A Double-Blind, Randomized Study Comparing Post-operative Pain Management Using Epidural Ropivacaine with Intravenous Ketorolac or Intravenous Ketorolac Alone Following Transabdominal Hysterectomy

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Abstract

Objective : The aim of this study is to compare the effect on postoperative pain of epidural ropivacaine in combination with intravenous ketorolac with intravenous ketorolac alone following transabdominal hysterectomy.

Design : A multi-center, randomized, double-blind study was conducted in Thailand and the Philippines to assess postoperative pain management in 107 patients given ketorolac alone or in combination with epidural ropivacaine following transabdominal hysterectomy. Pain score was assessed using a 100-mm visual analogue pain scale (VAS).

Results : The VAS scores for pain on coughing and at rest were significantly better in the ropivacaine group. The number of patients who asked for morphine in addition was higher in the ketorolac group compared to the ropivacaine + ketorolac group. The time taken to carry out the first three ambulatory steps was similar for both the two treatment groups. A higher degree of motor block was observed in the ropivacaine group over time. The adverse events observed were similar in both groups.

Conclusion : We demonstrated that epidural infusion of ropivacaine in addition with intravenous ketorolac gave superior pain relief at rest and on coughing in patients undergoing transabdominal hysterectomy when compared to the group receiving intravenous ketorolac alone.

Key word : Ropivacaine, Ketorolac, Pain Controlled, Hysterectomy

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Despite a growing trend for active acute pain management, there is still a high incidence of moderate to severe postoperative pain, which remains a significant health care problem[1]. Postoperative epidural analgesia with opioids, although effective is frequently associated with unwanted side effects, including pruritus, nausea, vomiting, sedation and respiratory depression. Epidural infusions of local anesthetics, usually bupivacaine may reduce the incidence and the severity of these side effects, but adequate doses to provide effective analgesia may also produce an unwanted degree of sensory, sympathetic and motor blockade[2].

A multimodal approach to the management of postoperative pain may achieve optimal analgesia through additive or synergistic drug effects. The advantage of such a strategy is a reduction in the individual drug dosages with a corresponding reduction in the number and frequency of side-effects.

Ropivacaine is a new long-acting local anesthetic which is chemically homologous to bupivacaine and mepivacaine[3]. Preclinical studies have shown that ropivacaine induced less central nervous system and cardiac toxicity than bupivacaine[4,5]. This decreased toxicity has been reported for ropivacaine given intravenously to human volunteers. Futhermore, ropivacaine induces less motor blockade than bupivacaine[6].

Ketorolac is the only nonsteroidal anti-inflammatory drug (NSAID) in widespread clinical use that is available in an injectable form. Though similar to aspirin and ibuprofen, it is much more potent. It is useful for treating postsurgical pain either alone or in combination with other pain relief strategies. For many types of pain, ketorolac is comparable in potency to opioids, though the mechanism by which it relieves pain is different. Ketorolac has a much longer duration than morphine or meperidine but has a slower onset[7].

The aim of this study is to compare the effect of epidural ropivacaine plus intravenous ketorolac with intravenous ketorolac alone on postoperative pain, motor blockade and the need for morphine following transabdominal hysterectomy.

PATIENTS AND METHOD

A multi-center, randomized, double-blind study with two parallel groups was performed in 8 centers; 5 in Thailand and 3 in the Philippines. For each center patients were randomized consecutively based on their enrollment in the study. They were assigned randomization codes that were generated by Astra Pain Control AB, Sodertalje, Sweden. Institutional Review Board or Hospital Ethics Committee approval was obtained at each center. Written informed consent was obtained from ASA 1 or 2 patients scheduled for elective transabdominal hysterectomy. Exclusion criteria included age less than 18 yr or more than 79 yr, weight less than 45 kg or more than 110 kg, height less than or equal to 145 cm, contraindications for epidural and general anesthesia, contraindications for NSAID's (dehydration, serum creatinine more than 2 mg per dL, history of haemorrhagic peptic ulcer and coagulopaties), pregnancy, significant drug abuse and also participation in any clinical study in the two-week period prior to this study.

