Original Article

Comparison of ultrasound-guided transversus abdominis plane block with bupivacaine and ropivacaine as adjuncts for postoperative analgesia in laparoscopic cholecystectomies

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ABSTRACT

Background and Aims: Transversus abdominis plane (TAP) block is a popular technique for post-operative analgesia in abdominal surgeries. The aim of the study was to evaluate the relative efficacy of bupivacaine versus ropivacaine for post-operative analgesia using ultrasound-guided TAP block in laparoscopic cholecystectomies. **Methods:** Sixty adults undergoing elective laparoscopic cholecystectomy were randomised to receive ultrasound-guided TAP block at the end of the surgical procedure with either 0.25% bupivacaine (Group I, n = 30) or 0.375% ropivacaine (Group II, n = 30). All patients were assessed for post-operative pain and rescue analgesic consumption at 10 min, 30 min, 1 h, 4 h, 8 h, 12 h and 24 h time points. Means for normally distributed data were compared using Student's t-test, and proportions were compared using Chi-square or Fisher's exact test whichever was applicable. **Results:** Patients receiving ultrasound-guided TAP block with ropivacaine (Group II) had significantly lower pain scores when compared to patients who received the block with bupivacaine (Group I) at 10 min, 30 min and 1 h. However, both the drugs were equivalent for post-operative analgesia and 24 h cumulative rescue analgesic requirement (median [interquartile range]) (75.00 [75.00–75.00] in Group I vs. 75.00 [75.00–93.75] in Group II, P = 0.366). **Conclusion:** Ultrasound-guided TAP block with ropivacaine provides effective analgesia in the immediate post-operative period up to 1 h as compared to bupivacaine. However, both the drugs are similar in terms of 24 h cumulative rescue analgesic requirement.

Key words: Bupivacaine, ropivacaine, transversus abdominis plane block

INTRODUCTION

Laparoscopic cholecystectomy, one of the most common surgical endoscopic interventions today, is associated with lesser intensity of incision-related pain than its 'open' variant counterpart. However, it may result in surgical stress-induced major post-operative patient discomfort. Pain after laparoscopic cholecystectomy arises from laparoscopy port sites, carboperitoneum-induced abdominal stretch, and hepatic bed disturbances due to cholecystectomy. Adequate post-operative analgesia is likely to contain stress response following surgery, decrease post-operative morbidity, and facilitate improved surgical outcome.[1] Not surprisingly, pain and duration of convalescence are the two substantial concerns after laparoscopic cholecystectomy.

Numerous modalities have been used to alleviate pain after laparoscopic cholecystectomy, which include non-steroidal anti-inflammatory drugs

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(parecoxib/valdecoxib, ketoprofen, paracetamol), opioids (intravenous [IV] patient-controlled analgesia), local anaesthetic (LA) infiltration (before and/or after pneumoperitoneum), thoracic epidural block and multi-modal analgesia.[2] Transversus abdominis plane (TAP) block inhibits abdominal neural afferents by introducing LA into the neurofascial plane between the internal oblique and transversus abdominis muscles. With the widespread availability of ultrasound guidance for more accurate localisation of TAP (than the 'blind' technique), the TAP block is now established as an important technique for reduction of post-operative pain following abdominal surgery.[3]

Various LA agents have been utilised for post-operative analgesia with ultrasound-guided TAP block.[1,3,4] Although ropivacaine (S-enantiomer of bupivacaine) and bupivacaine (long-acting amide-linked LA) share a similar pKa and plasma protein binding property and are commonly used as LA agent for the TAP block, they have never been compared for their relative effectiveness and efficacy. We investigated whether ropivacaine with its inherent advantages (anaesthetic potency, long duration of action, favourable toxicity profile) is superior to bupivacaine for providing post-operative analgesia when used for TAP block in patients undergoing laparoscopic cholecystectomy.

METHODS

After the Institutional Ethics Committee approval and written informed consent, sixty American Society of Anesthesiologists Physical Status I/II patients of either sex, aged 18–65 years, scheduled to undergo 4-port laparoscopic cholecystectomy were enrolled in this trial. Patients with a history of LA allergy, psychiatric illness, substance abuse, opioid tolerance, any uncompensated systemic illness (cardiovascular, respiratory, metabolic, neurologic and endocrine) and pregnant women were excluded from the study. The patients were randomly allocated (computer-coded sealed envelopes) to receive TAP block with either bupivacaine or ropivacaine containing solution.

