J Anesth (2010) 24:24–30
DOI 10.1007/s00540-009-0830-8

ORIGINAL ARTICLE

Dexamethasone before total laparoscopic hysterectomy: a randomized controlled dose–response study

Chitra Rajeswari Thangaswamy · Vimi Rewari · Anjan Trikha · Maya Dehran · Chandralekha

Received: 23 April 2009 / Accepted: 10 August 2009 / Published online: 6 January 2010

Abstract
Purpose A prospective, randomized, double blind, placebo-controlled study was undertaken to evaluate the efficacy of a single preoperative dose of dexamethasone, in different dosages, in providing postoperative analgesia in patients undergoing total laparoscopic hysterectomy (TLH).
Method The study included 55 patients randomly divided into three groups. Patients in Groups P, D4, and D8 received saline, 4, and 8 mg dexamethasone, respectively, intravenously, 2 h before induction.
Results The time to first analgesic requirement was significantly delayed in patients in the D8 group compared with the D4 group ($P = 0.01$) and placebo ($P = 0.01$). Total postoperative fentanyl consumption was significantly less in patients in the D8 group compared with the D4 group ($P = 0.01$) and placebo ($P = 0.01$). Use of 8 mg dexamethasone resulted in a 99.3 mcg decrease in total 24-h fentanyl consumption. Postoperative nausea and vomiting (PONV) was significantly less in the D8 group with a complete response rate (no emetic episodes and no rescue medication for 24 h) of 36.8% compared with the placebo group in which all the patients had PONV. No adverse effects were observed in any group.
Conclusion Dexamethasone at a dose of 8 mg given intravenously 2 h before induction, delays patient request for analgesia and reduces total fentanyl consumption and PONV in patients undergoing TLH.

Keywords Dexamethasone · Analgesia, postoperative · Hysterectomy, laparoscopic

C. R. Thangaswamy · V. Rewari · A. Trikha · M. Dehran · Chandralekha
Department of Anaesthesiology and Intensive Care, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India

V. Rewari (✉)
K-25, Jangpura Extn, New Delhi 110014, India
e-mail: vimirewari@gmail.com

Introduction

Since the introduction of laparoscopic surgery in gynecology, total laparoscopic hysterectomy (TLH) has become an option with clear advantages over abdominal hysterectomy [1]. Although TLH performed on an outpatient basis has been reported to be safe, well tolerated, and cost effective [2], pain and postoperative nausea and vomiting (PONV) are common reasons for hospital admission [3]. Opioids are the drug of choice for perioperative pain relief but are associated with common side effects such as sedation, drowsiness, urinary retention, PONV, reduced gastrointestinal motility, and paralytic ileus [4]. Multimodal analgesic regimes are advocated to reduce the need for opioids wherein various therapeutic modalities have been evaluated in patients undergoing laparoscopic procedures [5–8]. Glucocorticoids are well known for both their analgesic and antiemetic effects and several randomized, clinical trials have been conducted to examine the effect of perioperative single-dose corticosteroid administration, in various doses, on perioperative outcome [9, 10]. Glucocorticoids have demonstrated opioid-sparing effects in a number of clinical studies of postoperative pain, but procedure-specific data in relation to TLH are not available. Therefore, the objective of this prospective, double-blind, randomized, placebo-controlled study was to evaluate the effect of two different doses of dexamethasone on fentanyl consumption (primary end point), time to requirement of

the first analgesic, postoperative pain scores, PONV, and wound infection (secondary end points) in patients undergoing TLH.

Materials and methods

After approval of the Institutional Ethics Committee and written informed consent, 55 ASA I and II female patients aged 18–60 years scheduled for elective laparoscopic hysterectomy under general anesthesia were enrolled in this prospective, randomized, double blind, placebo-controlled study. The exclusion criteria were diabetes mellitus/impaired glucose tolerance, peptic ulcer disease, endocrine disorders, morbid obesity (BMI $>$ 30), history of motion sickness or postoperative nausea and vomiting (PONV) after general anesthesia, women on hormonal therapy, and patients on long-term steroids or non-steroidal anti-inflammatory drugs (NSAIDs). Before the surgery, all patients were instructed on the use of the patient controlled analgesia (PCA) device (Perfusor fm, B Braun Melsungen, Germany) for postoperative pain relief.

