The Effect of a Single Dose Dexamethasone on Postoperative Pain in Patients Undergoing Gynecological Laparotomy Surgery

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Background: *Acute postoperative pain is associated with many undesirable outcomes. Opioids are the mainstay for pain relief but their common side effects are still problematic. Many adjunctive agents such as NSAIDs and gabapentin have already been proved to be effective as multimodal analgesia. Dexamethasone has been reported to reduce postoperative nausea and vomiting but the analgesic effect is not well defined especially in open abdominal surgery.*

Objective: *To evaluate efficacy of a single perioperative dose of dexamethasone on postoperative pain in gynecological laparotomy surgery.*

Material and Method: *A prospective, randomized, double-blinded study was approved by the Institutional Review Board and registered with the Thai Clinical Trials Registry as TCTR20151116001. Fifty-two patients scheduled for elective gynecological laparotomy surgery were enrolled in the present study. Patients were randomized into two groups based on computer generated random number list. After induction, group D received intravenous dexamethasone 8 mg and group P received saline. Both groups were anesthetized in a standardized manner. Postoperative pain was managed with intravenous morphine using patient controlled analgesia. The primary outcome was total morphine consumption evaluated at 6- and 24-hour postoperatively. Pain score, nausea, and vomiting, shivering, sore throat, and adverse effects of dexamethasone were also recorded.*

Results: *The total dose of morphine (0 to 24 hour after surgery) was less in D group (15.88±9.59 mg) compared with P group (24.25±15.26 mg) (p = 0.027). The doses during hour 0 to 6 were smaller in D group (11.28±6.66 mg) than the placebo (15.79±12.50) (p = 0.435). The numerical rating scale for pain at rest did not differ in both study groups, but pain in motion was less in D group than P group at 6-hour (p = 0.03) and 24-hour (p = 0.039) after surgery. No adverse effect was observed in both groups.*

Conclusion: *A single perioperative dose 8 mg of dexamethasone is safe and significantly reduces pain at movement and morphine consumption in 24 hours after gynecological laparotomy surgery.*

Keywords: *Dexamethasone, Postoperative pain, Gynecology laparotomy*

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Acute postoperative pain is associated with many undesirable outcomes, for it delays mobilization, increases duration of hospital stay, and decreases patient's satisfaction. Patients who receive adequate analgesia recover faster and need shorter hospital stay.

Opioids are the mainstay for perioperative pain relief, but their common side effects such as postoperative nausea and vomiting, sedation, drowsiness, urinary retention, reduce gastrointestinal mobility, and paralytic ileus are still problematic. Many adjuvants such as gabapentin, paracetamol, nonsteroidal anti-inflammatory drugs, and ketamine have already been proved to be effective as multimodal analgesia.

Dexamethasone, a strong anti-inflammatory drug with long duration of action (36 to 72 hours) has many beneficial effects in surgical setting. Besides antiemetics, it has anti-inflammatory effect, reduce shivering, and sore throat, but the analgesic effect of dexamethasone is inconclusive[1-3]. There are several studies about dexamethasone and postoperative pain, but most of the surgical procedures were limited to laparoscopic surgery, tonsillectomy, breast surgery, and orthopedics surgery[4-6]. That was the reason the authors chose to investigate its analgesic effect in open abdominal surgery using pfannenstiel incision, a common surgical procedure but have never been studied yet.

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The aim of the present study was to evaluate the effect of a single perioperative dose of dexamethasone on postoperative pain in patients undergoing gynecological laparotomy surgery.

Material and Method

After the approval from the Ramathibodi Ethics Committee, Mahidol University and protocol of the present study was registered in Thai Clinical Trials Registry, coded: TCTR20151116001. We obtained the written informed consent from 52 patients, ASA physical status I or II, aged between 18 to 65 years, undergoing elective gynecological laparotomy surgery with pfannenstiel incision under general anesthesia consented to participate in the study. Patients with diabetic mellitus, treatment with steroids, obesity, use of opioid, or analgesic drug within one month prior to the study, history of alcohol or drug abuse, pregnancy, undergoing surgical staging surgery, history of chronic pain, history of peptic ulcer or gastritis, and those who refused the study were excluded.

The sample size of 26 per group were adequate to achieve 80% power to detect the difference of fentanyl consumption in 24 hours of 10% in the treatment group relative to placebo group value from a previous study by Thangaswamy et al[5] of 646.7±77.3, assuming a significance level α of 0.05, power of 80% and 20% drop-out.

