Original Article

Effect of a single bolus of dexamethasone on intraoperative and postoperative pain in unilateral inguinal hernia surgery

Muhammad Vaiz Asad, Fauzia Anis Khan

Department of Anaesthesiology, Aga Khan University, Karachi, Pakistan

Abstract

Background and Aims: Opioids are commonly used to provide perioperative analgesia, but have many side-effects. Addition of co-analgesics results in reducing the dosage and hence the side-effects of opioids. The objective of this study was to compare the analgesic efficacy of fentanyl (1 micro/kg^{-1}) administered alone, with fentanyl (0.75 micro/kg^{-1}) and dexamethasone (8 mg) combination, in patients undergoing day care unilateral inguinal hernia repair.

Material and Methods: Patients scheduled for the day care unilateral inguinal hernia repair were randomized to receive either saline and fentanyl 1 micro/kg^{-1} (control group) or 8 mg dexamethasone with fentanyl 0.75 micro/kg^{-1} (study group) immediately before induction of anesthesia in a double-blind clinical trial. Anesthesia technique and rescue analgesia regimen were standardized. Intraoperatively, pain was assessed based on hemodynamic variability and postoperatively by visual analog scale.

Results: The mean heart rate, systolic and the diastolic blood pressure at 1, 5, 20 and at 30 min after incision, were significantly higher in the control group ($P \leq 0.001$) when compared to the study group. Intra-operative rescue analgesia was required in 32 (100%) and 19 (59.4%) patients in control group and study group respectively ($P = 0.0002$). Mean pain scores measured at fixed time periods postoperatively were significantly higher in the control group when compared to study group ($P \leq 0.001$). Postoperative rescue analgesia was needed in 32 (100%) versus 24 (75%) patients in the control group and study group respectively, but this difference was not statistically significant ($P = 0.285$).

Conclusion: We conclude that the addition of 8 mg of preoperative intravenous dexamethasone to 0.75 micro/kg^{-1} fentanyl was effective in reducing intraoperative and postoperative pain in the 1st h after unilateral inguinal hernia surgery.

Key words: Analgesia, day care, dexamethasone, inguinal hernia, postoperative pain

Introduction

Postoperative pain is one of the main reasons of delayed discharge and unanticipated hospital admission in day care anesthesia. Opioids are traditionally used for both intra and postoperative analgesia but are associated with unwanted side-effects, e.g., respiratory depression, nausea and vomiting, itching, increased duration of postoperative ileus, and others. These side effects can be reduced with a reduction in the amount of opioid drugs administered, but this requires the addition of co-analgesic drugs. One such supplemental drug is dexamethasone. Its strong antiinflammatory effect contributes to postoperative analgesia as tissue injury plays a significant role in the pathophysiology of surgical pain.[1] The recommended analgesic dose of dexamethasone for this purpose is variable. A single dose of 8 mg of dexamethasone has been shown to be effective in reducing postoperative analgesic requirements after dental surgery[2] and thyroidectomy for up to 48 h.[3] On the other hand, Tan *et al*.[4]have showed that dexamethasone 10 mg is not effective in reducing postoperative pain after spinal anesthesia for inguinal hernia repair, therefore the role of dexamethasone as a co-analgesic remains unclear.

This study was undertaken to compare intraoperative and early postoperative pain in unilateral inguinal hernia repair, in patients who received fentanyl 1 ug/kg^{-1} alone with fentanyl 0.75 ug/kg^{-1} and 8 mg of dexamethasone combination at the time of induction.

Material and Methods

This randomized double-blind placebo-controlled study was approved by the local Ethics Review Committee

Address for correspondence: Dr. Fauzia Anis Khan,
Department of Anaesthesiology, Aga Khan University, P.O. Box 3500, Stadium Road, Karachi - 74800, Pakistan.
E-mail: fauzia.khan@aku.edu