The sample size was estimated based on mean 24 h morphine consumption (mg) from a previous study[3] where it was found that mean difference in morphine consumption in groups (standard and TAP group) was 22 mg with standard deviation (SD) of 18.5. In another study comparing bupivacaine and ropivacaine,[5] a sample size calculation was done so that a mean difference between groups in visual analogue scale (VAS) of 20 mm, with reduced pain scores in the bupivacaine group in comparison to the ropivacaine group, would permit a type 1 error rate of one-tailed $\alpha = 0.05$, and with the alternate hypothesis, the null hypothesis would be retained with a type II error of $\beta = 0.20$. The sizes came to 19 each, but we opted for 30 in each group to accommodate a bigger number and consider some dropouts.

Patients were randomly allocated into two groups, one group to undergo ultrasound-guided TAP block with 0.25% bupivacaine (plain) (Group I, $n = 30$) and other group to undergo ultrasound-guided TAP block with 0.375% ropivacaine (plain) (Group II, $n = 30$) [Figure 1].

Following a comprehensive pre-anaesthetic evaluation, all the patients were explained about verbal rating scale (VRS) for pain (0 - no pain, 10 - worst imaginable pain) and categorical scoring system (CSS) for nausea (0 - none, 1 - mild, 2 - moderate and 3 - severe) in their own vernacular language. They were electively fasted 8 h pre-operatively and were pre-medicated with oral ranitidine 150 mg and alprazolam 0.25 mg in the evening before and morning before the surgery.

In the operating room, routine monitoring was applied and venous access was secured. Following pre-oxygenation, the patients received IV fentanyl (2 μg/kg). Anaesthesia was induced with IV thiopentone sodium 5 mg/kg. Vecuronium bromide (0.1 mg/kg) IV was utilised to facilitate tracheal intubation. Anaesthesia was maintained with nitrous oxide (60%) and isoflurane (0.5–1%) in oxygen. The intra-abdominal pressures were maintained at 12 mm Hg in both the groups throughout the procedure.

At the end of the surgery, after ensuring full asepsis, ultrasound-guided TAP block was administered using a mid-axillary approach, under real-time guidance with a high-frequency (5–10 MHz) ultrasound probe (Micromaxx™ Sonosite, Inc., Bothell, WA 98021, USA). After confirming negative aspiration of blood, 20 ml of 0.25% plain bupivacaine or 0.375% plain ropivacaine was administered on each side as per the randomisation.

The anaesthesiologist who administered the TAP block and the investigator who assessed its outcome were blinded to the drug used. Thereafter, the residual neuromuscular block was antagonised by IV neostigmine and glycopyrrolate. Trachea was extubated once the