The patients were randomized to one of the three groups based on a computer generated random number list. The study solution to be given to the patient was concealed in a sealed envelope bearing the patient's number which was handed over by the second author to the ward nurse who was not involved in the study. The study solution was prepared by the ward nurse and administered to the patient intravenously 2 h before the start of the surgery. Group P was given 2 ml saline as placebo, Group D4 received 2 ml of 4 mg dexamethasone in saline and Group D8 received 2 ml of 8 mg dexamethasone. All patients were blinded to the nature of the drug administered. In the postoperative period the patients were monitored and followed up by the first author.

In the operating room, intravenous access was secured and routine monitoring in the form of electrocardiogram, non invasive blood pressure and pulse oximetry was established. All patients were premedicated with midazolam 0.03 mg/kg intravenously 10 min before induction of general anesthesia.

Anesthesia was induced with fentanyl 2 μg/kg and propofol 2–3 mg/kg, and endotracheal intubation was facilitated with vecuronium 0.1 mg/kg. Anesthesia was maintained with 33% oxygen in nitrous oxide and isoflurane (1–1.5%) with controlled ventilation to maintain normocarbia. Supplemental analgesia was provided with fentanyl 0.5 μg/kg if the heart rate or mean arterial blood pressure values exceeded 20% of baseline or if sweating and lacrimation were present. The total dose of fentanyl required intraoperatively was noted. Patients were hydrated by use of lactated Ringer's solution according to the standard departmental procedure. During the procedure, the patient was placed in the Trendenlenberg position and the abdomen insufflated with carbon dioxide with an intraabdominal pressure not exceeding 15 mmHg. At the end of the procedure, trachea was extubated after adequate reversal of neuromuscular blockade with neostigmine 50 μg/kg and atropine 20 μg/kg.

Postoperatively, patients were transferred to a postanesthesia care unit (PACU) where they were connected to a PCA device with fentanyl. The device was set to deliver a bolus of 20 μg fentanyl with a lockout interval of 5 min. In the PACU, a blinded investigator (first author) recorded the pain scores at rest and on movement (patient was asked to log roll to one side) and PONV at 0 min, 30 min, 1, 2, 4, 8, 12, and 24 h postoperatively. Pain intensity was measured using a 100 mm visual analog scale where 0 symbolized no pain and 100 represented the worst pain imaginable. The incidence of PONV was assessed by the presence of vomiting or nausea persisting for more than 5 min, for which the patient received ondansetron 0.1 mg/kg intravenously as a rescue antiemetic. The discharge criteria based on the postanesthetic discharge scoring system (PADSS) [11] were assessed every 30 min. The time taken to achieve a score of 9 or more was recorded as the patient's eligibility for discharge.

The primary outcome measured was total fentanyl consumption at 2, 4, 8, 12 and 24 h postoperatively. Secondary outcomes measured were time to requirement of the first analgesic, postoperative pain scores at rest and during movement, nausea and vomiting, and wound infection. Blood sugar levels 2 h before induction and at induction of anesthesia were also assessed. Postoperative complications specific to glucocorticoids, for example wound infection and delayed wound healing, were assessed on the 7th postoperative day.

Maintenance intravenous fluids (Ringer's lactate) were continued in the postoperative period. The PCA was discontinued after 24 h. Patients were transferred to the ward and advised to take oral ibuprofen (400 mg every 8 h) and paracetamol (1 g every 6 h) for pain relief.

Statistical methods

From a pilot study in 10 patients it was observed that the mean $\pm$ standard deviation of 24-h fentanyl consumption in Group D4 was 637 $\pm$ 65.5 μg and that in Group D8 was 550 $\pm$ 64.2 μg. To detect the difference of 87 μg in 24 h fentanyl consumption between D4 and Group D8, with 90% power and 5% level of significance, the sample size estimated was 15 per group.

