

DEXAMETHASONE ADDED TO BUPIVACAINE PROLONGS DURATION OF EPIDURAL ANALGESIA

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Abstract

Background: Different additives have been used to prolong regional blockade. We designed a prospective, randomized, double-blind, controlled clinical trial to evaluate the effect of dexamethasone added to bupivacaine-fentanyl on the duration of postoperative analgesia via epidural catheterization.

Methods: Seventy two adult patients scheduled for elective abdominal or thoracic surgery under epidural anesthesia were randomly allocated into two groups to receive either bupivacaine (0.5%) - fentanyl (50µg) and dexamethasone (8 mg) in lumbar or thoracic epidural anesthesia (Dexa group, n=36), or bupivacaine-fentanyl and saline normal (control group, n=36) via epidural catheter. Duration of analgesia, postoperative pain score and IV analgesic use at first 24 hours were recorded and compared.

Results: Two patients were excluded (one in each group) due to unsuccessful blockade. Age, gender and duration of surgery were similar in the two groups ($p>0.05$). The duration of analgesia (372 ± 58.1 vs. 234.6 ± 24.3 min) was significantly longer and pain score and pentazocine use were less in the Dexa than the control group (37.1 ± 19.7 mg v.s. 73.1 ± 17.6 mg, respectively; $p=0.001$).

Conclusions: This study revealed that dexamethasone added to bupivacaine-fentanyl solution in epidural analgesia prolongs the duration of analgesia in abdominal or thoracic surgery.

Key words: Epidural, Analgesia, Dexamethasone, Bupivacaine, Fentanyl.

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Introduction

Uncontrolled perioperative pain may potentiate some of pathophysiologicals and increase morbidity and mortality for patients. Attenuation of postoperative pain may decrease perioperative morbidity and mortality¹. Analgesia delivered through an indwelling epidural catheter is a safe and effective method for management of postoperative pain².

Increasing the duration of local anesthetic action is often desirable because it prolongs analgesia. Different additives have been used to prolong regional blockade. Two of the more studied adjuvants are epinephrine and clonidine^{3,4}. Epidural neostigmine and ketamin also were used as adjuvant drugs⁵⁻⁶. Some studies have demonstrated the analgesic effect of local spinal and systemic corticosteroids in combination with bupivacaine⁷.

Dexamethasone is a high-potency, long-acting glucocorticoid with little mineralocorticoid effect that has been used for prophylaxis of postoperative nausea⁸. Dexamethasone microspheres have been found to prolong the block duration in animal and human studies⁹⁻¹⁰, and adding methylprednisolone and dexamethasone to local anesthetic increases the duration of axillary brachial block¹¹. Biodegradable microcapsules containing bupivacaine and dexamethasone have been tested in humans and found to produce analgesia for several days in intercostal block¹². Epidural steroids were effective in the treatment of low back pain¹³. A double-blind study demonstrated postoperative pain reduction and analgesic requirements after epidural dexamethasone injection¹⁴. Nevertheless, the time of analgesia was not cleared in this study.

The safety of epidural steroid injections has been demonstrated¹⁵. Thomas et al. showed that epidural dexamethasone reduced postoperative pain and analgesic requirements in patients undergoing laparoscopic cholecystectomy¹⁶. Hanan et al. demonstrated efficacy of epidural dexamethasone on postoperative analgesia in patients undergoing lower abdominal surgeries¹⁷.

The aim of the current study is to evaluate the effect of dexamethasone added to bupivacaine on the duration of epidural analgesia for postoperative pain

management in patients undergoing lower and upper abdominal and thoracic surgeries.

Methods

After institutional approval, written, informed consent was obtained from each patient before inclusion in the study. Seventy-two ASA physical statuses I-II patients aged 23-79 years scheduled for elective abdominal or pelvic surgery were included in the study. Power analysis was done on the basis of authors' assumption that adding dexamethasone to epidural analgesia by bupivacaine prolongs the time of post-operative analgesia (240±45 min) up to 30 minutes; considering $\alpha=0.05$ and desired power=80% and using online power analysis software; URL: <http://www.stat.ubc.ca/~rollin/stats/ssize/n2.html>.

Each group included 36 patients.