Patients were taught how to use the 100-mm visual analogue pain scale (VAS) at the start of the study. Baseline hemodynamic parameters, including pulse rate, systolic and diastolic blood pressure were measured a day before the operation. Upon arrival at the operating theater, each patient received a standard intravenous infusion of balanced salt solution (10 ml per kg body weight) before an epidural catheter was inserted at the level of L2-3 or L3-4 interspace. 3 ml of lidocaine (20 mg/ml) together with 5 μg/ml of epinephrine was used as a test dose to confirm correct catheter location. 10 to 15 ml of ropivacaine (7.5 mg/ml) was used to induce epidural block up to at least the T10 dermatome (loss of pinprick sensation). Before induction of anesthesia, each patient received 1 mg of midazolam and 1 μg per kg body weight of fentanyl intravenously, followed by a combination of general and epidural anesthesia. 5 ml of ropivacaine (7.5 mg/ml) was added into the epidural space every two hours. Opioids were given only after the start of the postoperative epidural infusion. Standard ASA monitoring was used during surgery.

In the recovery room, immediately after the operation, patients were randomly allocated into one of two groups, to receive either the epidural solution of ropivacaine, (2 mg/ml), or normal saline, (0.9%) which was prepared in a 100-ml glass bottle and labeled with a enrolment code prepared by Astra, Sweden. All investigators, study nurses and patients were blinded to the treatment arms. An epidural infusion was started immediately after surgery at a rate of 8 ml per h without a bolus dose. The infusion rate was reduced by 2 ml per h if excessive block or unacceptable side effects were observed and to a further 4 ml per h if required. In patients who dis-

played excessive block or unacceptable side effects at an infusion rate of 4 ml per h, the epidural infusion was discontinued. Every patient received a 30-mg bolus of ketorolac intravenously, together with the epidural infusion. Three additional doses of 10-mg of intravenous ketorolac were administered every 8 h, during the 24 h postoperative period. The total dose of ketorolac was 60 mg.

Assessment began on arrival at the recovery room which was denoted as reference time 0. Repeated measurements of pulse rate, blood pressure, pain assessment and degree of motor blockage were recorded at 1,2, 4, 6, 8, 12, 16, 20 and 22 hours after operation. A visual analogue scale ruler was used for evaluation. Patients were asked to rate their wound pain at rest and on coughing by moving a pointer along the ruler to mark the distance from the "no pain" end.

Motor blockade was assessed bilaterally using a modified Bromage scale and the highest value was recorded. All patients were encouraged to ambulate between 12-22 hours postoperatively. Three ambulating steps were recorded which included the ability to rise from lying to sitting in bed, the ability to sit up with their legs outside the bed and the ability to walk with assistance from the bed to the chair. Immediately after attempting each step, patients were asked to rate wound pain on the VAS and discomfort experienced based on the seven-grade Likert scale shown below :

Scale 0 = No discomfort at all
Scale 1 = Minor discomfort
Scale 2 = Mild discomfort
Scale 3 = Moderate discomfort
Scale 4 = Quite severe discomfort
Scale 5 = Severe discomfort
Scale 6 = Very severe discomfort

If the patient complained of unacceptable pain, morphine was given intravenously or intramusculaly according to the usual method used at each center. All adverse events, both serious and minor, were recorded throughout the study.

A total of at least 70 patients with the "Intention to treat" (ITT) were recruited into the study. Data

Table 1. Reasons for patients being excluded from final analysis (25 cases out of 107 cases).

Center/ patient	Country	Treatment	Details
5/502	Thailand	Ropivacaine	Operative plan was changed
5/512	Thailand	Ropivacaine	Other adverse event, no study drug was given
7/703	Thailand	Ketorolac	Failure to insert epidural catheter
1/101	Philippines	Ropivacaine	Reduction of epidural infusion rate did not correspond to protocol
1/103	Philippines	Ketorolac	Delayed administration of Ketorolac
1/104	Philippines	Ropivacaine	Ketorolac was not given according to study protocol
2/201	Philippines	Ropivacaine	Ketorolac was not given according to study protocol
2/202	Philippines	Ketorolac	Ketorolac was not given according to study protocol
2/203	Philippines	Ketorolac	Ketorolac was not given according to study protocol
2/204	Philippines	Ketorolac	Ketorolac was not given according to study protocol
2/205	Philippines	Ropivacaine	Ropivacaine infusion was stopped at 21 hours instead of 22 hours
2/206	Philippines	Ropivacaine	Ketorolac was not given according to study protocol
2/207	Philippines	Ropivacaine	Ketorolac was not given according to study protocol
3/306	Philippines	Ropivacaine	Ketorolac was not given according to study protocol
5/507	Thailand	Ketorolac	Ketorolac was discontinued because of epigastric pain
5/511	Thailand	Ketorolac	Reduction of the epidural infusion rate did not corresponded to protocol
5/504	Thailand	Ketorolac	Height 144 cm. (exclusion criterion)
6/607	Thailand	Ropivacaine	Ketorolac was not given according to study protocol
6/608	Thailand	Ropivacaine	Epidural infusion was stopped temporarily as a result of communication failure
6/609	Thailand	Ketorolac	Epidural infusion was turn off at 13 hours, instead of 22 hours as a result of communication failure
6/613	Thailand	Ropivacaine	Height 144 cm. (exclusion criterion)
7/706	Thailand	Ropivacaine	Epidural infusion was stopped at 21 hours 20 minute instead of 22 hours
7/709	Thailand	Ropivacaine	Morphine was used for premedication and the epidural infusion was stopped at 19 hours
8/811	Thailand	Ketorolac	Epidural infusion rate didn't correspond to study protocol
8/813	Thailand	Ropivacaine	Epidural infusion was stopped temporarily as a result of communication failure