Statistical analysis was performed using SPSS version 15. Age, weight, and blood sugar were compared using

one-way ANOVA test. The total intraoperative dose of fentanyl, postoperative heart rate, blood pressure, VAS scores (at rest and during movement), first analgesic dose, and postoperative opioid consumption were compared using one way ANOVA test. Any statistical significance in between the groups was analyzed using post-hoc Bonferroni test. The incidence of PONV was analyzed using Fisher's exact test and the χ^2 test. The incidence of wound infection and wound healing were analyzed using one-way ANOVA. For all statistical analysis $P < 0.05$ was considered statistically significant.

Results

Sixty seven consecutive patients were considered for inclusion in the study. Fifty-five patients were included and randomly assigned to their treatment group (Fig. 1). The results are reported as mean (±SD). All groups were comparable with regard to patient characteristics and intraoperative details (Table 1). VAS scores at rest and on movement at all time intervals were comparable in all the three groups (Figs. 2, 3). The mean time to first analgesic requirement was significantly more in Group D8

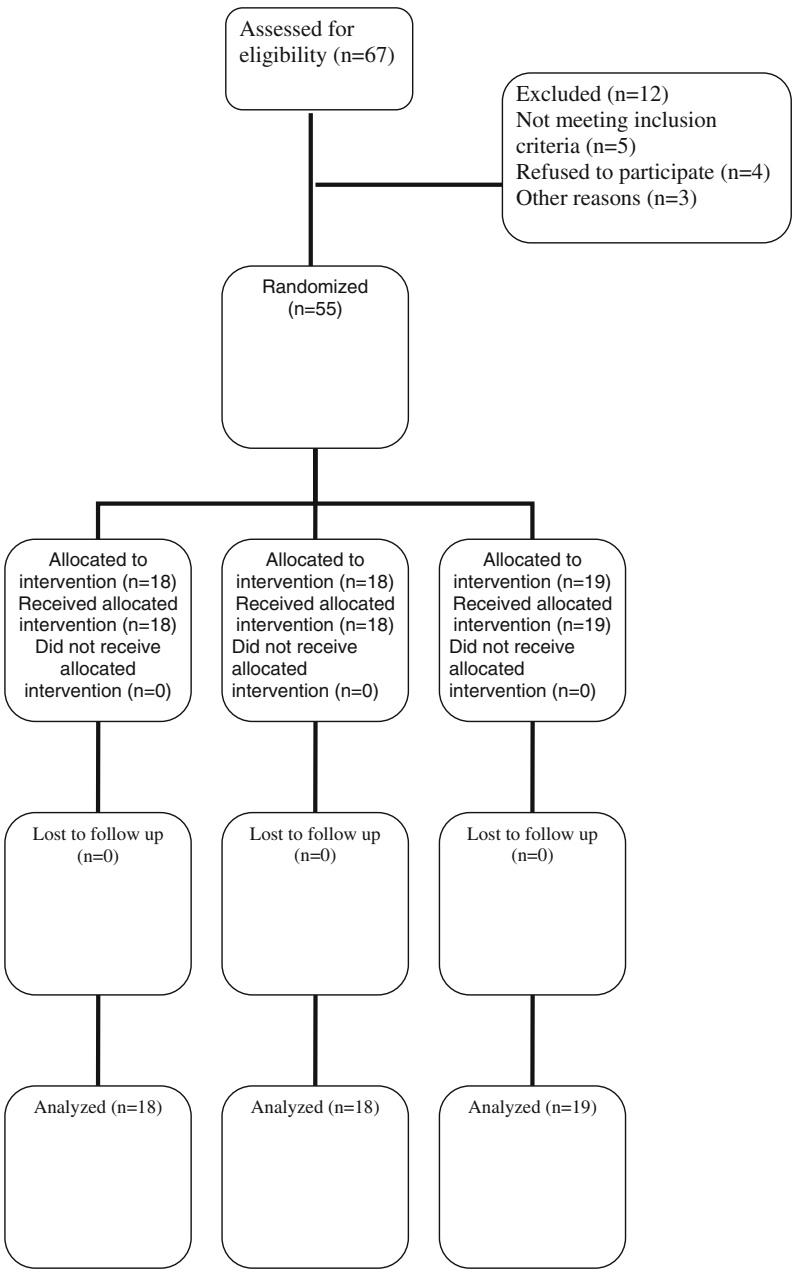

Fig. 1 Consort flow diagram of the trial

Table 1 Patient characteristics

	Group P	Group D4	Group D8
Patients (*n*)	18	18	19
Age (years)	36 ± 8	40 ± 9	42 ± 8
