The Effects of Single-Dose Preoperative Intravenous Dexamethasone on Clinical Outcome after Laparoscopic Cholecystectomy

Vichit Viriyaroj MD*, Thana Boonsinsukh MD*,
Thammanij Rookkachart MD*, Narongchai Yigsakmongkol MD*

** Department of Surgery, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand*

Background: *Laparoscopic cholecystectomy is one of the most common procedures in surgery. Post-operative pain and post-operative nausea and vomiting (PONV) are frequently events after laparoscopic cholecystectomy and cause distress to patients. Dexamethasones are known for analgesic, anti-inflammatory, immune-modulating and anti-emetic effects. Therefore, preoperative dexamethasone administration may reduce postoperative pain and postoperative nausea vomiting after laparoscopic cholecystectomy.*

Objective: *This study aims to determine the effects of single-dose preoperative intravenous dexamethasone on clinical outcome such as postoperative pain nausea and vomiting in patients undergoing laparoscopic cholecystectomy.*

Material and Method: *This is a prospective randomized controlled trial study. Eighty patients undergoing elective laparoscopic cholecystectomy were randomized to dexamethasone group and control group. Dexamethasone group received 8 mg (2 ml) of intravenous dexamethasone 60-90 minute before surgery whereas control group received 2 ml of normal saline 60-90 minute before surgery. Patients received a similar standardized anesthesia, surgical and multimodal analgesic treatment. The pain score, nausea and vomiting at 1, 6, 24 hours after surgery and before discharge including analgesic consumption and antiemetic required was recorded in both groups. Preoperative and postoperative erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured.*

Results: *No significant difference existed between two groups regarding age, sex, previous operation, operation time and hospital stays. All of the patients had no postoperative complication. Postoperative pain score, nausea and vomiting at 1st and 6th hours in dexamethasone group were significantly reduced in comparison with control group. Analgesic consumption, antiemetic requirement and CRP postoperative were significantly decreased in dexamethasone group.*

Conclusion: *Single-dose preoperative dexamethasone 8 mg 60-90 minute before induction of anesthesia improved clinical outcome in terms of significantly less nausea, vomiting, pain at first 6 hours and less inflammatory response after laparoscopic cholecystectomy compared to placebo. The preoperative dexamethasone should be used as routine in patients undergoing laparoscopic cholecystectomy.*

Keywords: *Dexamethasone, Laparoscopic cholecystectomy*

J Med Assoc Thai 2015; 98 (Suppl. 10): S112-S117
Full text. e-Journal: *http://www.jmatonline.com*

In recent years, laproscopic cholecystectomy has become a commonly performed minimally invasive procedure and is regarded as the standard for the management of gall bladder disease such as cholelithiasis, acute cholecystitis and gall bladder polyp. The advantages of laparoscopic cholecystectomy include less pain, reduced hospital stay and earlier recovery in comparison to conventional surgery. Laparoscopic cholecystectomy would appear to be an operation for ambulatory surgery. Postoperative pain and postoperative nausea vomiting (PONV) are frequently encountered events after surgery and are suffering problems for patients. Currently, multimodal analgesia is the standard approach in the management of PONV. Corticosteroids such as dexamethasone are known for analgesic, anti-inflammatory, immune-modulating and anti-emetic effects. Therefore, preoperative dexamethasone administration may reduce postoperative pain and postoperative nausea vomiting after laparoscopic

Correspondence to:
Viriyaroj V, Department of Surgery, Faculty of Medicine, Srinakharinwirot University, 62 Moo 7, Ongkharak, Nakhon Nayok 26120, Thailand.
Phone: +66-37-395085 ext. 11201
E-mail: vivichit@yahoo.com

cholecystectomy.

This study aims to determine the effects of single-dose preoperative intravenous dexamethasone on clinical outcome such as postoperative pain nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

Material and Method

This prospective randomized controlled trial was approved by Ethics committee and informed consent was obtained from all participants. Eighty patients undergoing elective laparoscopic cholecystectomy at Her Royal Highness Princess Maha Chakri Sirindorn Medical Center between 2013 and 2014 were enrolled. Patients with a history of chronic pain disease with the exception of gall bladder disease, patients with mental disorder, immunocompromized host, patients with alcoholism or drug abuse, patients with allergy to dexamethasone, patients who required conversions to laparotomy during surgery were excluded from the study. Patients were allocated randomly to receive either dexamethasone (dexamethasone group) or saline (control group) by sealed envelope technique. The dexamethasone group received 8 mg (2 ml) of intravenous dexamethasone approximate 60-90 minute before surgery, whereas the control group received 2 ml of intravenous normal saline.