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.161669

(1557-ANE-ERC-10.PI). Sixty-four American Society of Anesthesiologists (ASA) grade I and II patients between the ages of 18 and 70 years undergoing unilateral inguinal hernia surgery as day care anesthesia were recruited between November 1, 2010 and April 4, 2011. Only patients who opted for GA instead of regional anesthesia were enrolled for the study. A 50% reduction of pain [visual analog scale (VAS) score without study drug 6.4 ± 3.3, and with study drug 3.1 ± 2.2] with combination of fentanyl and dexamethasone when compared to fentanyl alone was considered clinically significant.[7] A sample size of 32 subjects in each group was sufficient to detect a 50% difference in pain score with alpha 0.01 and beta 0.01. We considered 50% reduction in postoperative VAS score as the primary outcome. All patients gave written informed consent. Patients with a history of allergy or hypersensitivity to study drugs, history of chronic usage of analgesic drugs, or use of steroids 30 days prior to surgery were excluded. Patients were randomly allocated into two groups by "sealed opaque envelope method." Randomization was done by pharmacy and drugs were prepared in identical syringes for each group by a pharmacist. Fentanyl was prepared in 5 ml syringes and labeled as "fentanyl study." Group A (control) syringe contained fentanyl 1micro/kg^{-1} and Group B (study) contained fentanyl 0.75 micro/kg^{-1}. The volume in both syringes was made up to 5 ml by adding normal saline 0.9%. A second syringe of 3 ml was labeled as "study drug." This contained 2 ml of normal saline 0.9% for Group A (control) and 8 mg (2 ml) of dexamethasone for Group B (study). Dexamethasone is a colorless solution and therefore indistinguishable from saline.

At the time of the preoperative visit, all patients were explained about the 10 cm VAS for pain in which 0 means no pain and 10 means worst imaginable pain. Midazolam tablet 7.5 mg was administered 1 h before surgery as premedication. In the preoperative area baseline heart rate, systolic, diastolic and mean arterial blood pressure was recorded, and an average of three readings was taken as a baseline. In the operating room, patient's lungs were preoxygenated for 3 min with oxygen at a flow rate of 6 L/min on a circle breathing system. Patients were administered the study drug by an assistant anesthetist who was not involved in taking observations. The patients and the anesthetist making observations were blind to the drugs administered. Each group received one syringe of fentanyl and another of study drug.

Anesthesia was induced with propofol 2 mg/kg^{-1} administered over 30 s followed by atracurium 0.6 mg/kg^{-1} intravenous (iv). Intraoperative monitoring was assessed via Datex-Ohmeda S/5 anesthesia monitor, and included electrocardiography, noninvasive blood pressure, pulse-oximetry and capnography, which was used in all patients. Maintenance of anesthesia was achieved with nitrous oxide (N_2O) 60% in oxygen (O_2), FiO_2 0.4, and isoflurane 0.6-1.2%. Ventilation was volume controlled and the tidal volume was kept between 8 and 10 ml kg^{-1} and respiratory rate was set to achieve normocapnia (end tidal carbon dioxide of 30-40 mmHg). Intraoperative rescue analgesia with pethidine 10 mg iv was given if the hemodynamic variables escalated above 20% of preoperative baseline values.

Reversal of the muscle relaxant was achieved with neostigmine 2.5 mg and glycopyrolate 0.5 mg iv given when spontaneous breathing was resumed by the patient. After tracheal extubation patient was shifted to the recovery room.

Visual analogue scale ranging from zero to ten was used to assess the pain in the recovery room and day care unit. Readings were taken on arrival in the recovery room followed at 10 min intervals for 30 min and then at 60 min at the time of discharge from the recovery room. The last observation was taken at time of discharge from day care unit at 120 min after surgery. Rescue analgesia with pethidine 10 mg iv was given if the patient had VAS score of three or above. This was administered by the nursing staff who was blinded to the treatment group, and who also noted the number of injections dispensed.

Unmasking of drugs administered was done after the study was completed. Statistical analysis was performed using Statistical Packages for Social Science version 19 (SPSS Inc., Chicago, IL). Mean and standard deviations were estimated for numerical outcome and analyzed by independent sample *t*-test while qualitative characteristics were presented in term of frequency and percentage and analyzed by Chi-square test. Normality assumption was also checked for quantitative variables, and Mann–Whitney U-test was applied for nonparametric data. Haemodynamic variables including blood pressure and heart rate were reported as mean and standard deviation at different time points and analyzed by repeated measures of ANOVA. $P \leq 0.05$ was considered as statistically significant.