Weight (kg)	58.3 ± 12.6	58.3 ± 7.4	60 ± 10.6
Blood sugar (mg/dl)			
Base line	101.2 ± 11	97.4 ± 13.2	101.2 ± 13
Before induction of anesthesia	111.4 ± 10.3	107.7 ± 12.2	112.1 ± 14
Duration of surgery	146.4 ± 30.96	149.4 ± 29.2	153.7 ± 40.2

Values are mean (SD) or number of patients. No significant differences among the groups were noted

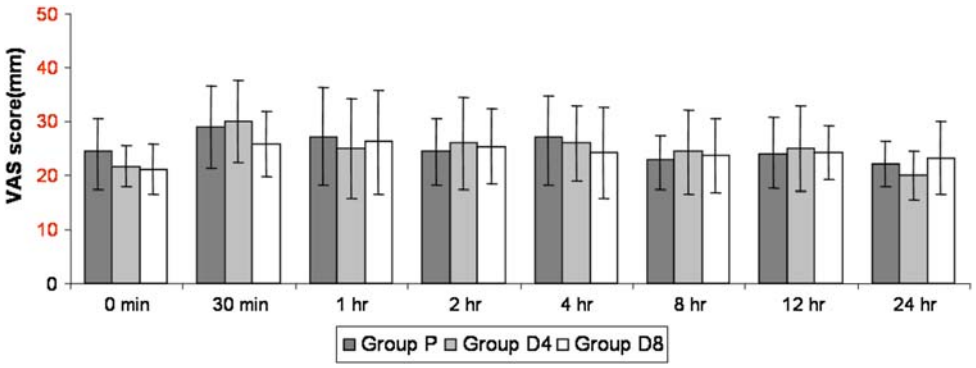

Fig. 2 VAS scores at rest at different times in the 24-h postoperative period. Values are expressed as mean (SD). No statistically significant difference was found between the three groups

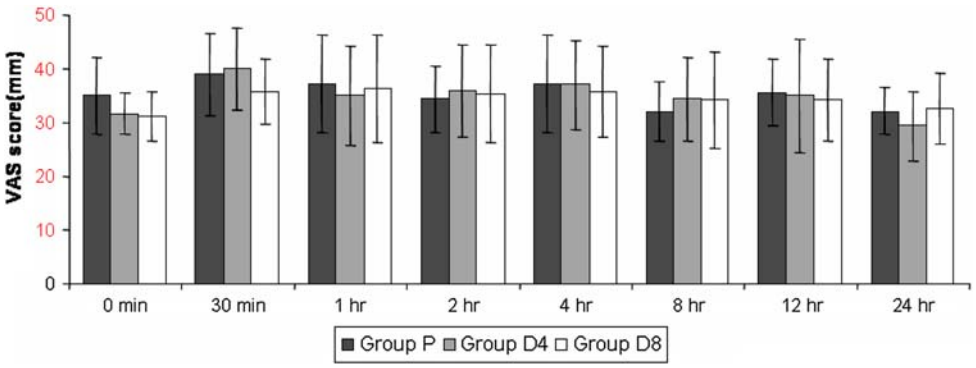

Fig. 3 VAS scores at movement at different times in the 24-h postoperative period. Values are expressed as mean (SD). No statistically significant difference was found between the three groups

(36.8 ± 10.0 min) than in Group D4 (23.1 ± 5.9 min; $P = 0.01$) and Group P (20.8 ± 8.4 min; $P = 0.01$). Postoperative fentanyl consumption at 2, 4, 8, 12 h was significantly less in Group D8 than in Group D4 ($P < 0.05$) and Group P ($P < 0.05$) . Total postoperative fentanyl consumption in the 24-h study period was significantly less in Group D8 (547.4 ± 69 μg) than in Group D4 (655.6 ± 73.7 μg, $P = 0.01$) and Group P (646.7 ± 77.3 μg, $P = 0.01$) (Table 2). Use of 8 mg dexamethasone resulted in a 99.3 μg decrease in total 24 h fentanyl consumption compared with placebo.