During the day before surgery, preoperative evaluation of the patients was done. Routine laboratory investigations include preoperative erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Patients was trained regarding how to assess pain intensity on visual analogue scale (VAS) with 0 = no pain and 10 = severe pain.

General anesthesia was standardized. Anesthesia was induced with midazolam (0.01 mg/kg), fentanyl (2 µg/kg), sodium thiopental (5 mg/kg) and atracurium (0.5 mg/kg). During surgery, patients were positioned in the reverse Trendelenburg position with the right side of the bed elevated. Four small incisions were performed at infraumbilical, epigastrium, right upper quadrant and right anterior axillary line. The all incision areas were locally infiltrated with 10 ml of 1% lidocaine with adrenaline before insertion the trocar. The abdomen was insufflated with carbon dioxide and intraabdominal pressure was maintained at 12 mmHg. Laparoscopic cholecystectomy was done by standard technique. CO_2 was evacuated at the end of surgery by suction and manual compression.

After surgery, a nurse with no knowledge of the patient group allocation measured intensity of pain with VAS at 1, 6, 24 hours after surgery and before hospital discharge. Nausea was evaluated on verbal rating scale (0 = no nausea, 1 = mild nausea, 2 = moderate nausea, 3 = severe nausea) and the number of vomiting episodes were registered (0 = none, 1 = 1 episode as mild, 2 = 2 or 3 episode as moderate, 3 = more than 3 as severe) at 1, 6, 24 hours after surgery and before discharge. Rescue analgesic (Meperdine) and antiemetic (Metoclopramide) was provided on patients' demand. Postoperative erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) was checked.

Considering power of study at 80% and confidence interval (CI) at 95%, sample sized was calculated based on the hypothesis that the total incidence of PONV in placebo group would be 60% and the incidence of PONV in treatment group would be 20%. The sample sized was calculated as 37 samples for each group. We enrolled 40 patients per group to allow dropout. All of the statistical data were reported as mean $\pm$ SD and to compare mean between 2 groups were analyzed by unpaired t-test. A value of $p<0.05$ was considered significant.

Results

80 patients were available for analysis and none were excluded from the study. Patients were divided into dexamethasone group and control group. Patient baseline characteristics and pre-operative data are shown in Table 1, in which there were no significant differences between the two groups (sex, age and previous surgery), duration of surgery and hospital stays. All of the patients had postoperative complication.

The outcomes of this trial are presented in Table 2. Pain score at 1st and 6th hours after surgery in dexamethasone group was significantly less than in control group. There were no differences in pain score at 24 hours and before hospital discharge. A significant reduction in the mean analgesic consumption is observed in the group receiving dexamethasone.

Postoperative nausea and vomiting (PONV) at 1st and 6th hours in dexamethasone group was significantly reduced but there were not differences at 24 hours and before hospital discharge. Mean antiemetic requirement was significantly reduced in dexamethasone group (Table 3).

The preoperative ESR and CRP showed no differences between the two groups. Postoperatively, the dexmethasone group had a significantly lower CRP level in comparison to the control group. No difference is seen in postoperative ESR level between the two groups.

Table 1. Patient characteristics and perioperative data

	Control group (n = 40)	Dexamethasone group (n = 40)	*p*-value
Sex (male)	13	14	0.895
Age (years) (mean ± SD)	47.98±12.69	53.18±16.65	0.196
Previous surgery (yes)	6	9	0.683
Duration of surgery (min) (mean ± SD)	72.25±16.90	65.25±18.94	0.188
Hospital stay (day) (mean ± SD)	3.13±0.40	2.95±0.38	0.061

Table 2. Postoperative visual analog score (VAS) and analgesic consumption

	Control group (n = 40) (mean ± SD)	Dexamethasone group (n = 40) (mean ± SD)	*p*-value
Pain score at 1 hour	7.13±1.64	3.30±2.11	<0.050
Pain score at 6 hour	6.60±1.25	4.95±2.17	<0.050
Pain score at 24 hour	4.25±1.75	4.03±2.23	0.618
Pain score at discharge	1.75±1.05	1.75±1.03	1.000
Analgesic consumption(mg)	65.25±33.30	34.00±27.87	<0.050

$p<0.05$ shows significant difference between groups

Table 3. Postoperative nausea and vomiting verbal rating score and antiemetic requirement