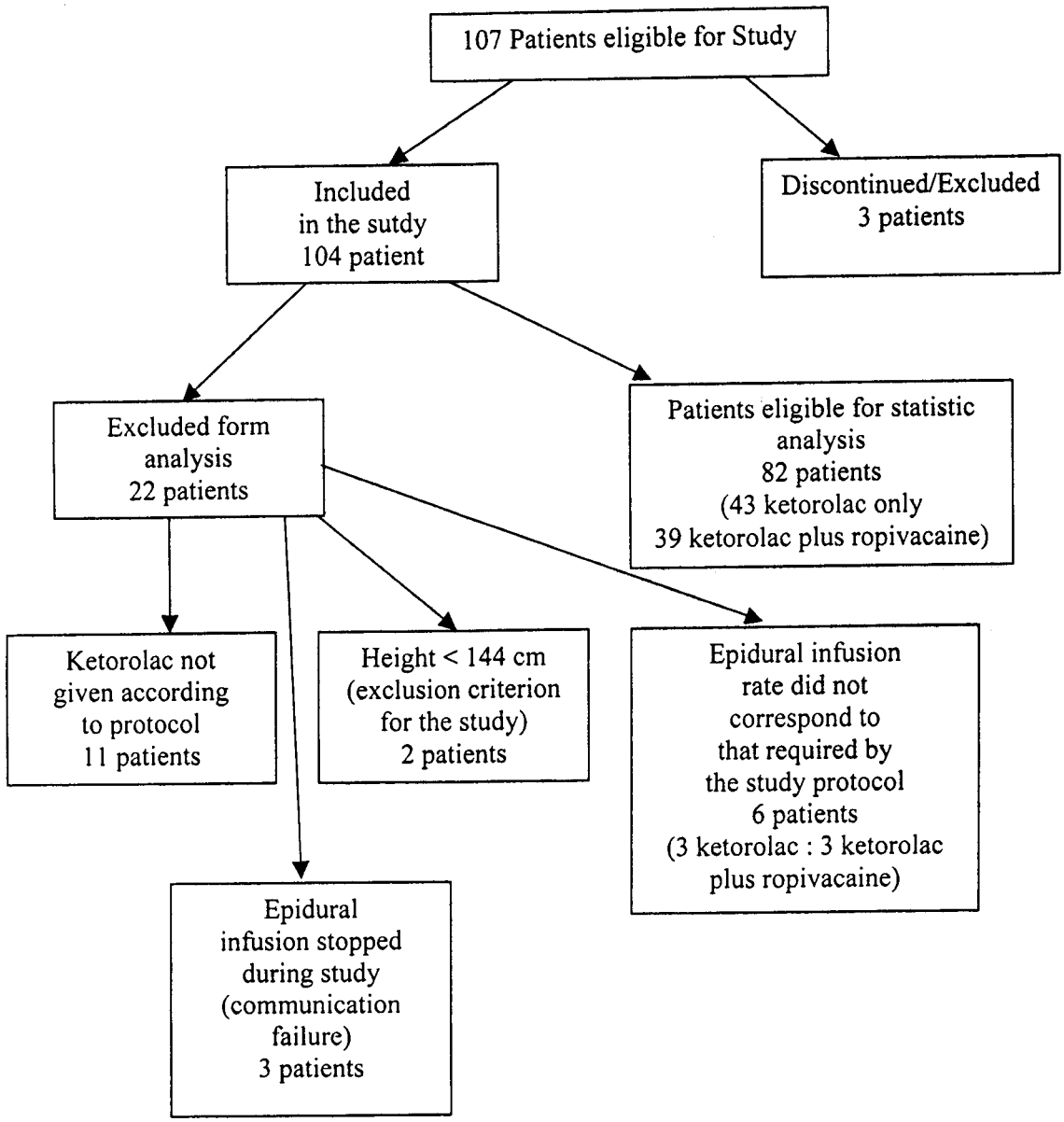

Fig. 1. Enrollment and exclusion of patients from statistical analysis.

entry, editing, and validation were performed by the AstraZeneca Asia data management unit.