Results

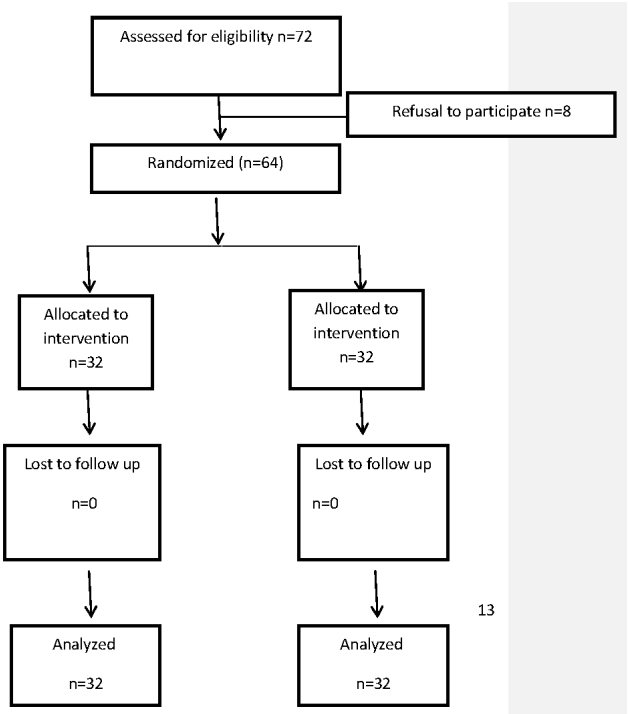
There were no dropouts, and all patients completed the study [Flow Diagram]. The two groups were comparable for demographic data and baseline variables [Table 1]. No statistical difference was observed between ASA status and baseline hemodynamic variables. Average duration of hernia and surgery were also not significantly different between groups.

Heart rate, systolic and diastolic blood pressure following

incision at 1, 5, 20 and 30 min were significantly higher in the control group compared to study group [Figures 1-3].

Intra operative rescue analgesia was required in all patients in the control group and 19 patients in study group. This difference was significant ($P = 0.0002$).

On arrival in the recovery room, 15 (47%) patients in the control group and eight (25%) in study group had pain score >3 but this was not statistically significant. During the first 60 min pain score was significantly higher in the control group than study group [Table 2].



At 120 min no comparison was possible as none of the patients complained of pain. Postoperative rescue analgesia was given in 32 (100%) and 24 (75%) patients in control

Table 1: Demographic data and other baseline variables

Variables	Group A (n = 32)	Group B (n = 32)	P value
Age (years)	50.4 (15.5)	43.9 (13.8)	0.08
Weight (kg)	69.3 (7.3)	70.5 (9.6)	0.60
Duration of hernia (months)	1.66 (0.65)	1.66 (1.0)	0.53
Duration of surgery (min)	60.1 (10)	62.2 (24.3)	0.97
Gender (%)			
Male	30 (93.8)	28 (87.5)	0.67
Female	02 (6.3)	4 (12.5)	
ASA status (%)			
I	14 (43.7)	17 (53.1)	0.62
II	18 (56.3)	15 (46.9)	

Values are in mean (SD). SD = Standard deviation, ASA = American society of anaesthesiologists

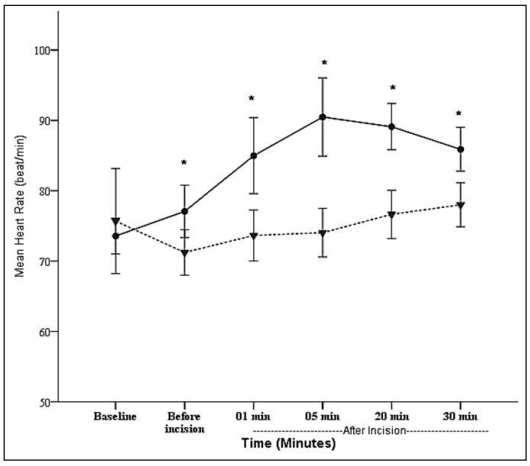


Figure 1: Comparison of intraoperative mean heart rate between fentanyl 1 micro/kg^{-1} (●) and fentanyl 0.75 micro/kg^{-1} and dexamethasone 8 mg (▼). *Significant difference between groups