	Control group (n = 40) (mean ± SD)	Dexamethasone group (n = 40) (mean ± SD)	*p*-value
Nausea score at 1 hour	0.53±0.90	0.03±0.15	0.001*
Nausea score at 6 hour	0.48±0.67	0.13±0.40	0.006*
Nausea score at 24 hour	0.13±0.46	0.08±0.35	0.588
Nausea score at discharge	0.00±0.00	0.00±0.00	-
Vomiting score at 1 hour	0.45±0.81	0.00±0.00	0.001*
Vomiting score at 6 hour	0.43±0.67	0.05±0.31	0.002*
Vomiting score at 24 hour	0.10±0.44	0.05±0.31	0.562
Vomiting score at discharge	0.00±0.00	0.00±0.00	-
Antiemetic requirement (mg)	9.25±11.85	0.15±0.48	< 0.05

*$p<0.05$ shows significant difference between groups

Discussion

Laparoscopic cholecystectomy is a minimally invasive procedure for gall bladder disease and is considered standard treatment. Postoperative pain and postoperative nausea vomiting are common events (53-72%)[1] and cause increased length of hospital stay. This study demonstrates that preoperative single-dose intravenous dexamethasone can reduce postoperative pain, nausea and vomiting during the first 6 hours postoperatively and can also decrease analgesic and antiemetic requirement in comparison to placebo.

In 1981, dexamethasone was reported to be an effective antiemetic agent in patients receiving cancer chemotherapy[2]. Since then, several studies reported that dexamethasone is effective in the prevention of nausea and vomiting after tonsillectomyin

Table 4. Preoperative and postoperative of ESR and CRP

	Control group (n = 40) (mean ± SD)	Dexamethasone group (n = 40) (mean ± SD)	*p*-value
ESR (preoperative)	22.80±17.24	30.88±25.57	0.102
ESR (postoperative)	35.55±14.31	28.43±20.88	0.079
CRP (preoperative)	2.00±3.203	4.65±10.17	0.120
CRP (postoperative)	24.39±18.47	14.60±15.82	0.013*

*$p<0.05$ shows significant difference between groups

pediatric[3,4] and gynecological surgery[5]. The outcomes of this study indicate that dexamethasone is also effective in the prevention of nausea and vomiting after laparoscopic cholecystectomy, other studies had also demonstrated similar results[6,7]. Nevertheless, Wang JJ et al[6] and Elhakim M et al[7] reported that while single-dose intravenous dexamethasone was effective in reducing postoperative nausea and vomiting, there was no effect on postoperative pain or the analgesic consumption. The results of our study revealed that preoperative single-dose intravenous dexamethasone can reduce postoperative pain at first 6 hours after cholecystectomy and decrease analgesic consumption. Lim SH et al[8] reported that intravenous injection of dexamethasone before and after laparoscopic cholecystectomy was effective in reducing post-operative pain. Mohtadi A et al[9] found that single-dose dexamethasone can reduce postoperative pain at first 12 hours after laparoscopic cholecystectomy in comparison with placebo. Also, Fukami Y et al[10] demonstrated that 8 mg of dexamethasone significantly decreases postoperative pain after laparoscopic cholecystectomy, the result of which is similar to this study. Dexamethasone is the most potent corticosteroids and had analgesic, anti-inflammatory and anti-emetic effects. Although the mechanism of the anti-emetic effect of dexamethasone is not clear but it is thought to inhibit production of serotonin at central and peripheral nervous system[11], central inhibition of the synthesis of prostaglandins[12]. The mechanism of analgesic effect remains unclear, but it seems to decrease cyclooxygenase and lipoxygenase production, via inhibition of peripheral phospholipase[13,14], as well as suppress tissue levels of bradykinin[15] and the release of neuropeptides from nerve endings[16]. This study found that dexamethasone group significantly decreased analgesic consumption and antiemetic requirement in comparison with placebo.

Dexamethasones are modifiers of the postoperative physiologic inflammatory, humoral and immunological responses by regulation of trauma induced humoral mediators. In our study, postoperative ESR and CRP were increased in both treatment groups but postoperative CRP increased significantly less in dexamethasone group compared with control group. Thus, our findings suggest that preoperative intravenous dexamethasone reduced the postoperative inflammatory response after laparoscopic cholecystectomy. This finding is consistent with the results of a study by Bisgaard et al[17] which demonstrated that preoperative dexamethasone reduced postoperative CRP levels, body temperature and fatigue score.

In conclusion, single-dose preoperative dexamethasone 8 mg 60-90 minute before induction of anesthesia improved clinical outcome in terms of significantly less nausea, vomiting, pain at first 6 hours and less inflammatory response after laparoscopic cholecystectomy compared to placebo. The authors suggest that preoperative dexamethasone should be used as routine in patients undergoing laparoscopic cholecystectomy.