The total incidence of PONV was significantly less in Group D8 (57.9%) than in Group D4 (100%) and placebo (100%) ($P = 0.01$). The incidence of early PONV (within 6 h) during the study period was significantly less in Group D8 (26.3%) than in Group D4(100%; $P = 0.01$) and Group P (100%; $P = 0.01$). After 6 h (late PONV), the incidence of PONV in Group P (77.8%) was significantly more than in both Group D4 (44.4%; $P = 0.02$) and Group D8 (36.8%; $P = 0.01$) (Table 2).

The average time required to achieve a discharge score of >9 (eligibility for discharge) was significantly less in Group D8 (333.5 ± 43.0 min) than in Group D4 (366.0 ± 43.0 min; $P = 0.03$) and Group P (367.5 ± 46.5 min; $P = 0.02$) (Table 2). No patients in any group had any adverse effects with regard to blood sugar values, wound infection, and healing.

Discussion

This study demonstrates that intravenous administration of 8 mg dexamethasone 2 h before induction of anesthesia delays the time to requirement of the first analgesic, and

Table 2 Intraoperative and postoperative fentanyl consumption in different time intervals, time to first analgesic requirement, incidence of PONV, and time to achieve eligibility for discharge

	Group P	Group D4	Group D8
Intraoperative fentanyl consumption (μg)	195.6 ± 96.3	173.9 ± 20.9	176.3 ± 29.9
Time to first analgesic requirement (min)	20.8 ± 8.4	23.1 ± 5.9	36.8 ± 10*,**
Fentanyl consumption			
At 2 h	130.0 ± 40.0	123.9 ± 25.0	102.1 ± 26.6*,**
Between 2 and 4 h	111.1 ± 33.0	110.6 ± 44	83.2 ± 30*,**
Between 4 and 8 h	127.8 ± 21.8	131.1 ± 24.9	112.6 ± 11.9*,**
Between 8 and 12 h	135.6 ± 25.3	137.8 ± 20.5	116.8 ± 22.4*,**
Between 12 and 24 h	167.8 ± 40.1	155.6 ± 34.7	124.2 ± 31.7*,**
Up to 24 h	646.7 ± 77.3	655.6 ± 73.7	547.4 ± 69*,**
PONV			
Early PONV	18 (100%)	18 (100%)	5 (26.3%)*,**
Late PONV	14 (77.8%)	8 (44.4%)*	7 (36.8%)*,**
Time to achieve eligibility of discharge	367.5 ± 46.5	366.0 ± 43.0	333.5 ± 43.0*,**

Values are mean ± SD or *n* (%)

* Statistically significant value ($P < 0.05$) compared with Group P; ** statistically significant value ($P < 0.05$) compared with Group D4

reduces total postoperative fentanyl consumption and PONV in women undergoing TLH. However, dexamethasone at a dose of 4 mg did not have an opioid-sparing effect but helped in the reduction of delayed PONV.

Dexamethasone has been shown to have potent anti-inflammatory properties and suppresses tissue levels of bradykinin [11] and the release of neuropeptides from the nerve endings [12]. The established reduction in prostaglandin production mediated by glucocorticoids might further contribute to analgesia by inhibiting the synthesis of cyclooxygenase-2 in peripheral tissues and in the central nervous system and by inhibition of other mediators of inflammatory hyperalgesia, for example TNF-α, IL-1, and IL-6 [13, 14]. Glucocorticoids have been demonstrated to lead to reduced pain after tonsillectomy [15], oral surgery [16], orthopedic surgery [17], spinal surgery [18], anorectal surgery [19], breast surgery [20], and laparoscopic cholecystectomy [21]. However, the role of dexamethasone in TLH has not been evaluated.

With advances in laparoscopic techniques, TLH is becoming an increasingly popular choice for both surgeons and patients. We chose to study these patients because the beneficial effects of dexamethasone are most reliably shown in studies of limited surgical trauma, for example tonsillectomies, dental procedures, and laparoscopic cholecystectomy vis a vis a major surgical procedure [22].