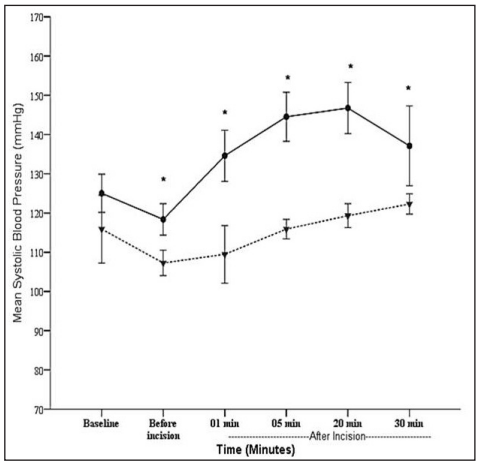


Figure 2: Comparison of intraoperative mean systolic blood pressure between fentanyl 1 micro/kg^{-1} (●) and fentanyl 0.75 micro/kg^{-1} and dexamethasone 8 mg (▼). *Significant difference between groups

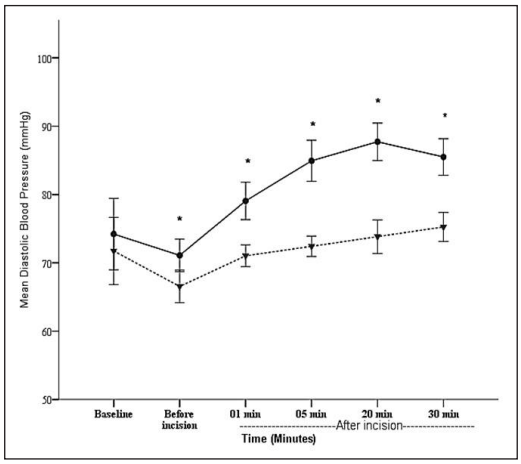


Figure 3: Comparison of intraoperative mean diastolic blood pressure between fentanyl 1 micro/kg^{-1} (●) and fentanyl 0.75 micro/kg^{-1} and dexamethasone 8 mg (▼). *Significant difference between groups

group and study group respectively. This difference was again not significant. A comparison of postoperative mean pain scores on VAS between the two groups is shown in Table 3.

Discussion

Postoperative pain after day care surgery can delay discharge from the hospital.

A multimodal or "balanced" analgesic approach using a combination of opioid and nonopioid analgesic techniques has been more appropriate. The adjunct agents that have been used to decrease the dose of narcotics include ketamine,[5] gabapentin,[6] paracetamol, and nonsteroidal antiinflammatory drugs.[7] Systematic reviews have demonstrated the benefit of these drugs in reducing postoperative pain and/or opioid consumption.[5-7]

Dexamethasone is a synthetic glucocorticoid that has little to no mineralocorticoid activity. It is now commonly used perioperatively to reduce postoperative nausea and vomiting[8] and because of its antiinflammatory effect may have a beneficial role in providing postoperative analgesia. It suppresses both inflammation and immune responses. At the molecular level, unbound glucocorticoid readily crosses cell membranes and binds with high affinity specific cytoplasmic receptors. This binding ultimately affects protein synthesis, which may inhibit leukocyte infiltration at the site of inflammation, interfering in the function of mediators of the inflammatory response, and suppress humoral immune responses. Some of the net effects include reduction in edema or scar tissue and a general suppression in immune response. The degree of clinical effect is normally related to the dose administered. The inflammatory mediators that are inhibited include interleukin, C-reactive protein, tumor necrosis factor α and leukocyte receptors.[9-11]

Table 2: Comparison of the number of patients undergoing inguinal hernia repair who had VAS pain scores >3 at different time points

