a rate of 1 mg/kg/min starting at 2 min after intravenous infusion of remifentanil until the patients lost consciousness (loss of consciousness referred to no responses to language and touch). Anesthesia was maintained with continuous intravenous infusion of propofol at a rate of 0.1 mg/kg/min. The operation started after patients lost consciousness. After operation, remifentanil and propofol were immediately stopped. If the body was moved during operation, a single dose of propofol (0.5 mg/kg) was injected intravenously. If intraoperative BP was lower than 80% of baseline BP,

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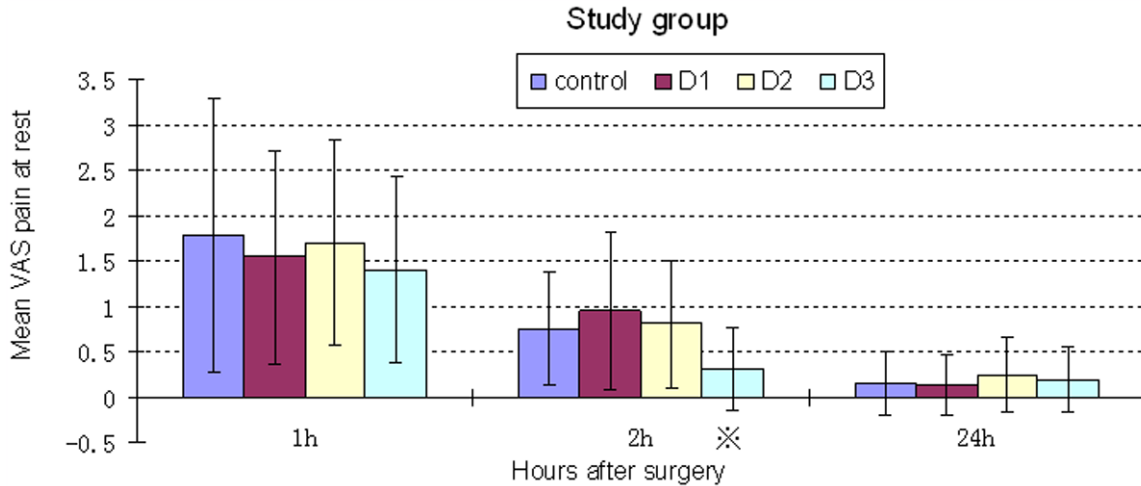


Figure 2. VAS scores at rest at 1, 2, and 24 h after operation in the control, D1 (0.1 mg dexamethasone), D2 (0.15 mg dexamethasone), and D3 (0.2 mg dexamethasone) groups.