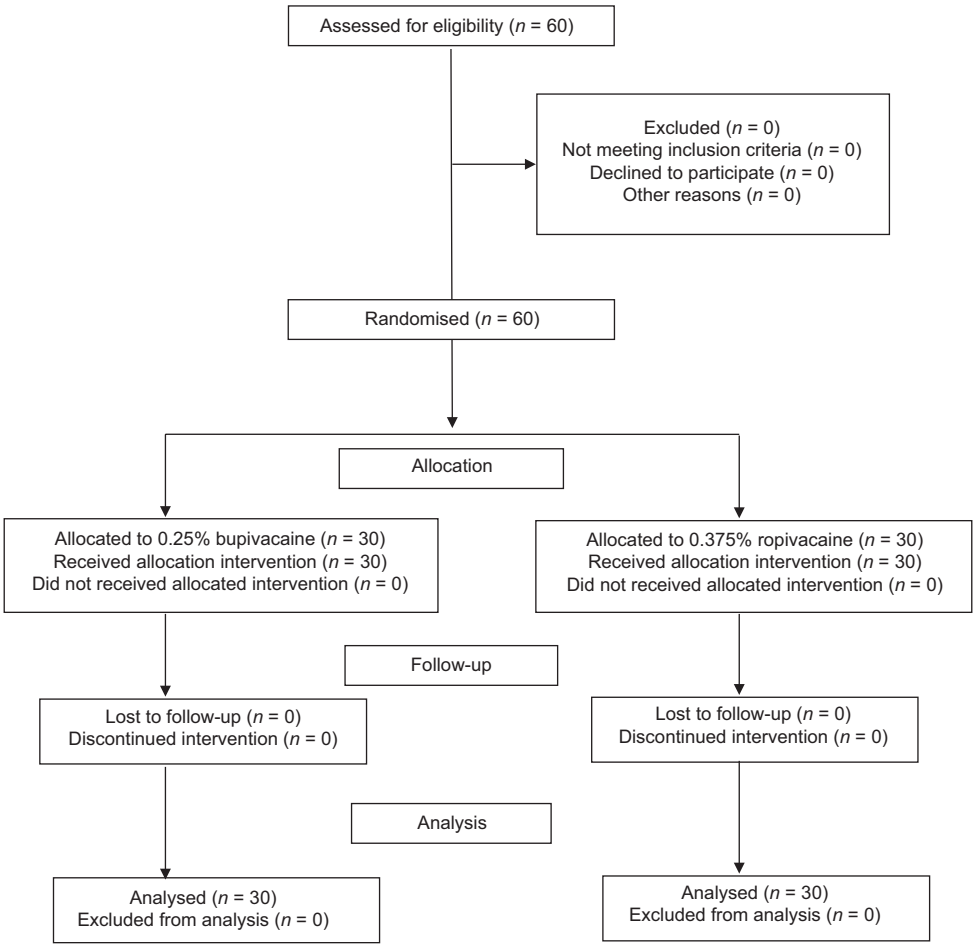

Figure 1: Consort flowchart

patients were wide awake. The patients were shifted to post-anaesthesia care unit (PACU). They were moved to the step-down ward after ensuring adequacy of pain relief (VRS <4) and absence of any overt side effects such as post-operative nausea vomiting (PONV). In PACU, the patients were monitored for vital parameters, pain (VRS score) and PONV (CSS) at 10 min, 30 min, 1 h, 4 h, 8 h, 12 h and 24 h. Rescue analgesic (diclofenac sodium: 75 mg IV diluted and given slowly if VRS score ≥4) and antiemetic (ondansetron: 0.1 mg/kg IV) were administered as appropriate. Total rescue drugs (analgesic, antiemetic) were noted at the end of the observation period. At all time-points, patients were monitored for any signs of LA toxicity, and the sites of injection of the TAP block were also inspected to detect haematomas or local infections. The dataset recorded in the respective case report forms of the study participants were decoded and analysed after the end of the study.

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA version 15.0 for Windows). All quantitative variables were estimated using measures of central location (mean, median) and dispersion (SD). Normality of data was measured by Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using Student's *t*-test. Qualitative or categorical variables were represented as frequencies and proportions. Proportions were compared using Chi-square or Fisher's exact test whichever was applicable. VRS scores, total rescue analgesic and rescue antiemetic used over 24 h and time-to-first analgesic and antiemetic used were compared using Mann–Whitney test. All statistical tests were two-sided and performed at a significance level of $\alpha = 0.05$.

RESULTS

All the sixty enrolled patients completed the study. There was no difference in the demographic data (age, gender, body weight and height) and duration of surgery in the two groups [Figure 2].