Patients were randomized into two groups: D (the study) and P (placebo), based on computer generated random number list (nQuery program). The study solution was prepared by a nurse not involved in the perioperative and postoperative care of the patient three hours before surgery. Then it was given to the patient in a sealed envelope, which was handed over to the anesthesiologist who was not involved in the study. All patients, anesthesiologists, and the follow-up team were blinded to the administered drugs.

In the operating room, after standard monitorings (electrocardiography, noninvasive arterial blood pressure, pulse oximetry), the patients were induced and intubated with propofol 1 to 2 mg/kg, fentanyl 0.5 mcg/kg and atracurium 0.5 mg/kg.

After intubation, group D received intravenous dexamethasone 8 mg and group P received saline in the same volume. A gastric tube was inserted to deflate the stomach, and was removed before extubation. Anesthesia was maintained with 1.0 to 2.5% sevoflurane and nitrous oxide in 50% oxygen, atracurium 10 mg every 30 minutes and morphine 0.1 mg/kg. At the end of surgery, endotracheal tube was extubated after reversal of neuromuscular blockade with neostigmine 2.5 mg and atropine 1.2 mg.

In the postanesthesia care unit, the patient controlled analgesia (PCA) device was connected. The device was set to deliver a PCA dose of morphine 1 mg/dose. The nurse who was blinded to the study drugs, assessed pain score at rest and movement by numerical rating scale. Total morphine consumption, nausea and vomiting, shivering, and sore throat were recorded, using four-point ordinal scale for PONV (0 = none, 1 = nausea, 2 = nausea with request for antiemetic, 3 = vomiting) and numerical rating scale (NRS) for sore throat. Patients were discharged from postanesthesia care unit by criteria based on the postanesthetic discharge scoring system.

At ward, the authors assessed pain score at rest and movement in 6-hour and 24-hour postoperatively. Morphine consumption, nausea and vomiting, shivering, sore throat, adverse event, and satisfaction score were recorded.

On the seventh postoperative day, pain and complications such as wound infection was assessed by telephone call or OPD visit.

The primary outcome was total morphine consumption at 6-hour and 24-hour postoperatively. The secondary outcomes were pain score, adverse events, and satisfaction score.

Results

Fifty-two patients undergoing gynecological laparotomy surgery were recruited. Three patients were excluded due to receiving succinylcholine for induction, operative time more than three hours, and having paracoxib for pain relief in the postanesthesia care unit.

There was no difference between groups in demographic data (Table 1). Group P was significantly

Table 1. Patients' characteristics

	Group D (n = 25)	Group P (n = 24)	*p*-value
Age (years)	43.40±9.28	41.67±10.05	0.533
Body weight (kg)	55.65±10.15	56.49±8.84	0.759
Height (cm)	156.64±5.23	155.04±5.72	0.312
Body mass index (kg/m^2)	22.99±4.23	23.50±3.47	0.650
ASA PS, n (%)			0.674
I	11 (44%)	12 (50%)	
II	14 (56%)	12 (50%)	

ASA PS = American Society of Anesthesiologists Physical Status
Data are mean ± SD unless otherwise stated

Table 2. Perioperative data

	Group D (n = 25)	Group P (n = 24)	*p*-value
Anesthesia time (minutes)	142.20±35.50	120.83±23.20	0.017*
Operative time (minutes)	120.20±35.43	101.04±28.70	0.040*
Blood loss (ml), median (min-max)	300 (10-1,500)	200 (30-1,000)	0.029*
Total intravenous fluid (ml), median (min-max)	1,700 (550-3,500)	1,150 (100-3,200)	0.002*

* Statistically significant at $p<0.05$
Data are mean ± SD unless otherwise stated

Table 3. Postoperative outcomes at ward

	Group D (n = 25)	Group P (n = 24)	*p*-value
Pain score			
At rest			
- 6-hour	4 (1-8)	5 (0-10)	0.118
- 24-hour	2 (0-6)	3 (0-5)	0.106
At movement			
- 6-hour	5 (2-10)	8 (1-10)	0.03*
- 24-hour	3 (0-6)	4 (0-9)	0.039*
Morphine consumption, mean ± SD			
6-hour	11.28±6.66	15.79±12.50	0.435
24-hour	15.88±9.59	24.25±15.26	0.027*
Nausea/vomiting, n (%)			
6-hour	8 (32.00)	11 (45.83)	0.32
24-hour	4 (16.00)	5 (20.83)	0.662
Shivering, n (%)	0 (0)	0 (0)	-
Sore throat score, mean ± SD			
6-hour	0.72±1.37	1.04±1.60	0.329
24-hour	0.40±1.12	0.96±1.57	0.037*
Hospital stay (days)	4 (4-5)	4 (3-6)	0.891
Satisfaction score	9 (7-10)	9 (9-10)	0.681

* Statistically significant at $p<0.05$
Data are median (min-max) unless otherwise stated

less in anesthetic time, operative time, blood loss, and total intravenous fluid administered than group D (Table 2).

