

Using Single Dose Systemic Dexamethasone Pre Operatively for Postoperative Pain as Part of Multimodal Analgesia in Laparoscopic Cholecystectomy

Hassan Sarhan Haider ,Bashar taha Enad ,
Mohammad Shakoor Mugheer

ABSTRACT:

BACKGROUND:

Pain after laparoscopy occurs for various reasons and a range of treatment have been suggested for the reduction in pain. There are reports that local anesthesia infiltration, removal of remaining carbon dioxide, administration of anti-inflammatory analgesia before surgery and dexamethasone are effective in post operative pain management. Recently multimodal analgesia methods, where a combination of the above methods are used, are recommended for their effectiveness.

METHOD:

Eighty patients aged 20-60 years; ASA class 1 & 2; undergoing laparoscopic cholecystectomy under general anesthesia were studied and divided into two groups: Group S(n = 40) received dexamethasone 8 mg before induction ; Group N received 2ml normal saline before induction. We measure the degree of pain of both groups with VAS at 1,3,6&24 hours after surgery.

RESULTS:

VAS score of Group S were lower than that of Group N during 24 hours after laparoscopic cholecystectomy and analgesia consumption of Group S were lower than that of Group N.

CONCLUSION:

A single dose of dexamethasone (8mg) intravenously given before induction was effective in reducing postoperative pain after laparoscopic cholecystectomy with multimodal analgesia.

KEY WORDS: dexamethasone ,laparoscopic cholecystectomy, postoperative pain.

INTRODUCTION:

Laparoscopic cholecystectomy has beneficial effect compared to laparotomy such as reduced hospitalization period, cost and use of analgesic with improved lung capacity and arterial oxygen tension^(1,2). Pain after laparoscopy occurs for various reasons and a range of treatment have been suggested for reduction in pain^(3,4). There are reports that local anesthesia infiltration⁽⁵⁾, removal of remaining carbon dioxide⁽³⁾, administration of anti-inflammatory analgesia before surgery⁽⁶⁾ and dexamethasone⁽⁷⁾ are effective in post operative pain management. Recently multimodal analgesia methods, where a combination of the above methods are used, are recommended for their effectiveness.

Moderate to severe acute pain ,regardless the site, can affect nearly every organ function and may adversely influence post operative morbidity and mortality ;so effective management of postoperative pain is not only humane, but is a very important aspect of postoperative care^(8,9).

Glucocorticoids inhibit the phospholipase enzyme and there for block both the cyclo-oxygenase and the lipo- oxygenase pathways in the inflammatory chain reaction ,they may be effective therefore in reducing pain by interfering with prostaglandins synthesis⁽¹⁰⁾. Dexamethasone is a corticosteroid with high glucocorticoid but minimal mineralocorticoid activity and long duration of action(half-life 36-72 hours),thus used where sustained activity is required but when water retention would be harmful (e.g. cerebral edema) , also used to reduced edema following dental surgery. It has been used to prevent nausea and vomiting associated with surgery and chemotherapy and to mature fetal lung in premature labor^(11,12,13) .

AIM OF THE STUDY:

The aim of the study was to investigate whether the administration of steroids affect postoperative pain management in patients undergoing multimodal analgesia in laparoscopic cholecystectomy.

Medical City Baghdad Teaching Hospital .

PATIENTS AND METHOD:

This prospective comparative double blind study was conducted in Baghdad Teaching Hospital during the period from the first of Jan till the end of April 2013.

Eighty patients aged 20-60 years; ASA class 1 & 2 ; undergoing laparoscopic cholecystectomy under general anesthesia were studied.

Patients with BMI over 30, diabetic patients , who switched to laparotomy during surgery and who were taking medication for chronic pain were excluded from the study. Subjects were randomly assigned to a control group (**Group N**) and to a group who received dexamethasone 8 mg before induction (**Group S**). There were no significant differences in gender, age, BMI, duration of surgery and duration of anesthesia between the groups. In a visit before surgery, the VAS (visual analog scale) was thoroughly explained (0= no pain, 10= unimaginably severe pain). Before induction of anesthesia **Group S** received 8mg dexamethasone while **Group N** received 2ml normal saline.

Induction of general anesthesia started by pre-oxygenation, Midazolam 1 mg, Fentanyl 100^{mcg}, Ketamine 0.5 mg /kg, Propofol 2mg/kg for the loss of consciousness. Intubation was done after 0.5mg/kg atracurium besylate and anesthesia was maintained with O₂ and Halothane 0.7%. Tidal volume and breathing rate were controlled to maintain a 35-40 mmHg end tidal CO₂. We

measure the degree of pain of both groups with VAS at 1,3,6&24 hours after surgery.

RESULTS:

Forty patients in Group N their mean ages $\pm$ SD were 41.70 $\pm$ 11.27 years, 13(32.5%) of them were males and 27 (67.5%) females, with male to female ratio 1:2.07. Forty patients in Group S their mean age $\pm$ SD were 40.25 $\pm$ 11.02 years, 16(40%) of them were males and 24 (60%) females with male to female ratio 1:1.5.

