



Original Article

A randomized placebo controlled trial comparison of pre-incision infiltration of a local anaesthetic drug to reduce postoperative pain after laparoscopic adrenalectomy

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Abstract

Objective: To study the efficacy of pre-incision infiltration of a local anaesthetic drug in postoperative pain following laparoscopic adrenalectomy.

Material and Method: In a randomized placebo controlled study, 52 patients listed for unilateral laparoscopic adrenalectomy were randomized into 2 groups. Group I (n=26) received subcuticular pre-incision infiltration with 0.5% bupivacaine and group II (n=26) received normal saline as a placebo; all the operations were performed with the same technique by only one experienced laparoscopic urologist. Postoperative pain was assessed using the Visual Analogue Scale at the 4th, 8th, 12th, 24th, and 48th hour postoperatively as primary outcomes. The secondary outcomes were the total postoperative analgesic consumption and time to the first analgesic demand.

Results: The average pain scores were significantly different at the 4th, 12th, 24th, and 48th hour postoperatively (p=0.00, 0.00, 0.001, 0.00), but insignificantly different at the 8th hour (p=0.311). There was no significant difference in nausea/vomiting, bruising score and wound infection (p=0.223, 0.298, 0.313). Postoperative analgesic consumption was significantly lower in the bupivacaine group, but time to the first analgesic demand was not significantly longer in this study.

Conclusion: Our study demonstrated that pre-incision infiltration of a local anaesthetic drug is highly effective for relief of postoperative pain after laparoscopic adrenalectomy in terms of pain perception and intravenous postoperative analgesic consumption without any effects on nausea/vomiting, bruising, and wound infection.

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Introduction

Even though laparoscopic adrenalectomy is made in order to reduce any injury to the surrounding tissue, blood loss, post-operative pain, and length of stay compare to open adrenalectomy in unilateral benign adrenal disease, such as pheochromocytoma, aldosterone-producing adenoma, Cushing's syndrome and non-functional adrenal tumor¹⁻⁴.

But postoperative pain is still a minor complication that concerns the author. Optimizing postoperative pain control is an important aspect in peri-operative patient care. Currently, there are many techniques to reduce post-operative pain. One of them is pre-emptive analgesic by pre-incision infiltration of a local anaesthetic drug⁵.

The author studied the efficacy of pre-incision infiltration of a local anaesthetic drug (using 0.5% bupivacaine) in postoperative pain following laparoscopic adrenalectomy.

Material and Method

In this randomized placebo controlled study that was conducted in Rajavithi Hospital from January 2015 to September 2018, a total of 60 patients who underwent unilateral laparoscopic adrenalectomy were recruited. In 6 patients the diagnosis was changed; patients with other analgesic modality or who were converted to open surgery were excluded from this study. Fifty-two patients were randomized into 2 groups. Group I (n=26) received a subcuticular pre-incision infiltration with 0.5% bupivacaine, and group II (n=26) received normal saline as a placebo in the control group.

After general anaesthesia was administered, in the patients of group I (bupivacaine group), the 24-gauge with 10 ml of 0.5% bupivacaine syringe was infiltrated into the subcuticular layer of the area of the camera and the other working port before the incision. Group II (placebo group) received 10 ml of normal saline instead with the same method. All the operations were performed with the same technique

by only one experienced laparoscopic urologist.

The demographic and clinical characteristics of the patients were recorded at the time of enrollment. Postoperative pain was assessed by medical officers in the urology department using the Visual Analogue Scale (VAS) at the 4th, 8th, 12th, 24th and 48th hour postoperatively as primary outcomes. The "0" on the scale meant no pain and the "10" meant very severe pain. The secondary outcomes were the total postoperative analgesic consumption, time to the first analgesic demand, and adverse effects. Intravenous morphine 3 mg was used in case of pain, at the request of the patient.

Statistical analysis

Statistical analysis was performed using SPSS version 17. Continuous variables were compared using the t-test for 2 independent samples. Categorical variables were compared using the Chi-square analysis. p-value <0.05 was considered to be statistically significant.

All patients provided written informed consent. Ethical approval was obtained from the Ethics and Research Committee of Rajavithi Hospital.

Results

Patient demographic data are shown in Table 1. The mean age of the bupivacaine group was 46.7 years old, whereas the placebo group was 48.7 years old. Most patients were female. The main diagnosis of adrenal disease in both groups was aldosterone-producing adenoma. The average tumor size was 2.0 and 2.1 cm, respectively. There were no significant differences between the 2 groups in age, underlying disease, sex, diagnosis, side and size of the tumor, operative time, number of working ports, placement of the drain, and blood loss.

