THE EFFECTIVENESS OF PATIENT-CONTROLLED EPIDURAL ANALGESIA WITH ROPIVACAINE 0.165% WITH FENTANYL 2.0 μG/ML OR LEVOBUPIVACAINE 0.125% WITH FENTANYL 2.0μG/ML AS A METHOD OF POSTOPERATIVE ANALGESIA AFTER MAJOR ORTHOPAEDIC SURGERY

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Abstract

This prospective randomized single-blinded study was conducted to determine whether there were differences in consumption, demand dosing and postoperative analgesia quality between PCEA using ropivacaine and levobupivacaine. Seventy patients with ASA classification I and II aged 18 to 80 years old scheduled for elective total knee replacement or total hip replacement were studied. All patients received CSE and then were randomly allocated to receive either ropivacaine 0.165% (Group A) or levobupivacaine 0.125% (Group B) both added with fentanyl 2.0μg/ml via epidural route. PCEA regime was offered for 48 hours with additional standard orthopaedic practice of oral analgesia (etoricoxib 120mg OD and paracetamol 1.0gm QID) on the second postoperative day. Basal infusion of PCEA was at 3.0ml/hour and discontinued after 24 hours following started of PCEA. The consumption of local anaesthetics used within the first 24 hours (basal + demand) and 48 hours (total basal + total demand) were recorded. The VAS pain score, sedation score, side effects and vital signs (blood pressure, heart rate and respiratory rate) were also recorded every four hours for 48 hours. This study showed that the total volume of drug used was significantly higher in Group A (163.31±29.01ml) than Group B (142.69±30.93ml) ($p<0.01$). The mean dose of Group A for the first 48 hours after surgery was 251.43±70.02mg and was significantly greater than the mean dose of Group B (178.91±42.33mg) ($p<0.01$). The numbers of PCEA boluses delivered (D) and PCEA attempts (A) were higher in the Group A (22.37±7.32 and 27.66±9.12) in contrast to Group B (17.63±7.71 and 24.40±11.51) but the differences were not statistically significant. The ratio D/A showed significantly higher in Group A (0.83±0.13) than Group B (0.74±0.15) ($p<0.02$). The VAS pain score was similar for both groups. One patient in Group B had vomiting and there was no sedation, hypotension, pruritus or motor block recorded in both groups. In conclusion this study showed that both PCEA using ropivacaine 0.165% with fentanyl 2.0μg/ml and levobupivacaine 0.125% with fentanyl 2.0μg/ml provided effective postoperative analgesia within the first 48 hours of major lower limb orthopaedic surgery despite clinically significant dose difference. There was no hypotension, pruritus, sedation or motor block recorded in both groups.

Key words: patient-controlled epidural analgesia, major lower limb orthopaedic surgery, VAS pain score.

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Introduction

At the present time, the use of epidural infusion of local anaesthetics with or without patient-controlled epidural analgesia (PCEA) to provide postoperative analgesia is becoming more popular. The benefits of PCEA over epidural infusion alone include avoidance of potential drug over-dosage, elimination of the "waiting time" and "peaks and valleys" of nurse-administered analgesics and the involvement of the patient in his/her own healthcare[1].

The high quality of postoperative pain relief is the main concerns for the patients. It is also the ultimate goal of both national health policy and the specialty of anaesthesiology. Nevertheless, postoperative pain relief is often inadequate[2]. Several studies have shown that epidural analgesia with local anaesthetics combined with opioid provides better postoperative analgesia than epidural analgesia or systemic opioid alone and improves the surgical outcome[3-5]. Initial reports suggest that PCEA may improve the quality of analgesia[6], patients' satisfaction and safety compared with conventional epidural infusion or bolus techniques despite lacking and limited experience concerning the efficacy and safety of this method[7].

Study done by Camorcia et al showed that ropivacaine and levobupivacaine were both less potent than bupivacaine and ropivacaine appeared to be 20% less potent than levobupivacaine[13]. However Polley et al reported that similar ED_{50} value for ropivacaine and levobupivacaine in parturients with cervical dilatation of up to 7 cm[14]. Two other studies performed in 1999 suggested that ropivacaine was 40% less potent than bupivacaine[10,11] whereas this difference was only 2% for levobupivacaine[12]. Casati et al[8] and De Cosmo et al[9] showed that lumbar and thoracic epidural catheter placement with levobupivacaine 0.125% provided satisfactory intraoperative and postoperative analgesia for major orthopaedic surgery and thoracotomies respectively.