Time	Group A (n = 32)	Group B (n = 32)	P value
On arrival in recovery room	15 (46.9)	8 (25)	0.07
10 min	30 (93.8)	20 (62.5)	0.005*
30 min	28 (87.5)	8 (25)	0.0001*
60 min	13 (40.6)	1 (3.1)	0.0001*
120 min	0 (0)	0 (0)	NA

*Values presented as n (%).*Significant difference between groups. VAS = Visual analogue scale, NA = Not available*

Table 3: Comparison of postoperative mean pain scores on VAS between the two groups

Time	Group A (n = 32)	Group B (n = 32)	P value
On arrival in recovery room	4.2 (2.1)	2.5 (1.8)	0.001
10 min	5.9 (1.3)	3.97 (1.4)	<0.0001
30 min	5.1 (1.1)	3 (0.98)	<0.0001
60 min	3.3 (1.3)	2.1 (0.8)	<0.0001
120 min	2.03 (0.47)	1.13 (0.34)	<0.0001

VAS = Visual analogue scale

A number of studies have been conducted to evaluate the analgesic effect of dexamethasone in adult patients undergoing different types of surgery in different doses ranging from 4 mg to 16 mg[10-12] but the optimal dose is still not defined. It has been used both orally and intravenously.[13,14] The time of administration also varies in the studies from 2 h before induction[17] to immediately before induction.[13-15] Some researchers have administered it postoperatively.[13] The evidence for its analgesic effect has not been convincing. Some studies have reported lowered pain scores, whereas others have reported no difference.[4-16]

Karanicolas *et al.*[17] conducted a systematic review of seventeen studies on the use of dexamethasone as an antiemetic in laparoscopic cholecystectomy. Analgesia was observed as a secondary outcome, and its effect was found to be inconclusive. Another recent meta-analysis by Oliveira *et al.*[18] included twenty-four randomized clinical trials. Comparisons were stratified by dose into three groups, low-dose (0.10 mg/kg^{-1}), intermediate-dose (0.11-0.20 mg/kg^{-1}), and high-dose (more than 0.21 mg/kg^{-1}) dexamethasone. They concluded that dexamethasone at doses more than 0.1 mg/kg^{-1} is an effective adjunct in multimodal strategies to reduce postoperative pain and opioid consumption after surgery.

In our study, the intraoperative pain assessed by hemodynamic variability was higher in the control group (Group A) with significantly more use of intraoperative rescue analgesia (P = 0.0002). Postoperative mean pain scores measured by VAS were also higher in the control as compared with the fentanyl dexamethasone combination study group (Group B). Although less number of patients in the study group required rescue analgesia 24 (75%) versus 32 (100%) of group a postoperatively, this difference was not statistically significant. One possible explanation could be the timing of administration of dexamethasone. Studies in which dexamethasone was administered early showed reduced postoperative pain scores and analgesic requirements.[14,19] In these studies, dexamethasone was administered 120, 90, 60 and 45 min before surgery. This may have resulted in improved peak levels of dexamethasone.

Jokela *et al.*[20] studied three different doses to identify the effective analgesic dose of dexamethasone after laparoscopic hysterectomy. Ten and 15 mg doses reduced the oxycodone consumption during the first 2 h after surgery, but 5 mg had no effect. Other authors were also unable to demonstrate

the analgesic effect of 4 mg and 5 mg.[10,20] In contrast Wu *et al*.[7] were able to demonstrate the analgesic effect of 5 mg of dexamethasone with reduced VAS pain scores in patients undergoing anorectal surgery. It's possible that different surgeries require different doses of dexamethasone based on the extent of surgery and the intensity of tissue trauma and hence the requirement for dexamethasone, therefore the dose that is adequate for one procedure may not be enough for another.

Our study has limitations. We did not observe patient satisfaction, and we did not study dynamic pain. Our method of assessment for administrating additional intraoperative analgesia was also simple. Additional use of depth of anesthesia monitor may have provided more information but would have considerably added to the cost. However, studies like ours have a special value in the developing and the less affluent countries. An important hurdle in the management of postoperative pain in the developing countries is related to erratic availability of potent narcotic analgesic drugs and their derivatives. Dexamethasone is an easily available and cheap drug, which when used as a co-analgesic not only reduces the narcotic dose requirement, but also prevent postoperative nausea and vomiting, and facilitates early discharge from hospital after day care surgery, thus reducing overall costs.