Exclusion criteria were history of peptic ulcer disease, hepatic or renal failure, psychological disease, allergy to narcotics, a contraindication to an epidural catheter, and use of any premedications (including opioids, benzodiazepines, and clonidine).

On arrival to the operating room, standard monitoring was established (pulse oximetry, electrocardiography, and noninvasive blood pressure monitoring). Patients were randomly divided into two groups (each n=36) using a table of random digits generated by a computer. The study was conducted as double-blinded manner so the patients were anesthetized and were unaware of drug choice. Anesthesia technician prepared the drugs and anesthesiologist only injected the coded-labeled syringes to the patients.

Before the induction of anesthesia, an epidural catheter was placed at the T10-11 or L3-4 intervertebral spaces (for thoracic and lumbar epidural catheter respectively), and correct positioning was confirmed by an injection of 3 ml of 2% lidocaine with 1:200,000 epinephrine. Patients that were under lumbar epidural catheterization in "Dexa group" received 15 ml of 0.5% bupivacaine, 50 µg (1ml) fentanyl, and 8mg (2ml) dexamethasone, and patients in "control group" received 15 ml of 0.5% bupivacaine, 50 µg (1ml) fentanyl, and 2ml of isotonic saline solution via

epidural catheter. Patients that were under thoracic epidural catheterization in Dexa group received 8 ml of 0.5% bupivacaine, 50 µg (1ml) fentanyl, and 4 mg(1ml) dexamethasone, and patients in control group received 8 ml of 0.5% bupivacaine, 50 µg (1 ml) fentanyl, and 1 ml of isotonic saline via epidural catheter. Epidural anesthesia was performed using epidural catheter in patients who underwent (lower or upper) abdominal surgeries. Epidural catheters were inserted via L4-L5 intervertebral space in abdominal surgeries and through T6-T7 intervertebral space in patients undergoing thoracic surgeries. Epidural catheter insertion was performed with 19-gauge Tuohy needle by hanging-drop method. General anesthesia was combined with epidural technique in patients undergoing thoracotomy. General anesthesia was induced with fentanyl 1 µg/kg, lidocaine 1 mg/kg, propofol 2 mg/kg, and atracurium 0.5 mg/kg, and patients were intubated.

All local anesthetic solutions and adjuvant drugs were prepared by an anesthesiologist not involved in performance of epidural catheterization, patient care, or data collection.

Postoperative pain management was performed via epidural catheter, and duration of analgesia and analgesic drug usage (if needed) was recorded. Intravenous pentazocine 10 mg bolus as analgesic drug was used if needed. Visual analogue scale (VAS) was used for estimate of pain degree in patients at 3, 6, 12 hours after surgery. Application of VAS was explained to the patients before operation.

Collected data were analyzed using SPSS statistical package v.17.0 (SPSS Inc. Chicago, IL, USA). For statistical analysis of demographic data and for comparison of groups, chi-square test and independent samples t-test were used. Level of significance considered $p \leq 0.05$.

Results

In this study, 72 patients were evaluated. Two patients were excluded from the study because of unsuccessful blockade. Demographic data and duration of surgery are presented in Table 1. There were no significant differences between the two groups with respect of age, gender, ASA physical status and

surgery duration. There was no significant difference between groups regarding lumbar or thoracic epidural catheterization ($p=0.49$). The duration of analgesia (372 ± 58.1 min in Dexa group vs. 234.6 ± 24.3 min in control group) was significantly longer in the Dexa than in the control group (Table 2).

Table 1

Background parameters in the two study groups

Variables	Dexa group (n=35)	Control group (n=35)	P value
Age (year)	56.2 ± 13.1	52.8 ± 10.4	0.24
Gender (male/female)	17 / 19	17 / 19	0.60
ASA class (I/II)	19 / 17	24 / 12	0.22
Surgery duration (min)	124 ± 32.4	125.8 ± 35.6	0.82

Visual analogue scale (VAS) at 3, 6 and 12 hours after surgery were lower in dexamethasone group than control group. Pentazocine use for pain control in first 24 hours after surgery was lower in dexamethasone group (37.1 ± 19.7 mg) than control group (73.1 ± 17.6 mg) (Table 2).