In our study, patients receiving 8 mg dexamethasone were eligible to be discharged significantly earlier than the other groups. It has been seen that when conducted with a proper anesthesia and analgesia protocol patients undergoing laparoscopic hysterectomy can safely be discharged early [23]. We wanted to evaluate the possible analgesic effect of this drug which, when incorporated in the multimodal analgesic regime, can help in achieving early discharge for these patients.

The analgesic effect of dexamethasone could be ascertained by the difference in the total postoperative consumption of fentanyl, which was significantly lower in Group D8 than in the placebo and D4 groups. Use of 8 mg dexamethasone resulted in 99.3 mcg decrease in total 24 h fentanyl consumption. The actual opioid-sparing effect of dexamethasone with regard to PCA fentanyl has not been studied previously. A recent metaanalysis on the effect of dexamethasone after laparoscopic cholecystectomy showed that patients treated with dexamethasone experienced moderately less postoperative pain and required less rescue analgesic than the control group [24].

No convincing documentation of effective analgesic dose of dexamethasone is available in the literature. In our study, 8 mg dexamethasone had an opioid-sparing effect whereas 4 mg dexamethasone had none. Numazaki and Fujii [25] also found that 8 mg dexamethasone effectively prevented PONV and aided management of postoperative pain compared with 4 mg, and that increasing the dose to 16 mg provided no further benefit, in patients undergoing dental surgery. Fujii and Nakayama [26] also found that 8 mg dexamethasone effectively reduced PONV and analgesic requirement after thyroidectomy. In another study, IV administration of 4 mg dexamethasone facilitated recovery to "home readiness" in outpatients undergoing anorectal surgery although there was no effect on postoperative pain [19].

Onset of the biological action of glucocorticoids takes 1–2 h because of changes in protein-synthesis by gene

transcription [27]. Therefore, we decided to administer dexamethasone 2 h before the induction of anesthesia. Similar to our results, Bisgaard et al. [21] found that dexamethasone 8 mg given 90 min before surgery reduced pain, fatigue, nausea and vomiting, and duration of convalescence when compared with placebo.

Intraoperatively, total fentanyl consumption was less in Group D8 than in Group P and Group D4 although it did not reach statistical significance. Also, patients in Group D8 remained pain-free for a longer period of time in the immediate postoperative period, as indicated by a significant delay in the requirement of the first analgesic dose. Some previous studies indicate that dexamethasone may not have enough analgesic efficacy to take care of the intense intraoperative nociceptive stimulus [21, 28]. However, in a recent study it was seen that betamethasone administered to outpatients before conscious sedation in gynecologic and obstetric surgery resulted in better control of intraoperative pain [29].

The incidence of PONV after TLH was found to be very high (100%). Previous studies in minor gynecological laparoscopic surgery have reported rates of 54–92% [30–32]. The very high incidence in our study could be related to the combination of risk factors namely, gynecological surgery, laparoscopy, long duration of surgery, and the intraoperative use of nitrous oxide. In a recent study it was seen that the incidence of PONV in patients undergoing operative laparoscopic gynecological surgery was 63% [33].This is less than the incidence of PONV in our study because these patients received multimodal analgesia in the form of wound infiltration with local anesthetic and indomethacin, instead of PCA fentanyl, for postoperative analgesia.

Dexamethasone in a dose of 8 mg reduced the incidence of PONV from 100 to 57.9% in our study, which is corroborated by similar results in other studies [34, 35]. In addition to the antiemetic effects of dexamethasone, the reduced PONV in Group D8 might also be attributed to the reduced total postoperative fentanyl consumption in this group. Dexamethasone in a dose of 8 mg reduced both early (within 6 h) and late (6–24 h) PONV. On the other hand, 4 mg dexamethasone was effective as an antiemetic only in the late postoperative period (6–24 h). Fujii and Nakayama [33] also found, in a similar group of patients, that the incidence of PONV was significantly less in the 8 mg dexamethasone group than in the 4 mg dexamethasone group. It is also noteworthy that in the placebo group the incidence of late PONV was high, despite receiving ondansetron as a rescue antiemetic, indicating the need for combination antiemetic therapy in these patients.