Combining the benefits of better analgesia with the advantages of patient control; it appears therefore that PCEA might offer the best option for postoperative analgesia. Currently PCEA is mainly used in obstetrics and the technique is not widely used outside this unit. However, a study done by Smet et al which used ropivacaine 0.165% plus sulfentanil 1.0μg/ml versus levobupivacaine 0.125% plus sulfentanil 1.0μg/ml in total knee and total hip arthroplasty suggested the volume consumed was higher in ropivacaine group than levobupivacaine group[15]. This study suggested either a potency difference between both local anaesthetics of more than 25% or a different duration of action. Therefore, it is going to be extremely difficult when performing comparative studies to decide what concentrations of local anaesthetics to select to give optimal analgesic care for post-operative patients.

General Objective

The purpose of this study was to determine whether there were differences in consumption, demand dosing and postoperative analgesia quality between PCEA using ropivacaine 0.165% with fentanyl 2.0μg/ml and levobupivacaine 0.125% with fentanyl 2.0μg/ml within the first 48 hours of major lower limb orthopaedic surgery.

Methods

This prospective single-blinded randomized study was conducted following approval by the Dissertation Committee of the Department of Anaesthesiology and Intensive Care, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and by the Research and Ethics Committee of UKMMC (Project Code: FF-288-2009).

Following written informed consent, seventy patients with ASA I and II aged between 18 to 80 years old scheduled for elective unilateral total knee replacement (TKR) or total hip replacement (THR) surgery were studied. Exclusion criteria included contraindications to central neuroaxial block (e.g. bleeding disorders), allergies to any drugs used and patients who had difficulty in understanding PCEA. Intra-operatively, all patients received combined spinal-epidural anaesthesia (CSE) under aseptic technique at level L_3/L_4 or L_4/L_5. The spinal component consisted of 3.0ml of hyperbaric bupivacaine 0.5% with fentanyl 25μg. If the spinal block proved insufficient for the surgery, epidural lignocaine 2% supplement was allowed to be given a maximum of 10ml, after which

the patients were put under general anaesthesia and were excluded from the study.

After CSE had been performed all the patients were then randomly allocated to Group A (ropivacaine 0.165% + fentanyl 2.0µg/ml) or Group B (levobupivacaine 0.125% + fentanyl 2.0µg/ml). Post-operatively, once the Bromage score had decreased to zero on the non-operated side, the PCEA regimen was started. This PCEA delivered 3.0ml/hr basal infusion for the first 24 hours with additional demand doses of 4.0ml with a lockout time of 20 minutes. After the first 24 hours, the basal infusion was stopped but the demand doses continued as required.

Every four hours, the ward nurses recorded the following variables: heart rate, arterial blood pressure, respiratory rate, Visual Analogue Scale (VAS) pain scores on a scale 0-10, sedation score (Ramsay score) and evidence of side effects (e.g. nausea, vomiting, pruritus) while the Acute Pain Service (APS) staff nurses assessed Bromage score twice daily. The observer recorded the volume of the local anaesthetic used within the first 24 hours (basal + demand) and 48 hours (total basal + total demand). The observer also recorded the number of successful PCEA boluses delivered (D) and the number of PCEA attempts made (A) and the ratio (D/A) for 48 hours was then calculated. All the epidural catheters were removed 48 hours after the start of the PCEA infusion.

After 24 hours, all patients were given supplementary analgesia in the form of oral etoricoxib 120mg OD and oral paracetamol 1.0gm QID. For patients who had insufficient analgesia, additional drug such as tramadol 50mg or opioids (e.g. morphine and pethidine) were given to the patients.

Statistical Analysis

Data calculated from previous study done by Smet et al[15] showed that sample of 70 patients who underwent major orthopaedic surgery were required to detect a 15% difference in the volume between the two groups. Thirty five patients were required in each group to obtain a study power of 0.85 with a '*p'* value of 0.05. Data was analyzed by using SPSS 17.0™ software (SPSS, Chicago, IL). ANOVA for repeated measures was used to compare VAS pain scores, heart rate and arterial blood pressure. Student's t-test was used to compare the volumes of epidural solution consumed, delivered/attempt (D/A) ratios, age and weight. A '*p'* value of < 0.05 was considered to be statistically significant.

Results

A total of 70 patients were enrolled in this study with 35 patients in each group. As shown in Table I, the two groups were comparable with respect to age, gender, eight, ASA classification and race.