Table 2

Clinical parameters in the two study groups

Variables	Dexa group (n=35)	Control group (n=35)	P value
Analgesia duration (min)	372 ± 58.1	234.6 ± 24.3	0.001
VAS* after 3 hours	0.51 ± 0.1	2.1 ± 0.3	0.001
VAS after 6 hours	1.4 ± 1.1	3.6 ± 1.3	0.001
VAS after 12 hours	2.2 ± 0.6	4.4 ± 1.37	0.001
Pentazocine use (mg) in first 24 hour after surgery	37.1 ± 19.7	73.1 ± 17.6	0.001

* VAS = Visual analogue scale.

Discussion

The results of current study indicate that the addition of dexamethasone (8mg, 4mg in lumbar and thoracic epidural catheterization, respectively) to bupivacaine and fentanyl for post-operative epidural analgesia, results in a significant increase in duration of analgesia.

Previous studies demonstrated that the addition of corticosteroid microspheres to local anesthetic prolonged duration of blockade of the peripheral nerves⁹⁻¹⁰. In one study, a prolonged percutaneous blockade of sciatic nerve in rat using bupivacaine-dexamethasone microspheres was demonstrated⁹. It was also reported that the intercostal injection of dexamethasone containing bupivacaine microcapsules produces a prolonged duration of anesthesia and analgesia¹⁰. Other preliminary data suggest methylprednisolone can increase the duration of sensory and motor block²¹. The authors concluded that the applicability of these findings to clinical practice should be verified in a randomized prospective clinical trial.

In one study (Thomas S, 2006) the addition of corticosteroid to epidural local anesthetic, demonstrated that dexamethasone reduced post-operative pain and analgesic requirements¹⁴ but this study was performed in laparoscopic cholecystectomy. In another study, Hanan et al. demonstrated the efficacy of epidural dexamethasone on postoperative analgesia in patients undergoing lower abdominal surgeries¹⁶.

However, in our study, both lumbar and thoracic epidural catheterization and postoperative analgesia were performed and applied for both lower and upper and thoracic surgeries. The mechanism of the analgesia induced by corticosteroids is not fully understood. However, this effect is suspected to be mediated by their anti-inflammatory or immune-suppressive effects²²⁻²³. Corticosteroids cause skin vasoconstriction effects on topical application. The vasoconstriction effects of topical steroids are mediated by occupancy of classical glucocorticoid receptors rather than by nonspecific pharmacological mechanisms²⁴⁻²⁵. According to the traditional theory of steroid action, steroids bind to intracellular receptors and modulate nuclear transcription.

In our study, dexamethasone produced a relatively rapid effect, which cannot be explained by

the above mechanism²⁶. Therefore, vasoconstriction, the presumed mechanism of action for epinephrine's adjunctive effect on local anesthetics, is probably not responsible for block prolongation by dexamethasone. Corticosteroids may have a local effect on the nerve and the dexamethasone effect may be related to this action²⁷.

Some authors believe that analgesic properties of corticosteroids are the result of their systemic effect²⁸. Because of our positive results, the question of whether these results were attributable to a local or systemic effect warrants further investigation.

The safety of dexamethasone use in intrathecal or epidural injections may raise some concerns. In one study, after approximately 2000 intrathecal injections of dexamethasone (8 mg) in 2000 patients for treatment of posttraumatic visual disturbance, no neurological disorders were found at 1-month follow up²⁹.

We used a dose of 8 mg dexamethasone in lumbar epidural and 4 mg in thoracic epidural cases because administration of this dose seems to be safe in adults. Adverse effects with a single dose of dexamethasone are probably extremely rare and minor in nature, and previous studies have demonstrated that short-term (<24 hours) use of dexamethasone was safe³⁰⁻³¹. Adding a steroid to local anesthetic solution may not be indicated for all patients. For example, diabetic patients may experience hyperglycemia and patients with a continuing infectious process may be detrimentally affected by the anti-inflammatory effects of steroids. This study led us to hypothesize that dexamethasone may be useful in situations in which epinephrine must be used with caution (e.g., hypertension, ischemic heart disease).

In conclusion, the addition of dexamethasone to bupivacaine solution in epidural postoperative analgesia prolongs the duration of blockade. Further studies are needed to evaluate the optimal dose of dexamethasone to be used for prolonged epidural analgesia as well as the mechanism of this effect.

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