What is already known on this topic ?

Several studies reported that dexamethasone is effective in the prevention of nausea and vomiting after tonsillectomy in pediatric[3,4]and gynecological surgery[5] but postoperative analgesic effect is uncertain.

What this study adds ?

Single-dose preoperative dexamethasone 8 mg before induction of anesthesia improved clinical outcome in terms of significantly less nausea, vomiting, pain at first 6 hours and less inflammatory response after laparoscopic cholecystectomy compared to

placebo.

Acknowledgement

The authors acknowledge Faculty of Medicine, Srinakharinwirot University Research Grant to support this work.

Potential conflicts of interest

None.

References

1. Thune A, Appelgren L, Haglind E. Prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. A prospective randomized study of metoclopramide and transdermal hyoscine. Eur J Surg 1995; 161: 265-8.
2. Aapro MS, Alberts DS. Dexamethasone as an antiemetic in patients treated with cisplatin. N Engl J Med 1981; 305: 520.
3. Splinter WM, Roberts DJ. Dexamethasone decreases vomiting by children after tonsillectomy. Anesth Analg 1996; 83: 913-6.
4. Pappas AL, Sukhani R, Hotaling AJ, Mikat-Stevens M, Javorski JJ, Donzelli J, et al. The effect of preoperative dexamethasone on the immediate and delayed postoperative morbidity in children undergoing adenotonsillectomy. Anesth Analg 1998; 87: 57-61.
5. Fujii Y, Uemura A. Dexamethasone for the prevention of nausea and vomiting after dilatation and curettage: a randomized controlled trial. Obstet Gynecol 2002; 99: 58-62.
6. Wang JJ, Ho ST, Liu YH, Lee SC, Liu YC, Liao YC, et al. Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. Br J Anaesth 1999; 83: 772-5.
7. Elhakim M, Nafie M, Mahmoud K, Atef A. Dexamethasone 8 mg in combination with ondansetron 4 mg appears to be the optimal dose for the prevention of nausea and vomiting after laparoscopic cholecystectomy. Can J Anaesth 2002; 49: 922-6.
8. Lim SH, Jang EH, Kim MH, Cho K, Lee JH, Lee KM, et al. Analgesic effect of preoperative versus intraoperative dexamethasone after laparoscopic cholecystectomy with multimodal analgesia. Korean J Anesthesiol 2011; 61: 315-9.
9. Mohtadi A, Nesioonpour S, Salari A, Akhondzadeh R, Masood RB, Aslani SM. The effect of single-dose administration of dexamethasone on postoperative pain in patients undergoing laparoscopic cholecystectomy. Anesth Pain Med 2014; 4: e17872.
10. 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.
11. Fredrikson M, Hursti T, Furst CJ, Steineck G, Borjeson S, Wikblom M, et al. Nausea in cancer chemotherapy is inversely related to urinary cortisol excretion. Br J Cancer 1992; 65: 779-80.
12. Aapro MS, Plezia PM, Alberts DS, Graham V, Jones SE, Surwit EA, et al. Double-blind crossover study of the antiemetic efficacy of high-dose dexamethasone versus high-dose metoclopramide. J Clin Oncol 1984; 2: 466-71.
13. Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev 2000; 21: 55-89.
14. Callery MP. Preoperative steroids for laparoscopic surgery. Ann Surg 2003; 238: 661-2.
15. Hargreaves KM, Costello A. Glucocorticoids suppress levels of immunoreactive bradykinin in inflamed tissue as evaluated by microdialysis probes. Clin Pharmacol Ther 1990; 48: 168-78.
16. Hong D, Byers MR, Oswald RJ. Dexamethasone treatment reduces sensory neuropeptides and nerve sprouting reactions in injured teeth. Pain 1993; 55: 171-81.
17. 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.

การศึกษาผลของการให้เด็กซ่าเมทาโซนทางเส้นเลือดหนึ่งครั้งก่อนการผ่าตัดต่อผลลัพธ์ทางคลินิกหลังการผ่าตัดถุงน้ำดีผ่านทางกล้อง