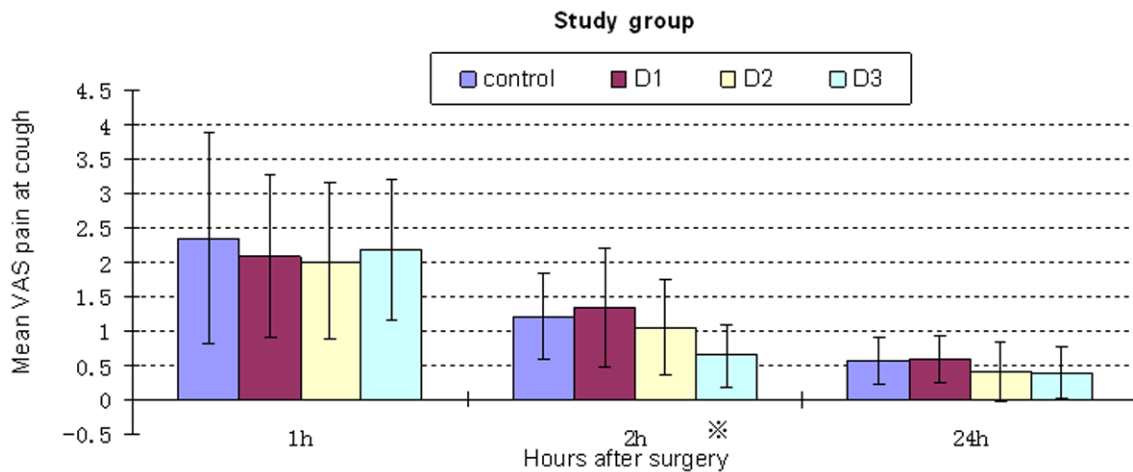


Figure 3. VAS scores during coughing at 1, 2, and 24 h after operation in the control, D1 (0.1 mg dexamethasone), D2 (0.15 mg dexamethasone), and D3 (0.2 mg dexamethasone) groups.

ephedrine (6 mg) was administered intravenously. If the HR was < 60 beats/min, atropine (0.2 mg) was administered intravenously. Oxygen was supplied with a low-oxygen oxygen mask. When SpO₂ was < 94%, artificial ventilation was performed. All surgeries were performed by the same obstetrician.

The anesthesia time, operation time, dosages of remifentanyl and propofol, and occurrence of hypotension and bradycardia were recorded. The visual analogue scale (VAS) score were evaluated during coughing and at rest at 1, 2 and 24 h after operation by a nurse blinded to the experimental condition, using a 10 cm

scale marked from 0 to 10, on which patients indicated the severity of pain. In the VAS, 0 means no pain, and 10 means maximal intolerable pain. In addition, the occurrence of nausea, vomiting and drug-induced side effects was recorded at 1, 2 and 24 h after operation. All patients were observed in the recovery room for 2 h after operation, and were discharged. The postoperative 24-h data were obtained via telephone follow-up after patients gave their consent.

Statistical analysis

Numerical values are presented as mean and standard deviation. Repeated measures analy-

Table 2. Occurrence of postoperative nausea and vomiting (PONV)

	Control group (n = 72)	Group D (n = 71)	Group D (n = 72)	Group D3 (n = 71)
0~1 h	2	0	1	0
1~2 h	0	0	0	0
2~24 h	0	0	0	0

sis of variance (ANOVA) was used to compare differences in the VAS score within the same group. One-way ANOVA was used to compare differences in the age, BMI, anesthesia time, operation time, and dosage of remifentanyl and propofol among groups. Categorical data including ASA score, occurrence of PONV, numbers of patients receiving ephedrine and atropine, and occurrence of nausea and vomiting were compared using chi square. Statistical significance was considered as $P < 0.05$.

Results

Of 287 patients, one patient was excluded due to postoperative use of oxytocin. **Figure 1** shows a flow chart describing the distribution of patients in the four groups of this study with exclusion reasons. **Table 1** summarizes the clinical characteristics of patients in the four groups. There were no significant differences in clinical characteristics among the four groups ($P > 0.05$, **Table 1**). There were no significant difference in the anesthesia time, operation time, and dosage of propofol and remifentanyl among the four groups ($P > 0.05$, **Table 1**). There was no significant difference in the number of patients with intraoperative use of ephedrine or atropine among the four groups ($P > 0.05$, **Table 1**).

The VAS scores at 1, 2 and 24 h after operation were not significantly different in Group D1 and D2 compared with the control group ($P > 0.05$). The VAS scores at rest and during coughing at 2 h after operation were significantly lower in Group D3 compared with the control group ($P < 0.05$, **Figures 2, 3**).

The frequency of occurrence of PONV in the control, D1, D2, and D3 groups was 2%, 0%, 0%, and 0%, respectively. There was no significant difference in the frequency of occurrence of PONV among the four groups ($P > 0.05$, **Table 2**).