Postoperative pain as the primary outcome evaluated using the VAS score is shown in Figure 1 and Table 2. The average VAS score at the 4th, 12th, 24th, and 48th hour post-operatively in the bupivacaine



group was 0.88 ± 1.84 , 2.08 ± 1.77 , 2.19 ± 1.50 , and 1.04 ± 1.76 , which was significantly lower compared with 5.31 ± 3.46 , 4.50 ± 2.23 , 4.00 ± 2.20 and 3.12 ± 2.07 in the placebo group (p-value=0.000, 0.001, 0.001, and 0.000), respectively. The postoperative VAS scores at the 8th hour post-operatively were not significantly different between the 2 groups.

Total intravenous analgesic (IV) consumption using morphine to control postoperative pain was

1.04 ± 1.89 mg in the bupivacaine group and 5.27 ± 4.18 mg in the placebo group (p-value=0.000). The first analgesic demand was not significantly different between the 2 groups (271.73 ± 918.21 minutes vs 164.42 ± 270.94 minutes, p-value=0.570), as shown in Table 3.

There were no statistical differences in nausea/vomiting, bruising wound and infected wound, as shown in Table 4.

Table 1. Demographic data.

Characteristic	0.5% Bupivacaine	0.9% NaCl	P-value
Age (years) \pm SD	46.69 ± 10.87	48.65 ± 11.66	0.533
Gender			0.482
- Male	4 (15.4%)	6 (23.1%)	
- Female	22 (84.6%)	20 (76.9%)	
Underlying disease			
- Diabetes mellitus	4 (15.4%)	3 (11.5%)	0.685
- Hypertension	24 (92.3%)	24 (92.3%)	1.000
- Dyslipidemia	4 (15.4%)	3 (11.5%)	0.685
Diagnosis			0.859
- Pheochromocytoma	3 (11.5%)	2 (7.7%)	
- Aldosterone-producing adenoma	19 (73.1%)	20 (76.9%)	
- Cushing's syndrome	2 (7.7%)	3 (11.5%)	
- Non-functional tumor	2 (7.7%)	1 (3.8%)	
Side of adrenal gland			0.358
- Left	17 (65.4%)	20 (76.9%)	
- Right	9 (34.6%)	6 (23.1%)	
Diameter of tumor (cm) \pm SD	2.07 ± 0.92	2.18 ± 1.05	0.676
Operative time (min) \pm SD	137.50 ± 41.33	133.85 ± 32.10	0.723
Number of Port \pm SD	3.12 ± 0.33	3.04 ± 0.53	0.530
Place of drain	17 (60.7%)	11 (30.3%)	0.095
Blood loss (ml) \pm SD	26.15 ± 21.74	35.00 ± 34.67	0.276

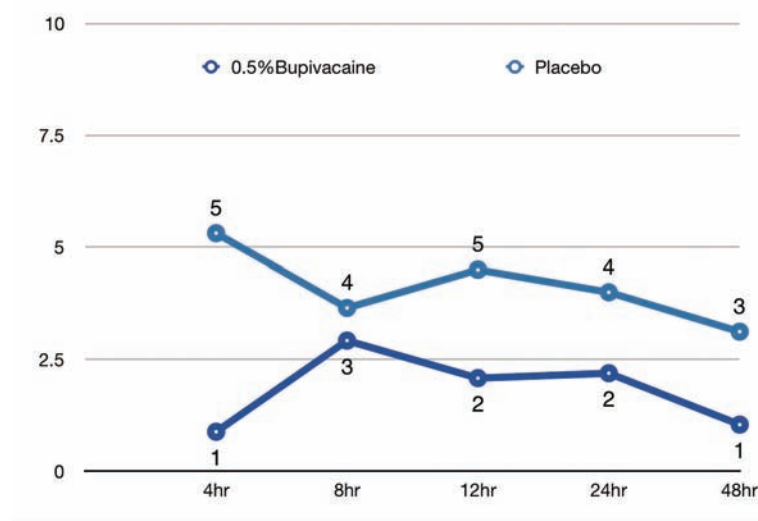


Figure 1.

Visual Analogue Scale at 4th, 8th, 12th, 24th, and 48th hour post-operatively.

Table 2. Visual Analogue Scale at 4th, 8th, 12th, 24th and 48th hour post-operatively.

Visual Analog Scale (VAS)	0.5% Bupivacaine	0.9% NaCl	P-value
VAS at 4 th hour	0.88 ± 1.84	5.31 ± 3.46	0.000
VAS at 8 th hour	2.92 ± 2.58	3.65 ± 2.58	0.311
VAS at 12 th hour	2.08 ± 1.77	4.50 ± 2.23	0.000
VAS at 24 th hour	2.19 ± 1.50	4.00 ± 2.20	0.001
VAS at 48 th hour	1.04 ± 1.76	3.12 ± 2.07	0.000

Table 3. Total intravenous analgesic consumption and time to first analgesic demand.