วิชิต วิริยะโรจน์, ธนา บุญสินสุข, ธรรมนิจ รุกขชาติ, ณรงค์ชัย ยิ่งศักดิ์มงคล

ภูมิหลัง: การผ่าตัดเอาถุงน้ำดีออกผ่านทางกล้องเป็นการผ่าตัดที่ทำบ่อยทางศัลยกรรม ปัญหาที่พบได้บ่อยและทำให้ผู้ป่วยทุกข์ทรมาน หลังการผ่าตัดเอาถุงน้ำดีออกผ่านทางกล้อง คือ อาการปวดหลังการผ่าตัดและอาการคลื่นไส้ อาเจียนหลังการผ่าตัด ยาเด็กซ่าเมทาโซนเป็นที่รู้จักกันว่าเป็นยาสำหรับแก้ปวด ต้านการอักเสบ ปรับภูมิคุ้มกันและต้านอาการคลื่นไส้อาเจียน ดังนั้นการให้ยาเด็กซ่าเมทาโซนก่อนการผ่าตัดอาจลดอาการปวดหลังการผ่าตัดและอาการคลื่นไส้อาเจียนหลังผ่าตัดเอาถุงน้ำดีออกผ่านทางกล้องได้

วัตถุประสงค์: ศึกษาผลของการให้เด็กซ่าเมทาโซนทางเส้นเลือดดำหนึ่งครั้งก่อนการผ่าตัดต่อผลลัพธ์ทางคลินิก เช่น อาการปวดหลังการผ่าตัดและอาการคลื่นไส้อาเจียนหลังผ่าตัดในผู้ป่วยที่ได้รับการผ่าตัดเอาถุงน้ำดีออกผ่านทางกล้อง

วัสดุและวิธีการ: เป็นการศึกษาแบบสุ่มไปข้างหน้า โดยมีกลุ่มประชากรเป้าหมาย 80 คนที่มารับการผ่าตัดถุงน้ำดีออกโดยสุ่มแยกผู้ป่วยออกเป็น 2 กลุ่มคือ กลุ่มที่ได้รับยาเด็กซ่าเมทาโซน 8 มิลลิกรัม (2 มิลลิลิตร) ทางเส้นเลือดดำก่อนการผ่าตัด 60-90 นาที กับกลุ่มควบคุมจะได้น้ำเกลือ 2 มิลลิลิตรทางเส้นเลือดดำก่อนการผ่าตัด 60-90 นาที ผู้ป่วยจะได้รับการดมยาสลบที่เป็นมาตรฐานแบบเดียวกัน การผ่าตัดและการได้ยาระงับอาการปวดแบบเดียวกันทั้ง 2 กลุ่ม หลังจากนั้นจะมีการเก็บข้อมูลอาการปวด อาการคลื่นไส้ อาเจียน หลังการผ่าตัด ชั่วโมงที่ 1, 6, 24 และก่อนกลับบ้าน รวมทั้งปริมาณการใช้ยาแก้ปวด ยาแก้คลื่นไส้ อาเจียน ผลตรวจทางห้องปฏิบัติการทั้ง ESR และ C-reactive protein (CRP) ก่อนผ่าตัดและหลังผ่าตัดทั้ง 2 กลุ่ม

ผลการศึกษา: พบว่าผู้ป่วยทั้ง 2 กลุ่ม ไม่มีความแตกต่างกันในเรื่อง อายุ เพศ ประวัติการผ่าตัดมาก่อน เวลาในการผ่าตัดและระยะเวลาในการนอนโรงพยาบาล ผู้ป่วยทุกคนไม่มีภาวะแทรกซ้อนหลังการผ่าตัดผู้ป่วยกลุ่มที่ได้รับยาเด็กซ่าเมทาโซนมีอาการปวด อาการคลื่นไส้ อาเจียน ในชั่วโมงที่ 1, 6 หลังการผ่าตัดน้อยกว่ากลุ่มควบคุมอย่างมีนัยสำคัญสถิติและปริมาณการใช้ยาแก้ปวด ยาแก้คลื่นไส้อาเจียนและ CRP หลังการผ่าตัดในกลุ่มที่ได้รับยาเด็กซ่าเมทาโซนน้อยกว่า

สรุป: การให้เด็กซ่าเมทาโซน 8 มิลลิกรัม ทางเส้นเลือดดำหนึ่งครั้งก่อนการผ่าตัด 60-90 นาที สามารถเพิ่มผลลัพธ์ทางคลินิก โดยสามารถลดอาการปวด อาการคลื่นไส้ อาเจียน ใน 6 ชั่วโมงแรกหลังการผ่าตัดและขบวนการอักเสบลดลงหลังการผ่าตัดเอาถุงน้ำดีออกเมื่อเทียบกับกลุ่มที่ไม่ได้ยาเด็กซ่าเมทาโซน ผู้นิพนธ์จึงแนะนำว่าควรจะให้เด็กซ่าเมทาโซนก่อนการผ่าตัดในผู้ป่วยที่จะได้รับการผ่าตัดเอาถุงน้ำดีออกผ่านทางกล้อง