The total morphine consumption (at 24-hour) in group D (15.88±9.59 mg) was significantly less compared with group P (24.25±15.26 mg) ($p = 0.027$). The dosage during hour 0 to 6 were smaller in group D (11.28±6.66 mg) than the placebo (15.79±12.50) but there was no statistically significance ($p = 0.435$) (Fig. 1, 2). The numerical rating scale for pain at rest did not differ in both study groups but pain in motion was less in group D than group P at 6-hour ($p = 0.03$) and 24-hour ($p = 0.039$) after surgery (Table 3). Nausea/vomiting, shivering, and sore throat score was similar in both groups.

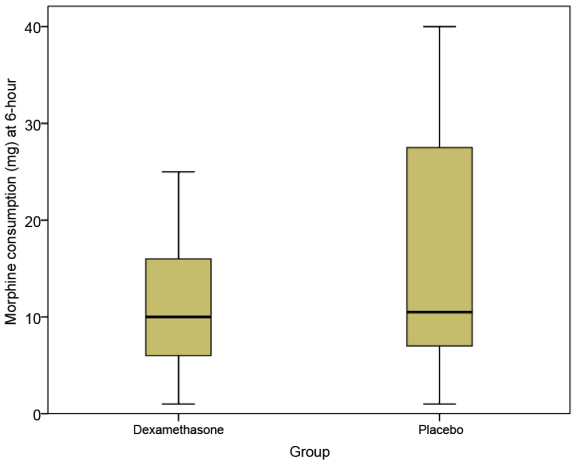

Fig. 1 Morphine consumption (mg) at 6-hour after surgery; there was no statistically difference between group D (11.28±6.66 mg) and the placebo (15.79±12.50 mg) ($p = 0.435$).

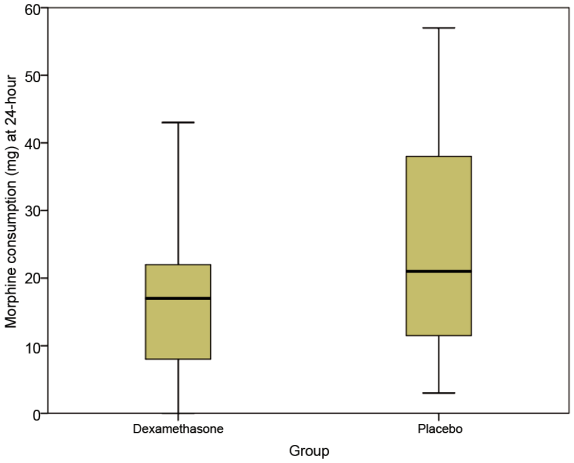

Fig. 2 Morphine consumption (mg) at 24-hour after surgery; the doses were smaller in group D (15.88±9.59 mg) than the placebo (24.25±15.26 mg) ($p = 0.027$).

Discussion

Dexamethasone has been reported to reduce postoperative nausea and vomiting, shivering, sore

throat. The analgesic effect of dexamethasone is not well defined. Mechanism of dexamethasone that could explain the analgesic effect might be the inhibition of the synthesis of cyclooxygenase 2 and other mediators that involve in inflammatory process such as TNF, IL-1, and IL-6. It also decreases the release of neuropeptides from the nerve endings.

Dexamethasone has been reported to reduce postoperative pain in tonsillectomy, laparoscopic cholecystectomy, breast surgery, and total laparoscopic hysterectomy but does not include laparotomy surgeries[4-6].

The meta-analysis by Oliveira et al[12] reported that intermediate dose of dexamethasone (0.11 to 0.2 mg/kg) has benefit on postoperative pain and reduction in opioid consumptions. From this meta-analysis, the authors decided to use a single dose of 8 mg dexamethasone.

Despite the onset of dexamethasone, the patients received a single dose of dexamethasone immediately after intubation. This was more practical to routine practice rather than giving two hours prior to the operation. This technique got rid of burning sensation at the perineal[13].