In our study, no patient had any adverse effects related to rise in blood sugar or infectious complications. Glucocorticoids can give a marked but transient elevation in blood glucose [9]. However, in our study, administration of dexamethasone was not associated with a significant rise in blood sugar. Most evidence in the literature also indicates that single doses of corticosteroids are unlikely to impair wound healing in man [36].

The limitation of our study is that it would have been of more clinical value to the explore benefits of combining drug strategies, so that the PCA fentanyl could be avoided, to reduce the incidence of opioid-related side effects. In addition, there is probably a need to study the opioid-sparing effect of higher doses of dexamethasone.

Acknowledgments This work was supported by institutional sources only.

References

1. Kluivers KB, Johnson NP, Chien P, Vierhout ME, Bongers M, Mol BW. Comparison of laparoscopic and abdominal hysterectomy in terms of quality of life: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2008;136:3–8.
2. Thiel J, Gamelin A. Outpatient total laparoscopic hysterectomy. J Am Assoc Gynecol Laparosc. 2003;10:481–3.
3. Kahn BS, Byrd K, Furlong D, Park S, Willems J. Outpatient laparoscopic hysterectomy. J Minim Invasive Gynecol. 2008;15:S21.
4. Bowdle TA. Adverse effects of opioid agonists and agonist-antagonists in anesthesia. Drug Saf. 1998;19:173–89.
5. Wheatley SA, Millar JM, Jadad AR. Reduction of pain after laparoscopic sterilisation with local bupivacaine: a randomised, parallel, double-blind trial. BJ OG. 1994;101:443–6.
6. Ding Y, White PF. Comparative effects of ketorolac, dezocine, and fentanyl as adjuvants during outpatient anesthesia. Anesth Analg. 1992;75:566–71.
7. Aho MS, Erkola OA, Scheinin H, Lehtinen AM, Korttila KT. Effect of intravenously administered dexmedetomidine on pain after laparoscopic tubal ligation. Anesth Analg. 1991;73:112–8.
8. Alexander JI. Pain after laparoscopy. Br J Anaesth. 1997;79:369–78.
9. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am Coll Surg. 2002;195:694–712.
10. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg. 2000;90:186–94.
11. Hargreaves KM, Costello A. Glucocorticoids suppress levels of immunoreactive bradykinin in inflamed tissue as evaluated by microdialysis probes. Clin Pharmcol Ther. 1990;48:168–78.
12. Hong D, Byers MR, Oswald RJ. Dexamethasone treatment reduces sensory neuropeptides and nerve sprouting reactions in injured teeth. Pain. 1993;55:171–81.
13. Ferreira SH, Cunha FQ, Lorenzetti BB, Michelin MA, Perretti M, Flower RJ, et al. Role of lipocortin-1 in the anti-hyperalgesic actions of dexamethasone. Br J Pharmacol. 1997;121:883–8.
14. Li W, Xie W, Strong JA, Zhang ZM. Systemic anti-inflammatory corticosteroid reduces mechanical pain behaviour, sympathetic sprouting, and elevation of proinflammatory cytokines in a rat model of neuropathic pain. Anesthesiology. 2007;107:469–77.
15. Afman CE, Welge JA, Steward DL. Steroids for posttonsillectomy pain reduction: meta-analysis of randomized controlled trials. Otolaryngol Head Neck Surg. 2006;134:181–6.