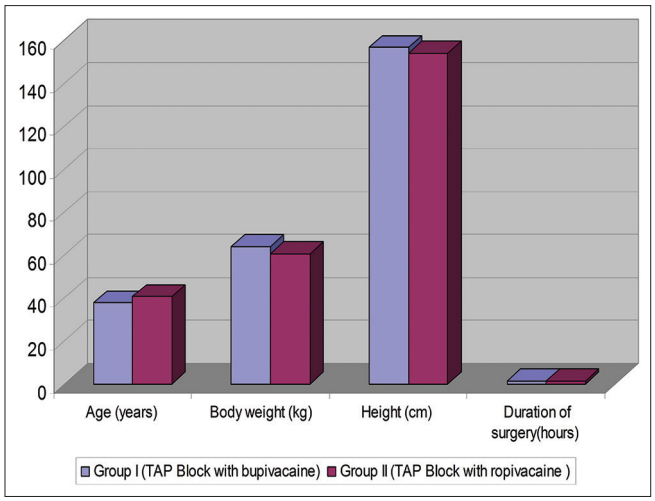

Figure 2: Demographic profile

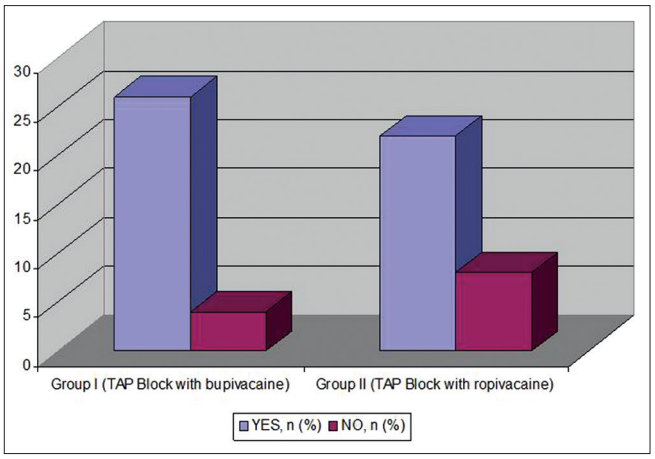

Figure 3: Number of patients requiring analgesics in the two groups

Table 1: Post-operative pain scores (median (interquartile range))

Time	Median (IQR)		*P*
	Group I (TAP block with bupivacaine)	Group II (TAP block with ropivacaine)	
10 min	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.044
30 min	1.00 (0.00-1.00)	0.00 (0.00-0.00)	0.003
1h	1.50 (0.75-2.25)	0.00 (0.00-2.00)	0.020
4 h	2.00 (1.00-5.00)	2.00 (1.00-4.00)	0.441
8 h	2.00 (1.00-2.00)	2.00 (1.00-4.25)	0.164
12 h	1.50 (1.00-2.00)	2.00 (1.00-2.00)	0.803
24 h	1.00 (1.00-2.00)	1.00 (1.00-2.00)	1.000

IQR – Interquartile range; TAP – Transversus abdominis plane

Table 2: Cumulative diclofenac consumption

Group	Cumulative diclofenac consumption (in mg) in 24 h median (IQR)
Group I (TAP block with bupivacaine)	75.00 (75.00-75.00)
Group II (TAP block with ropivacaine)	75.00 (75.00-93.75)

P=0.366, i.e. statistically non-significant (*P*>0.05). IQR – Interquartile range; TAP – Transversus abdominis plane

The pain scores were significantly lower at 10 min, 30 min and 1 h post-operatively in Group II as compared to Group I [Table 1]. Twenty-four out of 30 patients in Group I and 22 out of 30 patients in Group II required rescue analgesic in 24 h [Figure 3]. Out of these patients requiring rescue analgesic, the median cumulative diclofenac consumption in 24 h post-operative period was comparable (median [interquartile range (IQR)]) (75.00 [75.00–75.00] in Group I vs. 75.00 [75.00–93.75] in Group II, $P = 0.366$) [Table 2]. The two groups were also comparable for time-to-first analgesic requirement (median [IQR]) (4.00 [3.00–7.25] h in Group I vs. 5.65 [4.00–9.00] h in Group II, $P = 0.145$).

No complications such as LA toxicity, liver trauma, local infection or haematoma were seen in any of the two groups.

DISCUSSION

The present study showed that when administered via ultrasound-guided TAP block, the plain solution of ropivacaine (0.375%) provides more effective pain relief in the immediate post-operative period as compared to bupivacaine (0.25%). The findings are in sync with the previous studies, which found ropivacaine to be more effective than bupivacaine when administered through various routes.[6,7] However, the results also highlighted that after a time interval of 1 h, the quality of pain relief is comparable irrespective of the LA agent used. The related analgesia index, i.e. the time-to-first analgesic was also equivocal for the two groups. Interestingly, the choice of LA agent used did not have any bearing on PONV parameters, including cumulative antiemetic use and time-to-first rescue antiemetic.