Steroids may involve with hyperglycemia, decrease immune response with increase infection rate in chronic user. Bolac et al[7] showed that single dose dexamethasone did not increase postoperative wound complication in patients underwent laparotomy endometrial cancer surgeries. Murphy et al[11], Nazer et al[8] also reported that a single dose dexamethasone did not significantly increase perioperative blood glucose level. Even with high dose, from systematic review by Sauerland et al[9], single perioperative steroids did not increase the incidence of adverse effect.

At recovery room, pain score and morphine consumption was similar in both groups. These results could be explained by every patient receiving intraoperative morphine bolus dose 0.1 mg/kg that was adequate for the immediate postoperative pain management period.

At ward 6-hour after surgery, patients who received dexamethasone had significantly less pain score at movement. The dose of morphine consumption in dexamethasone group was not significantly less than the placebo group.

Patients who received dexamethasone reported significantly reduced pain at movement and morphine consumption in 24-hour postoperatively. No patients had adverse effect related to infection complication or wound healing.

Conclusion

A single perioperative dose of 8 mg dexamethasone after intubation is safe and significantly reduces movement related pain in 24-hour after gynecological laparotomy surgery.

What is already known on this topic?

Dexamethasone is known for its anti-inflammatory effect, antiemetic, sore throat, and shivering reduction. The analgesic effect of dexamethasone is not well defined. There are many mechanisms that could explain its analgesic effect such as inhibition of cyclooxygenase 2 synthesis, decrease neuropeptide release, and its anti-inflammatory effect. There are also several studies about dexamethasone and postoperative pain, which was well documented in laparoscopic surgery, tonsillectomy, breast, and orthopedic surgery.

What this study adds?

This study showed that, not only in laparoscopic surgery, tonsillectomy, breast, and orthopedic surgery, dexamethasone also reduces postoperative pain and morphine used in gynecological laparotomy surgery without increasing the incidence of adverse effect.

The finding supports using dexamethasone as part of postoperative multimodal analgesia.

Acknowledgments

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Potential conflicts of interest

None.

References

1. Bilgin TE, Birbicer H, Ozer Z, Doruk N, Tok E, Oral U. A comparative study of the antiemetic efficacy of dexamethasone, ondansetron, and metoclopramide in patients undergoing gynecological surgery. Med Sci Monit 2010; 16: CR336-41.
2. Entezariasl M, Isazadehfar K. Dexamethasone for prevention of postoperative shivering: a randomized double-blind comparison with pethidine. Int J Prev Med 2013; 4: 818-24.
3. Thomas S, Beevi S. Dexamethasone reduces the severity of postoperative sore throat. Can J Anaesth 2007; 54: 897-901.
4. Fukami Y, Terasaki M, Okamoto Y, Sakaguchi K,

Murata T, Ohkubo M, et al. Efficacy of preoperative dexamethasone in patients with laparoscopic cholecystectomy: a prospective randomized double-blind study. J Hepatobiliary Pancreat Surg 2009; 16: 367-71.
5. Thangaswamy CR, Rewari V, Trikha A, Dehran M, Chandralekha. Dexamethasone before total laparoscopic hysterectomy: a randomized controlled dose-response study. J Anesth 2010; 24: 24-30.
6. Carr MM, Williams JG, Carmichael L, Nasser JG. Effect of steroids on posttonsillectomy pain in adults. Arch Otolaryngol Head Neck Surg 1999; 125: 1361-4.
7. Bolac CS, Wallace AH, Broadwater G, Havrilesky LJ, Habib AS. The impact of postoperative nausea and vomiting prophylaxis with dexamethasone on postoperative wound complications in patients undergoing laparotomy for endometrial cancer. Anesth Analg 2013; 116: 1041-7.
8. Nazar CE, Echevarria GC, Lacassie HJ, Flores RA, Munoz HR. Effects on blood glucose of prophylactic dexamethasone for postoperative nausea and vomiting in diabetics and non-diabetics. Rev Med Chil 2011; 139: 755-61.
9. Sauerland S, Nagelschmidt M, Mallmann P, Neugebauer EA. Risks and benefits of preoperative high dose methylprednisolone in surgical patients: a systematic review. Drug Saf 2000; 23: 449-61.
10. Gali B, Burkle CM, Klingele CJ, Schroeder D, Jankowski CJ. Infection after urogynecologic surgery with the use of dexamethasone for nausea prophylaxis. J Clin Anesth 2012; 24: 549-54.
11. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear T, Vender JS, et al. The effect of single low-dose dexamethasone on blood glucose concentrations in the perioperative period: a randomized, placebo-controlled investigation in gynecologic surgical patients. Anesth Analg 2014; 118: 1204-12.
12. De Oliveira GS Jr, Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology 2011; 115: 575-88.
13. Neff SP, Stapelberg F, Warmington A. Excruciating perineal pain after intravenous dexamethasone. Anaesth Intensive Care 2002; 30: 370-1.