Discussion

It has been reported that 10 mg dexamethasone can reduce the analgesic dosage within 2 h after laparoscopic hysterectomy, and 15 mg dexamethasone can reduce the amount of postoperative analgesic dosage within 24 h after surgery [5]. However, in another study, 4 mg dexamethasone was shown to be ineffective for postoperative analgesia [6]. These studies suggest that the analgesic effect of dexamethasone is dose-dependent. In addition, several studies have shown that the VAS scores at rest are not significantly different in patients receiving dexamethasone compared with control patients [7-13]. This result is likely due to postoperative use of analgesics in these studies. In the present study, to investigate the analgesic effect of dexamethasone, we did not use any analgesics postoperatively. In addition, to reduce the effect of intraoperative analgesics on postoperative pain, we selected remifentanyl, an opioid analgesic with a short half-life that does not accumulate in the body. The incidence of PONV is approximately 20-80%, and the incidence for PONV is higher in females and risk factors for PONV include the use of opioid analgesics, non-smoking, and a history of PONV and motion sickness. Therefore, in the present study, we selected painless abortion patients, with three risk factors of PONV as study subjects.

In the present study, we found that the VAS scores at 1, 2 and 24 h after operation were not significantly different in patients receiving 0.1 and 0.15 mg/kg dexamethasone compared with control patients. The VAS scores at 2 h after operation were significantly lower in patients receiving 0.2 mg/kg dexamethasone compared with the control patients. Our findings suggest that dexamethasone at the dose of 0.2 mg/kg can obviously produce analgesic effects, which is consistent with a previous report by De Oliveira et al. [14]. To date, it is generally believed that the analgesic effect of dexamethasone is associated with its anti-inflammatory action, including inhibition of leukocyte migration, maintenance of intact cell membrane, reduction of lysosome release, and reduction of fibroblast proliferation [15-17]. In the present study, we found that the VAS scores at 1 h after operation were not significantly different in patients receiving 0.2 mg/kg dexamethasone compared with control patients.

This may be associated with a slow onset of dexamethasone. Ritva et al. [18] reported that the maximum analgesic effect of dexamethasone occurred at 2-4 h after intravenous injection. Therefore, at 1 h after operation, dexamethasone does not produce its analgesic effect, and at 2 h after operation, dexamethasone starts to exert its analgesic effect, which can explain our finding that the VAS scores at 2 h after operation were significantly lower in patients receiving 0.2 mg/kg dexamethasone compared with the control patients. These findings agree with a previous report by Romundstad et al. [19] showing that methylprednisolone (125 mg) produced its maximum analgesic effect at 1 h after intravenous injection. In addition, it has been reported that dexamethasone can reduce the postoperative dosage of analgesics within 2 h after operation, suggesting that the rapid onset of dexamethasone may be associated with its action on the membrane-bound receptors [20, 21]. In the present study, we found that the VAS scores at 24 h after operation were low and similar in both control and dexamethasone groups, suggesting that painless abortion resulted in a small trauma and weak inflammation.

In the present study, we found that of 288 patients, PONV only occurred in 3 patients. The frequency of occurrence of PONV in the present study is lower than that in previous studies (25-30%) [22, 23]. The low frequency of occurrence of PONV is likely associated with the specific surgical feature of painless abortion. Although we selected female nonsmoker patients and used opioid analgesics during operation, the anesthesia time is very short for painless abortion, and only short-acting remifentanyl without accumulation in the body was used. In addition, during operation, we used propofol, which can reduce PONV.

The side effects of dexamethasone include hyperglycemia, gastrointestinal ulcer, and increased risk for infection. In the present study, we excluded patients with diabetes, gastrointestinal ulcer, and infection from this study. In addition, several studies have shown that the risk of these side effects is negligible when a single low dose of dexamethasone is used [24-26]. Therefore, in the present study, we did not find any side effects in patients receiving 0.2 mg/kg dexamethasone.

In summary, compared with the control group, intravenous injection of 0.2 mg/kg dexamethasone before induction of anesthesia can significantly reduce the severity of pain at 2 h after painless abortion.

Disclosure of conflict of interest

None.

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