Statistical methods

Descriptive statistics were used for continuous variables. Pain score on coughing was compared between both treatment arms, by calculating the area under the curve based on repeated measurements up to 22 hours after operation using a trapezoidal rule. A stratified Wilcoxon (mid) rank sum test was used to adjust for the different centers. Corresponding point estimates and the 95 per cent confidence interval was used to compare primary and secondary efficacy variables.

RESULTS

A total of 107 patients from 8 centers, 3 centers (27 patients) from the Philippines and 5 centers

Table 2. Demographic characteristics and risk category. All patients were female and oriental, no significant difference was observed between groups.

	ITT data set		PP data set	
	Ketorolac	Ropivacaine	Ketorolac	Ropivacaine
All patients	53	51	43	39
Age (years)				
mean ± SD	44.1 ± 7.3	44.5 ± 7.8	43.9 ± 6	44.2 ± 6.9
range	27 - 68	32 - 72	28 - 56	34 - 72
Weight (kg)				
mean ± SD	56.7 ± 8.1	59.7 ± 9.4	57.2 ± 8.6	60.2 ± 8.5
range	45 - 75	45 - 90	45 - 75	45 - 81
Height (cm)				
mean ± SD	155.1 ± 4.3	155.2 ± 5.4	155.4 ± 4.2	155.2 ± 4.9
range	144 - 167	144 - 166	147 - 167	145 - 166
ASA classification				
1 : 2	30 : 23	27 : 24	26 : 17	22 : 17
Allergic history				
Yes : No	8 : 45	3 : 48	7 : 36	2 : 37

ITT data set included all patients who were recruited in the study.
PP data set included patients who were eligible for statistically analysis.

Table 3. Total dosage administered by epidural infusion.

Total dose (ml)	Ketorolac	Ropivacaine
Mean	170.4	147.1
Standard deviation	16.8	33.3
Minimum	175.9	160.6
Maximum	191.9	191.9
Average per hour (ml/h)	7.7	6.2

(80 patients) from Thailand, were enrolled into the study. Of the 107 patients, 53 were randomized to receive ropivacaine plus intravenous ketorolac and 54 were randomized to receive intravenous ketorolac alone. Of the three patients who discontinued treatment, two of them did not receive any study drugs. The first patient underwent a myomectomy, the second patient had an unexpected intraoperative bigemini without hypotension, and the third patient's treatment was discontinued due to technical failure.

After the start of the study, twenty-two patients were excluded from statistical analysis for the following reasons: there were eleven cases, in which ketorolac was not given according to the protocol, two cases which the height was 144 cm and six cases (3 in ketorolac and 3 in ropivacaine group) in which subjects received epidural infusion at a rate and duration that did not correspond to the protocol. For the last three cases, epidural infusion was stopped as a result of communication failure (Table 1 and Fig. 1).

Only 82 patients were eligible for statistically analysis, of these 43 were from the ketorolac group and 39 from the ropivacaine group. All of them were female and oriental. Demographic distribution (age, height, weight), risk category by ASA classification and allergy history were similar between the two treatment groups (Table 2).

For both groups the epidural catheter was usually inserted at the 2^{nd}-3^{rd} lumbar space using a size 16-18 gauge Tuohy needle. All 104 intention to treat (ITT) patients were given 10-15 ml of 0.75 per cent ropivacaine prior to surgery according to the protocol. All patients achieved adequate anesthesia dermatome level of more than T_{10} before the induction of general anesthesia. The duration of surgery was similar for both groups.

The mean total dosage of epidural infusion during the 22 hour postoperative period was 170.4 ml for the ketorolac group and 147.1 ml for the ropivacaine plus ketorolac group (Table 3). The average epidural infusion rate was 7.7 ml per h for the ketorolac group and 6.2 ml per h for the ropivacaine group. The median epidural infusion rate was 6 ml per h in the ketorolac group. In the ropivacaine plus ketorolac group, a steady epidural infusion rate of 4 ml per h was given in 14 patients, 6 ml per h in 20

patients and 8 ml per h in 5 patients. No patients in either group received an epidural infusion rate of more than 8 ml per h.