ผลของ dexamethasone ต่อการระงับปวดหลังการผ่าตัดเปิดช่องท้องทางนรีเวช

พรภัทรา อารีรักษ์, วิชัย อิทธิชัยกุลฑล, ศิวพร เติมพรเลิศ, ธนิศร์ ประวิตรางกูร, จิตรภัทรา งันลาโสม, ชลธิชา เจริญทรัพย์, เกศินี ทองจุลเจือ

ภูมิหลัง: *ภาวะเจ็บปวดหลังผ่าตัด สามารถนำมาซึ่งภาวะไม่พึงประสงค์ต่อผู้ป่วยหลายประการ วิสัญญีแพทย์จึงควรควบคุมความปวดนี้ให้ดี โดยปัจจุบันมีการใช้ opioid เป็นการรักษาหลัก ในการระงับปวดหลังผ่าตัด และมีการใช้ยากลุ่มอื่น ๆ เช่น NSAIDs, Gabapentin ร่วมด้วย เพื่อลดปริมาณการใช้ opioid ได้ สำหรับ dexamethasone เป็นยาที่มีการใช้แพร่หลายในการลดการอักเสบ และลดภาวะคลื่นไส้อาเจียนหลังผ่าตัด แต่ผลในแง่การระงับปวดหลังการผ่าตัดเปิดช่องท้องนั้นยังไม่มีการศึกษาชัดเจน*

วัตถุประสงค์: *เพื่อประเมินผลในการระงับปวดของการให้ dexamethasone ในระหว่างการผ่าตัดเปิดช่องท้องทางนรีเวชวิทยา โดยหวังว่าในอนาคตจะสามารถใช้เป็นหนึ่งใน multimodal analgesia ได้*

วัสดุและวิธีการ: *หลังจากได้รับการพิจารณาทางจริยธรรมแล้ว แบ่งผู้ป่วย 52 ราย ที่มาเข้ารับการผ่าตัดเปิดช่องท้องทางนรีเวช ออกเป็นสองกลุ่ม โดยการใช้ computer generated random number list หลังจากนำสลบ กลุ่ม D จะได้รับ dexamethasone 8 mg กลุ่ม P ได้ normal saline ในปริมาตรที่เท่ากัน หลังผ่าตัด มีการให้ยาระงับปวดด้วย PCA morphine โดยมี primary outcome คือ ปริมาณการใช้ morphine รวมที่ 6 และ 24 ชั่วโมง หลังผ่าตัด นอกจากนี้ยังมีการวัดภาวะข้างเคียง อาการคลื่นไส้อาเจียน อาการเจ็บคอ และภาวะแทรกซ้อนอื่น ๆ หลังผ่าตัดร่วมด้วย*

ผลการศึกษา: *พบว่าปริมาณการใช้ morphine ในช่วง 24 ชั่วโมง หลังผ่าตัดในกลุ่ม D (15.88±9.59) น้อยกว่ากลุ่ม P (24.25±15.26) อย่างมีนัยสำคัญ ($p = 0.027$) เช่นเดียวกับปริมาณการใช้ในช่วง 6 ชั่วโมง หลังการผ่าตัด ส่วนการให้คะแนนความปวดขณะพักของสองกลุ่มไม่แตกต่างกัน แต่คะแนนความปวดเวลาขยับ ในกลุ่ม D น้อยกว่ากลุ่ม P อย่างมีนัยสำคัญ ทั้งที่ 6 ชั่วโมง ($p = 0.03$) และ 24 ชั่วโมง ($p = 0.039$) โดยไม่พบภาวะแทรกซ้อนในทั้งสองกลุ่ม*

สรุป: *การให้ dexamethasone 8 mg ในระหว่างการผ่าตัด สามารถลดความปวดขณะขยับ และลดการใช้ morphine ในช่วงเวลา 24 ชั่วโมง หลังการผ่าตัดเปิดช่องท้องทางนรีเวชได้อย่างมีนัยสำคัญ*