Table I
Demographic and surgical data. Values expressed as mean ± SD and number (%) as appropriate

		Group A (n=35)	Group B (n=35)
Mean age (years)		63.3±11.4	66.1±8.0
Gender	Male	6 (17.1)	7 (20.0)
	Female	29 (82.9)	28 (80.0)
Weight (kg)		66±8.6	68±7.6
ASA	I II	15 (21) 18 (25)	20 (28) 17 (24)
Race	Malay	16 (45.7)	13 (37.1)
	Chinese	16 (45.7)	19 (54.3)
	Indian	1 (2.9)	2 (5.7)
	Others	2 (5.7)	1 (2.9)
Surgery	TKR THR	27 (38.6) 8 (11.4)	23 (32.9) 12 (17.1)

Table II shows that after 48 hours, the cumulative volumes of drugs used were higher in Group A compared to Group B and the difference was significant at 24 hours (*p<0.02*) and 48 hours (*p<0.01*). The mean

Table II
Volume and amount of drugs used, number of PCEA delivered (D), number of PCEA attempt (A) and ratio D/A. Values expressed as mean ± SD and number (n) as appropriate

	Group A (n=35)	Group B (n=35)	*p* value
Volume 24 hr (ml)	118.17±20.36	105.54±22.03	0.02*
Volume 48 hr (ml)	163.31±29.01	142.69±30.93	0.01*
Amount of drug used 48 hr (mg)	251.43±70.02	178.91±42.33	0.01*
PCEA bolus delivered (D)	22.37±7.32	17.63±7.71	0.19
PCEA attempts (A)	27.66±9.12	24.40±11.51	0.17
Delivered/Attempted	0.83±0.13	0.74±0.15	0.02*

* Significant '*p*' values.

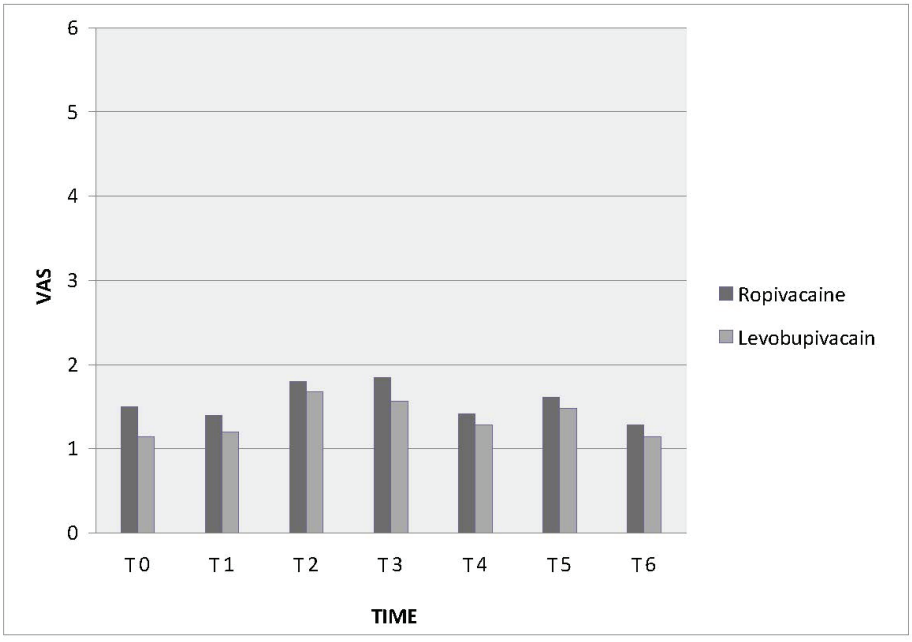
± SD dose of Group A for the first 48 hours after surgery was significantly ($p<0.01$) greater than the dose of Group B.

The numbers of PCEA boluses delivered (D) and PCEA attempted (A) were higher in the Group A in contrast to Group B but the differences were not statistically significant. However the delivered/attempt ratio (D/A) was significantly higher in Group A ($p<0.02$) than Group B.

Figure 1 shows VAS pain scores presented as means ± SD at different time intervals for both drugs. T_0 at the start of PCEA, T_1 at 8 hour, T_2 at 16 hour, T_3 at 24 hours, T_4 at 32 hours, T_5 at 40 hours and T_6 at 48 hours. There were no statistically significant differences.