For both treatments, primary efficacy was evaluated using the visual analogue scale scores for pain on coughing during the 22-hour postoperative period. The mean VAS score was found to be similar for both groups at the beginning and the end of 22 hour post operative period (Fig. 1). During the 2-20 hour peroid, the mean score was found to be consistently lower in the ropivacaine plus ketorolac group compared to the group receiving ketorolac alone (Table 4). The largest difference between the groups was observed 4 hours after initiating the epidural infusion. The area under the curve for repeated measurements made at 22 hours, 0-4 hours, 4-12 hours and 12-22 hours was consistently lower in the ropivacaine plus ketorolac group. The largest difference was observed between 4-12 hours (Table 5). Treatment across the various centers were adjusted by using the stratified Wilcoxon mid rank sum test. The point estimate difference and the corresponding 95 per cent confidence interval were statistically significantly different for area under the curve measurements (AUCM) at 0-22, 0-4 and 4-12 but not for the 12-22 h period (Table 6). A consistent statistical difference was observed in Thai patients but not in Filipino patients.

The mean VAS score at rest was similar to the mean VAS score on coughing (Fig. 2 and 3). This too, was found to be consistently lower in the ropivacaine plus ketorolac group for all corresponding AUC measurements i.e. AUCM 22, AUCM 0-4, AUCM 4-12 and AUCM 12-22. The largest difference was also observed in the AUCM at 4-12 hours. The stratified Wilcoxon mid rank sum test was used to adjust for the various centers (Table 7). The point estimates for treatment differences were less than 0 for all summary measurements. The results showed that pain at rest was lower in the ropivacaine plus ketorolac group compared to the group receiving ketorolac alone. A statistical difference ($p \leq 0.05$)

Table 4. Mean pain score on coughing using VAS scores during the 22-hour postoperative period between the two groups of study. Displayed both by country and pooled sites.

Hours postoperative	Pooled sites		Philippines		Thailand	
	Ketorolac	Ropivacaine	Ketorolac	Ropivacaine	Ketorolac	Ropivacaine
1	20.4	18.2	30.9	26.3	16.9	15.2
2	29.2	19.1	29.1	25.4	29.3	16.7
4	50.5	24.1	56.5	28.4	48.5	22.4
6	48.1	29.3	42.6	31.6	50.0	28.4
8	51.5	34.1	45.1	36.8	53.6	33.0
12	48.7	38.2	44.7	43.4	50.0	36.3
16	47.0	38.8	43.9	36.8	48.0	39.5
20	40.9	36.0	38.5	31.5	41.6	37.7
22	40.7	41.6	41.4	37.1	40.5	43.4

Table 5. Summary measurement of the area under the curve measurement (AUCM) of pain on coughing between the two groups. Displayed by pooled sites and country.

AUCM	Pooled site		Philippines		Thailand	
	Ketorolac	Ropivacaine	Ketorolac	Ropivacaine	Ketorolac	Ropivacaine
AUCM 22	45.3	33.5	43.0	35.0	46.1	33.0
AUCM 0-4	34.8	20.6	38.5	26.5	33.6	18.3
AUCM 4-12	49.8	32.7	45.8	36.1	51.1	31.4
AUCM12-22	44.9	38.1	42.2	36.6	45.5	38.7

AUCM 22 = Area under curve measurement during 22 hours
AUCM 0-4 = Area under curve measurement during 0-4 hours
AUCM 4-12 = Area under curve measurement during 4-12 hours
AUCM 12-22 = Area under curve measurement during 12-22 hours