The mean $\pm$ SD of age ,BMI, duration of surgery and duration of anesthesia between both groups showed little differences which are statistically not significant. P value were 0.944, 0.617, 0.616 and 0.383 respectively.

ASA Status of the two groups showed no statistical differences, P value = 0.105.

The amount of tramadol I.V injected during the 24 hours postoperatively was significantly reduced in Group S compared to Group N, P value was 0.002.

ANOVA analysis results regarding the repeat measurements of VAS confirmed that steroid administration cause a significant decrease in VAS in Group S during 6 and 24 hours postoperatively compared to Group N.

Intravenous dexamethasone was effective in the postoperative pain management of patients undergoing multimodal analgesia after laparoscopic cholecystectomy.

Table 1 : Changes in postoperative pain between the two groups during postoperative periods.

VAS Score	Group N		Group S		* P value
	Mean	SD	Mean	SD	
1 hour	4.30	0.723	4.13	0.607	0.245
3hour	3.20	1.018	2.95	0.597	0.184
6 hour	2.68	0.616	2.35	0.483	0.010
24 hour	2.50	0.599	2.20	0.405	0.010

Table 2: Demographic Data.

Demographic Data	Group N		Group S		*P value
	Mean	SD	Mean	SD	
Age(year)	41.70	11.27	40.25	11.02	0.944
BMI	24.11	2.93	23.78	3.06	0.617
Duration of surgery(min.)	45.28	9.80	44.18	9.93	0.616
Duration of anesthesia (min.)	62.58	10.70	60.63	9.38	0.383

DISCUSSION:

After laparoscopic cholecystectomy, patients complain of pain from the incision of the skin, of visceral pain and of shoulder pain from diaphragm stimulation⁽¹⁴⁾. Since pain is caused by various reasons, a range of treatment methods has been introduced for the reduction of pain^(3,4).

In the case of local anesthetic infiltration, there are various results according to research, and while local anesthetic infiltration in the incision area is the recommended pain management method in laparoscopic cholecystectomy, infusion of local anesthesia into the abdominal cavity is reported to be more effective in obstetrics and gynecology laparoscopy^(5,8,15).

There are also reports that the remaining CO₂ in the abdominal cavity is related to the postoperative pain so thorough removal of the remaining CO₂ is effective⁽³⁾. There are reports that dexamethasone is effective in pain reduction after laparoscopic cholecystectomy⁽⁷⁾. Recently however, a multimodal analgesic method, which combines and utilizes the above methods, is recommended⁽¹⁴⁾.

The mechanisms of the pain relief for the effects of dexamethasone are not clear yet, but the decrease in cyclooxygenase and lipoxygenase products by suppressing phospholipases in the periphery plays a major role^(16,17). Additionally, reduced bradykinin, which reinforces pain in the inflamed tissue and operated area, and the concentration of nerve proteins secreted from the peripheral nervous system are involved in the pain relief effect^(18,19).

In this study, when compared to the control group, the use of dexamethasone showed a decrease in VAS at 1,3,6 and 24 hours postoperatively and a decrease in the use of analgesics. Bisgaard et al⁽⁷⁾ also reported similar results but were different to this study in that the VAS was not different to the control group at 24hr postoperatively. The reason for this difference may be partially that Bisgaard et al prescribe NSAID at regular intervals even without pain after surgery.

Considering the fact that 1-2 hrs is needed for the onset of the medication, to reduced the inflammatory response after surgery, the timing of the administration of the steroid before or during surgery is important⁽¹⁶⁾. Bisgaard et al reported that when 8 mg of dexamethasone was IV injected 90 minutes before laparoscopic cholecystectomy, the postoperative pain and required amount of opioids were reduced

approximately 50% compared to the placebo group.

Elhakim et al⁽¹⁵⁾ reported that there was no pain relief effect when dexamethasone was IV injected directly before incision of the skin. Elhakim et al used infusion of local anesthesia into the abdominal cavity in combination, but since the pain relief effect of this method is not clear in laparoscopic cholecystectomy, its use is not generally recommended⁽¹⁴⁾.

In addition, the different purposes of the research, the differences in surgery time due to the expertise of the operating surgeon, and subjective characteristics of the patients responding to the pain could all be involved with the differences in results between the 2 studies, and thus, further research regarding this may be necessary.

When steroid are used, complications such as delays in recovery, post-operative inflammation, glucose intolerance and ulcers in the gastric mucous membrane can occur. Sauerland et al⁽²⁰⁾ reported in their meta-analysis that there was no significant increase in complications when 15-30 mg/kg of methylprednisolone was used in one dose, and this is 50 times the amount of the 8 mg of dexamethasone.