16. Skjelbred P, Lokken P. Post-operative pain and inflammatory reaction reduced by injection of a corticosteroid. A controlled trial in bilateral oral surgery. Eur J Clin Pharmacol. 1982;21:391–6.
17. Romundstad L, Breivik H, Niemi G, Helle A, Stunbhaug A. Methylprednisolone intravenously 1 day after surgery has sustained analgesic and opioid-sparing effects. Acta Anaesthesiol Scand. 2004;48:1223–31.
18. Aminmansour B, Khalili HA, Ahmadi J, Nourian M. Effect of high-dose intravenous dexamethasone on postlumbar discectomy pain. Spine. 2006;31:2415–7.
19. Coloma M, Duffy LL, White PF, Tongier WK, Huber PJ Jr. Dexamethasone facilitates discharge after outpatient anorectal surgery. Anesth Analg. 2001;92:85–8.
20. Romundstad L, Breivik H, Roald H, Skolleborg K, Haugen T, Narum J, et al. Methylprednisolone reduces pain, emesis, and fatigue after breast augmentation surgery: a single-dose, randomized, parallel-group study with methylprednisolone 125 mg, parecoxib 40 mg, and placebo. Anesth Analg. 2006;102:418–25.
21. Bisgaard T, Klarskov B, Kehlet H, Rosenberg J. Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy: a randomized double-blind placebo-controlled trial. Ann Surg. 2003;238:651–60.
22. Callery MP. Preoperative steroids for laparoscopic surgery. Ann Surg. 2003;238:661–2.
23. de Lapasse C, Rabischong B, Bolandard F, Canis M, Botchorischvili R, Jardon K, et al. Total laparoscopic hysterectomy and early discharge: satisfaction and feasibility study. J Minim Invasive Gynecol. 2008;15:20–5.
24. Karanicolas PJ, Smith SE, Kanbur B, Davies E, Guyatt GH. The impact of prophylactic dexamethasone on nausea and vomiting after laparoscopic cholecystectomy—a systematic review and meta-analysis. Ann Surg. 2008;248:751–62.
25. Numazaki M, Fujii Y. Reduction of postoperative emetic episodes and analgesic requirements with dexamethasone in patients scheduled for dental surgery. J Clin Anesth. 2005;17:182–6.
26. Fujii Y, Nakayama M. Efficacy of dexamethasone for reducing postoperative nausea and vomiting and analgesic requirements after thyroidectomy. Otolaryngol Head Neck Surg. 2007;136:274–7.
27. Haynes R, Murad F. Adrenocorticotropic hormone, adrenocortical steroids and their synthetic analogs: Inhibitors of adrenocortical steroid biosynthesis. In: Hardman JG, Limbird LE, Gilman AG, editors. Goodman and Gilman's the pharmacological basis of therapeutic. Tenth ed. New York: McGraw–Hill; 2001. p. 1466–95.
28. Elhakim M, Ali NM, Rashed I, Riad MK, Refat M. Dexamethasone reduces postoperative vomiting and pain after pediatric tonsillectomy. Can J Anaesth. 2003;50:392–7.
29. Pace MC, Palagiano A, Passavanti MB, Iannotti M, Sansone P, Maistro M, et al. The analgesic effect of betamethasone administered to outpatients before conscious sedation in gynecologic and obstetric surgery. Ann NY Acad Sci. 2008;1127:147–51.
30. Bodner M, White PF. Antiemetic efficacy of ondansetron after outpatient laparoscopy. Anesth Analg. 1991;73:250–4.
31. Sniadach MS, Alberts MS. A comparison of the prophylactic antiemetic effect of ondansetron and droperidol on patients undergoing gynecological laparoscopy. Anesth Analg. 1997;85:797–800.
32. Raphael JH, Norton AC. Antiemetic efficacy of prophylactic ondansetron in laparoscopic surgery: randomized, double-blinded comparison with metoclopromide. Br J Anaesth. 1993;71:845–8.
33. Fujii Y, Nakayama M. Dexamethasone for reduction of nausea, vomiting and analgesic use after gynecological laparoscopic surgery. Int J Gynaecol Obstet. 2008;100:27–30.
34. Wang JJ, Ho ST, Liu HS, Ho CM. Prophylactic antiemetic effect of dexamethasone in women undergoing ambulatory laparoscopic surgery. Br J Anaesth. 2000;84:459–62.
35. Huang JC, Shieh JP, Tang CS, Tzeng JI, Chu KS, Wang JJ. Low-dose dexamethasone effectively prevents postoperative nausea and vomiting after ambulatory laparoscopic surgery. Can J Anaesth. 2001;48:973–7.
36. Sauerland S, Nagelschmidt M, Mallmann P, Neugebeuer EA. Risks and benefits of preoperative high dose methylprednisolone in surgical patients: a systematic review. Drug Saf. 2000;23:449–61.