Pain following laparoscopic cholecystectomy may be substantial enough to delay the ambulation and hence nullify the early discharge objective of outpatient anaesthesia. To this effect, a number of modalities have been utilised to provide adequate post-operative pain relief.[2,8-13] TAP block is a regional analgesic technique, wherein effective pain relief is achieved by blocking the nerves of the abdominal wall (intercostal nerves:T7-T12 and ilioinguinal and iliohypogastric nerves: L1), which traverse the intervening plane between the internal oblique and transversus abdominis muscles.[14] Thus, even though gall bladder is a supra-umbilical organ, 4-port laparoscopic

cholecystectomy involves the use of infra-umbilical ports also and the pain caused by abdominal distension as a result of pneumoperitoneum is taken care of by the TAP block. The use of ultrasound has virtually surpassed the limitations of the conventional blind technique of anatomical landmark facilitated approach by providing direct visualisation of the target plane.[3,15] TAP block has also been used as an effective analgesic modality for abdominal surgeries in patients with compromised cardiac status. In a study done in a high-risk patient with gall bladder rupture and gallstone ileus, with multiple co-existing diseases, TAP block has been effectively used for an emergency laparotomy.[16]

Although bupivacaine and ropivacaine have been compared previously in different concentrations, in context of different surgical procedures,[6,7,17,18] there has been a dearth of evidence for the comparison of these LA agents when used in TAP block for laparoscopic cholecystectomy. The present study was designed to compare the amide LA agents for their relative efficacy in providing post-operative pain relief when administered for TAP block. There have been studies comparing the potency of 0.5% bupivacaine and 0.75% of ropivacaine in other blocks.[19-21] These studies have demonstrated a similar efficacy of ropivacaine and bupivacaine when used in above-mentioned concentrations. We, therefore, presumed that using half concentration of the test drugs, i.e. 0.25% bupivacaine and 0.375% ropivacaine, would also be equipotent. In a study involving rats, it has been seen that ropivacaine, at equipotent doses of bupivacaine, has lesser toxicity profile and is a safer drug.[22] The volume of LA to be deposited was derived from previous TAP block studies.[1,3,23,24]

There are studies with conflicting evidence which reports higher pain scores in patients receiving TAP block with either bupivacaine (0.25–0.5%) or ropivacaine (0.375–0.75%) for various non-laparoscopic abdominal/gynaecological surgeries.[3,25-27] Statistically significant reduction in post-operative opioid consumption has been reported in patients who received TAP block with 0.25% bupivacaine,[28] but the total consumption of rescue analgesic (diclofenac) in the present study is perceptibly lower. Although diclofenac sodium was utilised as a rescue analgesic in our study as compared to opioids agents in other studies, the lower post-operative analgesic requirements in our study is consistent with the results of various other studies where similar reduction in the requirement of rescue analgesic was seen following application of TAP block.[15,25-28]

A meta-analysis published on TAP block used for various abdominal surgeries has also reported statistically significant reduction in post-operative opioid consumption at 6 h and 24 h, respectively which is independent of the timing of injection or block approach adopted.[29]

Another study[14] reported reduced post-operative pain scores and rescue analgesic requirement in laparoscopic cholecystectomy patients who received TAP block with varying concentration of levobupivacaine (0.25–0.5%). In another clinical study done in non-laparoscopic gynaecological surgeries,[26] 0.375% ropivacaine was used for TAP block and the reported pain scores were lower when compared for the patients who did not receive TAP block; higher VAS scores were observed when 0.75% of ropivacaine was used in TAP block, attributed to different pain profile in the 'open' large incision used for the surgery. In the present study, patients in the bupivacaine group had a higher incidence of PONV in the first post-operative hour as compared to ropivacaine group. A correlation between higher 1st h pain scores in the bupivacaine group and higher PONV incidence cannot be ruled out. Interestingly, the PONV scores were comparable when the pain scores were comparatively lower in either of the study groups.

The present study has certain limitations. The pain scores at movement have not been taken into account despite the fact that laparoscopic surgeries are aimed to facilitate early ambulation. The serum concentrations of the drugs administered in the TAP were not estimated. Evaluation of sensory block level was not undertaken, for they were performed in anaesthetised patients.

The conclusions of this study are based upon the TAP block given at the end of surgery, but it is difficult to conclude whether the outcome would have been same if the TAP block is given before the start of surgery; hence, further studies are required to prove the same.

CONCLUSION

In patients undergoing laparoscopic cholecystectomy, the ultrasound-guided deposition of ropivacaine 0.375% in the TAP provided superior analgesia in the early post-operative period in comparison to

bupivacaine 0.25%. However, both the drugs may be considered to be at par for analgesia for the later part of the post-operative period.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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