In a meta-analysis regarding postoperative nausea and vomiting, one IV injection of dexamethasone did not increase the occurrence of inflammation or other complications⁽²⁾. In addition, in our study, there were no observations of complications related to dexamethasone.

Gildasio S et al concluded that dexamethasone at doses more than 0.1 mg/kg is an effective adjunct in multimodal strategies to reduce postoperative pain and opioid consumption after surgery⁽²¹⁾.

Intermediate dose of dexamethasone (0.11-0.2mg/kg) is a safe and effective multimodal pain strategy after surgical procedures. The preoperative administration of the drug provides a greater effect on postoperative pain⁽²¹⁾.

Liu et al, Murphy GS et al and Kim et al concluded that pain scores and requirements for analgesics were reduced after steroid administration in laparoscopic cholecystectomy.

CONCLUSION:

Through this study, it could be concluded that intravenous injection of 8mg of dexamethasone can be helpful in the pain management of patients undergoing the multimodal analgesic method after laparoscopic cholecystectomy.

Recommendations

We recommend to use single dose IV dexamethasone before induction of anesthesia in laparoscopic cholecystectomy if there is no contraindication.

REFERENCES:

- Joris J, Cigarini I, Legrand M, Jacquet N, De Groote D, Franchimont P, et al. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. *Br J Anaesth* 1992;69:341-45.
- Grace P A, Quereshi A, Coleman J, Keane R, McEntee G, Broe P, et al. Reduced postoperative hospitalization after laparoscopic cholecystectomy. *Br J Surg* 1991;78:160-62.
- Alexander JI. Pain after laparoscopy. *Br J Anaesth* 1997;79:369-78.
- Wills VL, Hunt DR. Pain after laparoscopic cholecystectomy. *Br J Surg* 2000;87:273-84.
- Lee IO, Kim SH, Kong MH, Lee MK, Kim NS, Choi YS, et al. Pain after laparoscopic cholecystectomy: the effect and timing of incisional and intraperitoneal bupivacaine. *Can J Anaesth* 2001; 48:545-50.
- Joshi GP, Viscusi ER, Gan TJ, Minkowitz H, Cippolle M, Schuller R, et al. Effective treatment of laparoscopic cholecystectomy pain with intravenous followed by oral COX-2 specific inhibitor. *Anesth Analg* 2004;98: 336-42.
- 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.
- Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: a critical assessment of the evidence. *Anesthesiology* 2006;104:835-46.
- Lubenow TR, Ivankovich AD, Barkin RL. Management of acute postoperative pain. In: Barash PG, et al. *Clinical anesthesia*. 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2006:1411.
- Turk R and John A. Cidlowski. Anti-inflammatory Action of Glucocorticoids-NEW Mechanisms for Old Drugs. *N Engl J Med* 2005;353:1711-23.
- Peter J. Anti-inflammatory actions of glucocorticoids: molecular Mechanisms. *Clinical Science* 1998; 94:557-72.
- Essential of Medicinal Pharmacology. 6th edition, Jaypee publisher, 2008: 453-68.
- Joseph Dipiro, Robert L Talert. *Pharmacotherapy: A Pathophysiologic Approach*, Eighth Edition. McGraw Hill Professional, 2011: 1703-12.
- Bisgaard T, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. *Pain* 2001;90:261-69.
- Elhakim M, Nafie M, Mahmoud K, Atef A. Dexamethasone 8 mg in combination with ondansetron 4mg appears to be the optimal dose for the prevention of nausea and vomiting after laparoscopic cholecystectomy. *Can J Anaesth*. 2002;49:922-26.
- 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.
- Callery MP. Preoperative steroids for laparoscopic surgery. *Ann Surg*. 2003;238:661-62.
- 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.
- Hong D, Byers MR, Oswald RJ. Dexamethasone treatment reduces sensory neuropeptides and nerve sprouting reaction in injured teeth. *Pain*. 1993;55:171-81.
- 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.
- Gildasio S, De Oliveira, Almeida, Marcela D, Benzon, Honorio T, McCarthy, Robert J. Perioperative Single Dose Systemic Dexamethasone for postoperative pain: A Meta-analysis of Randomized Controlled Trials. *Anesthesiology*. 2011; 115:575-88.
- Liu K, Hsu CC, Chia YY. Effect of dexamethasone on postoperative emesis and pain. *Br J Anaesth*. 1998;80:85-86
- Murphy GS, Szokol JW, Greenberg SB, Avram MJ, Vender JS, Nisman M, Vaughn J. Preoperative dexamethasone enhances quality of recovery after laparoscopic cholecystectomy: effect on in-hospital and

- post discharge recovery outcomes.
Anesthesiology. 2011; 114:882-90.
24. Kim HY, Lee MJ, Park PE, Koo JW. The effect of dexamethasone on postoperative pain and nausea and vomiting after laproscopiccholecystectomy in younger and older patients. Korean J Anesthesiol. 2008;54:651-55.