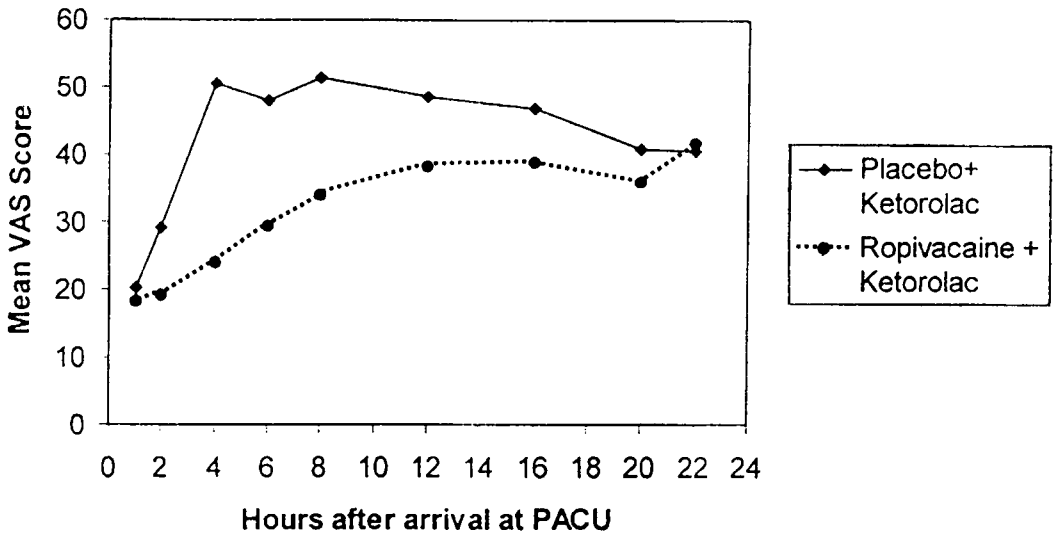

Fig. 2. **Pain on coughing. Note the similarity between the two treatments at the beginning and the end of the 22 hour postoperative period. The biggest difference between the two groups was observed 4 h after starting the epidural infusion.**

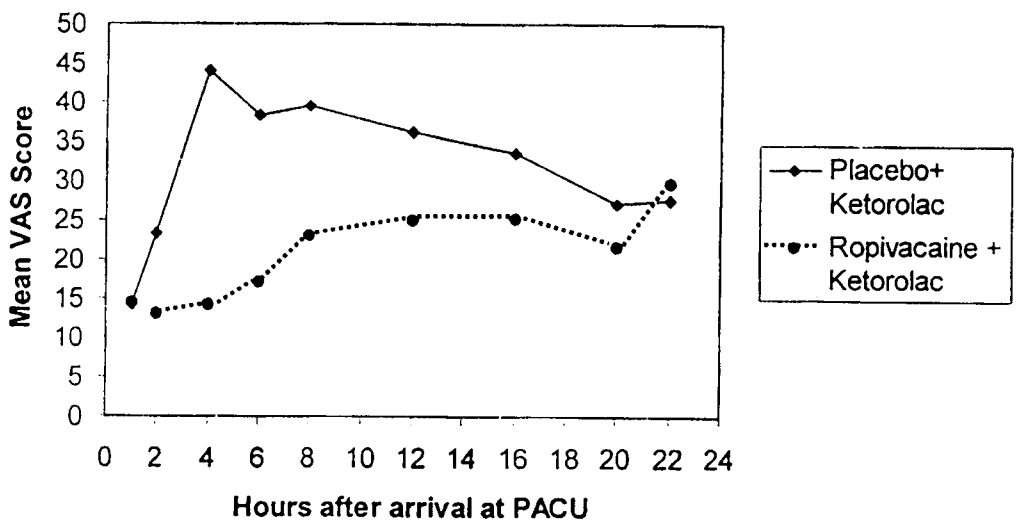

Fig. 3. **Pain at rest. Note the similarity between the two treatments at the beginning and the end of the 22 hour postoperative period. The biggest difference between the two groups was observed between 4-12 h.**

Table 6. Formal statistical comparisons between the two treatments for the summary measurements (AUCM) of pain on coughing.

Pain on coughing	Point estimate of the treatment differences*	95% confidence limit		2-tailed p-value
		Lower	Upper	
AUCM 22	-11.2	-20.0	-2.8	0.010
AUCM 0-4	-13.7	-23.0	-5.7	0.001
AUCM 4-12	-17.5	-28.8	-5.8	0.002
AUCM 12-22	-5.5	-16	4.6	0.288

* = The direct of difference is Ropivacaine and Ketorolac minus ketorolac and placebo

Table 7. Formal statistical comparisons between the two treatments for the summary measurements (AUCM) of pain at rest.

Pain at rest	Point estimate of the treatment differences*	95% confidence limit		2-tailed p-value
		Lower	Upper	
AUCM 22	-11.6	-19.0	-4.0	0.002
AUCM 0-4	-14.7	-22.7	-7.0	<0.001
AUCM 4-12	-18.1	-26.3	-8.4	<0.001
AUCM 12-22	-5.0	-13.4	1.3	0.150

* = The direct of difference is Ropivacaine and Ketorolac minus ketorolac and placebo

Table 8. Time to achieving full ambulation (all three steps) and pain on mobilization using VAS score for the two groups.