Characteristic	0.5% Bupivacaine	0.9% NaCl	P-value
Total intravenous analgesic consumption - morphine (mg)	1.04 ± 1.89	5.27 ± 4.18	0.000
Time to first analgesic demand (min)	271.73 ± 918.21	164.42 ± 270.94	0.570

Table 4. Adverse effect.

Adverse effect	0.5% Bupivacaine	Placebo	P-value
Nausea and vomiting	2 (7.6%)	5 (19.2%)	0.223
Bruising wound	1 (3.8%)	3 (11.5%)	0.298
Infected wound	0 (0%)	1 (3.8%)	0.313



Discussion

When the tissue is injured, it will send the nociceptive signal via the peripheral nerve (a fiber and polymodal C fiber nociceptors) to the central nervous system called “central sensitization,” which causes persistent post-injury change in the central nervous system, resulting in pain hypersensitivity⁶. “Pre-emptive analgesia” by infiltration of a local anesthetic drug before incision, which blocks the sodium channel, can reduce the signal from the peripheral nerve, resulting in a decrease in central sensitization and a decrease in post-operative pain⁵.

Bupivacaine (trading name “Marcaine”) is a local anaesthetic drug that is a commonly used peri-operative; it can be used in both peripheral nerve block and epidural nerve block. The mechanism of action is sodium-channel blockers, which prevent Na⁺ influx, resulting in a decrease in depolarisation, a decrease in nociceptive signal, and a decrease in central sensitization⁷.

The benefit of pre-incision infiltration of a local anaesthetic drug was demonstrated in previous studies of oto-rhino-laryngology, general surgery, and gynecology, such as thyroid surgery, laparoscopic cholecystectomy, and hysterectomy where bupivacaine was used as an anaesthetic agent.

A. Bagul et al.⁸ (2005) conducted a prospective randomized study on the efficacy of pre-incision infiltration of 0.5% bupivacaine in 39 patients; 19 patients were included in the bupivacaine group (10 ml of 0.5% bupivacaine infiltration) and 20 patients in the control group (normal saline infiltration). Pain scores (as linear analogue scores 0-100) were significantly different at 6 hours post-operatively (p-value=0.0341), with mean scores in the bupivacaine group = 33 and the control group = 50, but this difference disappeared at 24 hours. No patients received IV morphine in the bupivacaine group compared to 5 patients (25%) in the control group. There was no significant difference in the mean bruising scores (p-value=0.8864) and mean cosmetic scores (p-value=0.3339) at discharge.

F. Cantore. et al.⁹ (2008) reported on 50 patients who underwent laparoscopic cholecystectomy; 25 patients were randomized into pre I group (pre-incision infiltration of levobupivacaine) and 25 patients into post I group (post-operative infiltration). The results showed different analgesic consumption between the 2 groups: In pre I group, the mean intravenous dose of ketorolac post-operative used was 124 mg while in the post I group it was 339 mg. The mean VAS was 10.7 in the post I group while in the pre I group it was 5.1, which also was statistically significant.

Minoo Yaghmaei, et al.¹⁰ (2013) reported on 60 patients with ASA class I or II scheduled for abdominal hysterectomy. The patients were randomly assigned to receive pre-incision skin infiltration of either lidocaine or normal saline. Patients in the saline group complained of more pain than the lidocaine group in the recovery room (p-value<0.001). However, the patients were similar with respect to their post-operative pain scores and analgesic requirements. They were also similar regarding satisfaction rates during the first 24 hours post-operatively.

Presently there is an absence of studies in laparoscopic adrenalectomy or any urologic procedure. Our study has shown the benefit and safety of pre-incision infiltration of a local anaesthetic drug in relieving postoperative pain, leading to lower consumption of an IV analgesic drug (morphine). However, time to the first analgesic demand was not different between the 2 groups.

From subgroup analysis: There was not any significant difference at the 8th hour post-operatively. Figure 1 shows the decreasing pain score at the 8th hour post-operatively in the placebo group. The author suggests that the reason may be the result of the placebo group receiving an IV analgesic drug (morphine) on demand at 164 minutes (4th hour post-operatively), as shown in Table 2. The effect of the morphine was still involved at the 8th hour post-operatively, resulting in temporary pain relief.



Conclusion

Our study demonstrated that pre-incision infiltration of a local anaesthetic drug is effective for relief of postoperative pain after laparoscopic adrenalectomy in terms of pain perception and reducing intravenous postoperative analgesic consumption without any effects on nausea/vomiting, bruising or wound infection. However, time to the first analgesic demand was not significantly longer in this study. A larger study is needed in order to assess the efficacy of this technique.

Conflict of interest

The authors declare no conflict of interest.

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