We conclude that 8 mg of the preoperative iv dexamethasone when combined with a lower dose of fentanyl is effective in reducing intraoperative and immediate postoperative pain in the 1st h after unilateral inguinal hernia surgery.

Acknowledgment

Financial support: The cost of the study drug was funded by the departmental research fund of the Department of Anesthesiology, Aga Khan University, Karachi, Pakistan.

References

1. Salerno A, Hermann R. Efficacy and safety of steroid use for postoperative pain relief. Update and review of the medical literature. J Bone Joint Surg Am 2006;88:1361-72.
2. 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.
3. Worni M, Schudel HH, Seifert E, Inglin R, Hagemann M, Vorburger SA, *et al.* Randomized controlled trial on single dose steroid before thyroidectomy for benign disease to improve postoperative nausea, pain, and vocal function. Ann Surg 2008;248:1060-6.
4. Tan PH, Liu K, Peng CH, Yang LC, Lin CR, Lu CY. The effect of dexamethasone on postoperative pain and emesis after intrathecal neostigmine. Anesth Analg 2001;92:228-32.
5. Bell RF, Dahl JB, Moore RA, Kalso EA. Perioperative ketamine for acute postoperative pain. Cochrane Database Syst Rev 2006;Issue 1.Art.No.:CD004603.DOI:10.1002/14651858.CD004603.pub2.
6. Ho KY, Gan TJ, Habib AS. Gabapentin and postoperative pain — A systematic review of randomized controlled trials. Pain 2006;126:91-101.
7. Ong CK, Seymour RA, Lirk P, Merry AF. Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: A qualitative systematic review of analgesic efficacy for acute postoperative pain. Anesth Analg 2010;110:1170-9.
8. Gan TJ, Meyer TA, Apfel CC, Chung F, Davis PJ, Habib AS, *et al.* Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2007;105:1615-28.
9. Tsuei SE, Moore RG, Ashley JJ, McBride WG. Disposition of synethetic glucocorticoids. I. Pharmacokinetics of dexamethasone in healthy adults. J Pharmacokinet Biopharm 1979;7:249-64.
10. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: Pathophysiologic effects and clinical implications. J Am Coll Surg 2002;195:694-712.
11. 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.
12. 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.
13. 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.
14. Worni M, Schudel HH, Seifert E, Inglin R, Hagemann M, Vorburger SA, *et al.* Randomized controlled trial on single dose steroid before thyroidectomy for benign disease to improve postoperative nausea, pain, and vocal function. Ann Surg 2008;248:1060-6.
15. Al-Qudah M, Rashdan Y. Role of dexamethasone in reducing pain after endoscopic sinus surgery in adults: A double-blind prospective randomized trial. Ann Otol Rhinol Laryngol 2010;119:266-9.
16. Tolver MA, Strandfelt P, Bryld EB, Rosenberg J, Bisgaard T. Randomized clinical trial of dexamethasone versus placebo in laparoscopic inguinal hernia repair. Br J Surg 2012;99:1374-80.
17. 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.
18. 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.
19. Gómez-Hernández J, Orozco-Alatorre AL, Domínguez-Contreras M, Oceguera-Villanueva A, Gómez-Romo S, Alvarez Villaseñor AS, *et al.* Preoperative dexamethasone reduces postoperative pain, nausea and vomiting following mastectomy for breast cancer. BMC Cancer 2010;10:692.
20. Jokela RM, Ahonen JV, Tallgren MK, Marjakangas PC, Korttila KT. The effective analgesic dose of dexamethasone after laparoscopic hysterectomy. Anesth Analg 2009;109:607-15.

How to cite this article: Asad MV, Khan FA. Effect of a single bolus of dexamethasone on intraoperative and postoperative pain in unilateral inguinal hernia surgery. J Anaesthesiol Clin Pharmacol 2015;31:339-43.
Source of Support: The cost of study drug 'Dexamethasone' was funded by the departmental research fund, **Conflicts of Interest:** None declared.