	Duration (hours) mean ± SD		VAS (mm) mean ± SD	
	Ketorolac	Ropivacaine	Ketorolac	Ropivacaine
Patient able to rise from lying to sitting position in bed	17.9 ± 3.5	18.1 ± 2.8	34.4 ± 27.1	36.1 ± 25
Patient able to sit with legs outside bed	19.5 ± 2.1	18.9 ± 2	34.8 ± 29.4	38.1 ± 28.2
Patient able to ambulate with assistance from bed to chair	19.6 ± 2	20.2 ± 5.1	39.8 ± 29.6	41.3 ± 26.7

No statistically significant difference between study groups.

between the treatment groups was observed in the AUCM 22, AUCM 0-4 and AUCM 4-12 but not in the AUCM at 12-22. This too was found to be consistently significant in Thai patients but not in Filipino patients.

The time taken to carry out the first three ambulatory steps was found to be similar for both treatment groups (Table 8). Almost all patients achieved all ambulatory steps within a 30 hour postoperative period. Only one patient in the ropivacaine plus ketorolac group took 42.9 hours to achieve step 3. VAS scores and the Likert scale were used to record pain and discomfort for each ambulatory step. A stratified Wilcoxon mid rank sum test was used to adjust for the pooled sites, to allow for treatment comparisons. No statistically significant treatment difference was observed for any of the ambulatory steps between the two groups. There were three cases who demonstrated excessive motor blockade between 12-22 hours, and were not able to ambulate at 22 hours. All of them were in the ropivacaine plus ketorolac group.

The number of patients who asked for supplemental morphine was higher in ketorolac only group (48/53) compared to the ropivacaine plus ketorolac group (36/51) but the amount of morphine used by each patient was not statistically different between the two groups. Motor blockade was found to be similar for both treatment groups at the start of the study. The majority of the patients in the ketorolac

only group did not experience any motor blockade 4 hours after surgery. Patients in the ropivacaine plus ketorolac group demonstrated some degree of motor blockade for up to 22 hours. Four hours after starting the epidural infusion 6 (15.3%) patients could not raise extended legs; at 22 hours seven patients (17.9%) could not flex their knee and at 12 hours five (12.8%) could not flex their ankle joints.

Baseline vital signs were similar for both treatment groups. During the 22 hour post operative period the mean pulse rate, systolic and diastolic blood pressure at almost all time points were found to be slightly lower in patients receiving the ropivacaine plus ketorolac combination but this was not statistically significant.

There was no significant difference in the incidence of adverse events between the two groups. Twenty-seven patients in the ketorolac only group and eighteen in ropivacaine plus ketorolac group reported mild abdominal discomfort and one reported nausea and vomiting. Half of them needed to be given one dose of 10 mg metoclopramide intravenously.

DISCUSSION

Epidural analgesia with local anesthetics after lower abdominal surgery is a powerful method of relieving postoperative pain[8]. In addition, epidural local anaesthetics may reduce gastrointestinal paralysis and postoperative nausea and vomiting by inhibiting visceral activity and reducing the need for perioperative opioids[9].

The problem of persistent motor blockade limits the usefulness of epidural infusions with local anaesthetics. Although controversial, it has been claimed that ropivacaine produces comparable sensory, but less intense motor blockade compared to bupivacaine[10-12]. In the present study we investigated the effect of 0.2 per cent of epidural ropivacaine + ketorolac against ketorolac alone on postoperative pain following transabdominal hysterectomy.

We initially started the epidural infusion at 8 ml per h, but later reduced it to 4-6 ml per h as this was found to be sufficient to produce improved postoperative analgesia and decreased morphine requirement when compared with saline. We agreed not to test the sensory level during the study period to keep the investigators blinded to the study drug. The dose used was much lower than that used in other studies. In a dose-finding study, Scott and colleagues showed that 0.2 per cent ropivacaine at a rate of 10 ml per h provided the best balance between analgesia and motor blockade[13]. In another study, Etches and colleagues investigated the effect of epidural 0.2 per cent ropivacaine at a rate of 6, 8, 10, 12 or 14 ml per h after lower abdominal surgery. They found that ropivacaine at 10-14 ml per h (but not 6 or 8 ml per h) reduced PCA morphine requirement but had little effect on pain scores[2]. The differences observed maybe attributed to the lower body mass index of the oriental population.