None of the patient developed hypotension or sedation. There was only one incidence of vomiting occurred in one patient in Group B. Other incidences such as pruritus and motor block were not detected in this study.

Fig. 1
VAS pain score at different time intervals. Values expressed as mean ± SD and number (n) as appropriate



Discussion

Patient-controlled epidural analgesia provides us with a valuable and informative research tool in terms of comparing the efficacy of various concentrations of different local anaesthetics, either alone or in combination with opioids. Varying lockout periods, bolus and infusion dose with PCEA may also provide useful information for managing pain in acute setting.

There were several studies comparing ropivacaine and levobupivacaine for postoperative epidural analgesia. Casati et al compared PCEA ropivacaine 0.2% with levobupivacaine 0.125% (with baseline infusion rate 5.0ml/hour) for intraoperative and postoperative analgesia for major orthopaedic surgery and concluded that the quality of analgesia was similar for both local anaesthetics but

their study observation was only for the first 12 hours after surgery[8]. In our study we found that PCEA ropivacaine 0.165% or levobupivacaine 0.125% provided effective postoperative analgesia. However in our study, fentanyl 2.0 µg/ml was added to the local anaethetics and our observation was done up to 48 hours.

A nearly similar study done by Smet et al found that both PCEA ropivacaine 0.125% and levobupivacaine 0.125% (sufentanyl 1.0µg/ml was added to both local anaesthetics but no basal infusion was given) provided effective analgesia for major orthopaedic surgery. Smet et al chose sulfentanil whereas in our study we used fentanyl because it's availability, widely used and cost-effective[15]. The addition of an opioid may have affected local analgesic quality and duration. However, there is no evidence that opioid added to local anesthetic solution would alter the potency difference between them[16].

Our study showed significantly larger volumes and doses of ropivacaine were used than levobupivacaine during 48 hours of PCEA regime. The mean volume of ropivacaine was 13% greater than that of levobupivacaine. The boluses delivered/attempted ratio was also greater in ropivacaine group. In Smet et al study, the volume and dose used was 25% higher in those receiving ropivacaine than levobupivacaine[15]. The volume and dose difference may suggest different population studied and additional standard oral analgesic given. Therefore the higher amount of ropivacaine used probably reflects the potency difference between the two local anaesthetics.

Possible explanation for higher requirement of ropivacaine in both studies may be due to shorter duration of action of ropivacaine. However it would be unwise to believe that a higher dose can be explained entirely by a difference in duration of action alone. Furthermore, the ideal combination of local anaesthetic and opioid for PCEA is yet to be discovered.

In another study conducted by Senard et al using PCEA levobupivacaine 0.1% and ropivacaine 0.1% (both were combined with an epidural infusion morphine 0.1mg/hour) they did not find any difference in terms of postoperative pain relief between PCEA these two drugs in which was added morphine background infusion over a 48 hours period. However this study was conducted on patients undergoing abdominal surgery[17].

There were no side effects documented except for one patient in levobupivacaine group who had vomited twice within 24 hours postoperative without episode of hypotension observed. In a study by Smet et al[15], the incidence of hypotension and vomiting were very low, but mild pruritus was reported by 13% and 10% of patients in the ropivacaine and levobupivacaine groups respectively. Lack of side effects is probably related to the potency of the drug. The previous studies done by Capogna et al[11] and Lyon et al[12] showed that ropivacaine was 2% less potent than levobupivacaine but Camorcia et al[13] reported that ropivacaine was 20% less potent than levobupivacaine. Despite different potency described from these studies, there were no differences in analgesic qualities.

The other aspect of the study design needs further discussion. A background infusion may not be useful for epidural opioid alone[16] but with combination of both local anaesthetics and opioids, the use of basal infusion seems to be common practice, although there is lack of studies demonstrating benefit from this. In this study, a basal infusion was used for the first 24 hours. We found this basal rate infusion was beneficial during the first 24 hours after surgery when patients were not yet familiar with the PCEA pump. It was also noted, frequent additional demands had been observed despite of basal infusion of local anesthetic to obtain

optimum pain control. However, frequent demands may affect patient satisfaction and sleep quality.

Conclusion

This study showed that both PCEA using ropivacaine 0.165% with fentanyl 2.0µg/ml and levobupivacaine 0.125% with fentanyl 2.0 µg/ml provided effective postoperative analgesia within the first 48 hours of major lower limb orthopaedic surgery despite clinically significant dose difference. There was no hypotension, pruritus, sedation or motor block recorded in both groups.

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