The primary goal of postoperative epidural analgesia with local anesthetics is to improve analgesia, reduce the requirement for supplemental opioids, and minimize motor blockade to permit early ambulation, with an acceptable incidence of side-effects. In the present study, VAS scores for pain on coughing and at rest were found to be significantly better in the ropivacaine plus ketorolac group 4-12 hours after starting the epidural infusion. However, the mean scores were virtually identical in both groups at 22 hours. This is not surprising, since patients could request supplementary morphine in order to achieve sufficient analgesia to obtain similar VAS pain scores. Also, the number of patients who requested supplementary morphine was higher in ketorolac only group compared to the ropivacaine plus ketorolac group.

A higher degree of motor blockade was observed in the ropivacaine plus ketorolac group over time compared to the ketorolac group. A possible explanation for the higher intensity of motor block observed in the combined treatment group could be a synergistic effect on the central nervous system. The most frequently reported adverse event during the 22 hour postoperative period was mild abdominal discomfort with one case of nausea and vomiting. The adverse events occurred with similar frequencies for both groups and may be attributed to the ketorolac. Ketorolac was used as the basic analgesic because equipment used for patient controlled analgesia could not be made available to every patient. Also intravenous ketorolac has been reported in a number of studies to control postoperative pain to some degree.

In conclusion we demonstrated that an epidural infusion of ropivacaine plus ketorolac gave superior pain relief at rest and on coughing in patients undergoing transabdominal hysterectomy when compared to those receiving ketorolac alone.

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การศึกษาความสามารถในการระงับปวดด้วยวิธีหยดยา ropivacaine เข้าช่องอิพิดูรัล ร่วมกับการฉีด ketorolac เข้าหลอดเลือดดำเปรียบเทียบกับการใช้ ketorolac เพียงอย่างเดียว

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วัตถุประสงค์ : การศึกษานี้เพื่อเปรียบเทียบความสามารถในการระงับปวดจากการใช้ epidural infusion ด้วย 0.2% ropivacaine ร่วมกับการฉีด ketorolac เข้าทางหลอดเลือดดำกับการใช้ ketorolac เพียงอย่างเดียวภายหลังการผ่าตัดมดลูกออกทางหน้าท้อง

วิธีการศึกษา : ทำการศึกษา ณ สถาบัน 8 แห่งในประเทศไทยและฟิลิปปินส์ ด้วยวิธี randomized และ double-blind โดยประเมินความสำเร็จในการระงับปวด ภายหลังการผ่าตัดมดลูกทางหน้าท้องในผู้ป่วยทั้งหมด 107 ราย โดยเปรียบเทียบระหว่างผู้ป่วยที่ได้รับการฉีด ketorolac เข้าทางหลอดเลือดดำเพียงอย่างเดียวกับ ผู้ป่วยที่ได้รับ ketorolac เข้าหลอดเลือดดำ ร่วมกับ epidural infusion ด้วย 0.2% ropivacaine ทำการประเมินคะแนนของความเจ็บปวด (pain score) โดยใช้ 10 มม visual analogue pain scale (VAS)

ผลการศึกษา : พบว่าความเจ็บปวดในผู้ป่วยที่ได้รับการหยดยา ropivacaine เข้าช่องอิพิดูรัลร่วมกับได้ ketorolac มีคะแนนน้อยกว่ากลุ่มที่ได้รับ ketorolac เพียงอย่างเดียว ทั้งขณะพักและเมื่อผู้ป่วยไอ ซึ่งเป็นค่าที่มีนัยสำคัญทางสถิติ นอกจากนี้ผู้ป่วยกลุ่ม ropivacaine + ketorolac ยังต้องการมอร์ฟีนน้อยกว่ากลุ่มที่ได้รับketorolac เพียงอย่างเดียว แต่พบว่าผู้ป่วยทั้ง 2 กลุ่มสามารถลุกจากเตียงในลำดับต่าง ๆ โดยไม่แตกต่างกัน นอกจากนี้พบว่าผู้ป่วยกลุ่มที่ได้รับ epidural ropivacaine มีอาการอ่อนแรงของกล้ามเนื้อมากกว่ากลุ่มที่ไม่ได้รับยานี้

สรุป : จากการศึกษานี้พบว่าการใช้ epidural infusion ด้วย 0.2% ropivacaine ร่วมกับการฉีด ketorolac เข้าทางหลอดเลือดดำ มีผลระงับปวดหลังการผ่าตัดมดลูกออกทางหน้าท้องมากกว่าผู้ป่วยได้รับ ketorolac เพียงอย่างเดียว

คำสำคัญ : ropivacaine, ketorolac, ระงับปวด, ผ่าตัดมดลูก

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