The continuous epidural infusion of ropivacaine 0.1% with 0.5 μg·mL^{-1} sufentanil provides effective postoperative analgesia after total hip replacement: a pilot study

[La perfusion continue de ropivacaïne à 0,1 % additionnée de 0,5 μg·mL^{-1} de sufentanil produit une analgésie postopératoire efficace après l'arthroplastie totale de hanche : une étude pilote]

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Purpose: To assess the analgesic efficacy and functional outcome of postoperative epidural infusion of ropivacaine combined with sufentanil in a randomized, controlled trial.

Methods: Thirty-two ASA I–III patients undergoing elective total hip replacement (THR) were included. Lumbar epidural block using 0.75% ropivacaine was combined with either propofol sedation or general anesthesia for surgery. On arrival in the recovery room, the epidural infusion was commenced at a rate in mL calculated as follows: (height in cm – 100) × 0.1. Eleven patients received an epidural infusion of ropivacaine 0.1% with 0.5 μg·mL^{-1} sufentanil (Group R+S0.5), ten patients ropivacaine 0.1% with 0.75 μg·mL^{-1} sufentanil (Group R+S0.75), and 11 patients ropivacaine 0.1% with 1 μg·mL^{-1} sufentanil (Group R+S1) over a postoperative study period of 44 hr. All patients had access to *iv* piritramide via a patient-controlled analgesia (PCA) device. Postel-Merle-d`Aubigné scoring system (PMA score) was assessed preoperatively, three weeks after surgery, and three months after surgery by an orthopedic surgeon blinded to study group.

Results: Motor block was negligible in all three groups. After eight hours of epidural infusion, sensory block had regressed completely in all patients. There was no significant difference with regard to visual analogue scale (VAS) scores (at rest: $P = 0.55$, on movement: $P = 0.63$), consumption of rescue medication ($P = 0.99$), patient satisfaction ($P = 0.22$), and the incidence of adverse events. All treatment regimens provided effective postoperative analgesia with only a minimal use of supplemental opioid PCA. There was no difference between groups regarding orthopedic PMA score (pain: $P = 0.24$, mobility: $P = 0.65$, and ability to walk: $P = 0.44$).

Conclusion: Ropivacaine 0.1% with 0.5 μg·mL^{-1} sufentanil for postoperative analgesia after THR provides efficient pain relief and, compared with 0.75 and 1 μg·mL^{-1} sufentanil, reduces sufentanil consumption without compromise in patient satisfaction, VAS scores, and functional outcome.

Objectif : *Évaluer, par une étude randomisée et contrôlée, l'efficacité analgésique et les effets fonctionnels d'une perfusion péridurale postopératoire de ropivacaïne combinée au sufentanil.*

Méthode : *L'étude a été menée auprès de 32 patients d'état physique ASA I–III, devant subir une arthroplastie totale de hanche (ATH). Le bloc péridural lombaire réalisé avec de la ropivacaïne à 0,75 %, a été combiné à une sédation au propofol ou à une anesthésie générale pour l'intervention chirurgicale. La perfusion péridurale, débutée dès l'arrivée en salle de réveil, avait un débit en mL calculé comme suit : (la taille en cm - 100) x 0,1. Onze patients ont reçu une perfusion péridurale de ropivacaïne à 0,1 % combinée à 0,5 μg·mL^{-1} de sufentanil (Groupe R+S0,5), dix ont eu de la ropivacaïne à 0,1 % et 0,75μg·mL^{-1} de sufentanil (Groupe R+S0,75) et onze, de la ropivacaïne à 0,1 % avec 1 μg·mL^{-1} de sufentanil (Groupe R+S1) pendant les 44 h postopératoires de l'étude. Tous les patients avaient accès à une analgésie autocontrôlée (AAC) iv avec piritramide. Le score de Postel-Merle d'Aubigné (score PMA) a été évalué avant l'opération, trois semaines et trois mois après l'opération, par un chirurgien orthopédique impartial.*

Résultats : *Le blocage moteur a été négligeable dans les trois groupes. Après huit heures de perfusion péridurale, le bloc sensitif avait complètement régressé chez tous les patients. Il n'y a pas eu de différence significative des scores de l'échelle visuelle analogique (au*

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repos : P = 0,55, au mouvement : P = 0,63), de consommation de médication de secours (P = 0,99), de satisfaction des patients (P = 0,22) et d'incidence d'événements indésirables. Tous les schémas posologiques ont produit une analgésie postopératoire efficace et n'ont nécessité qu'un usage minimal d'opioïde supplémentaire en AAC. Le score orthopédique PMA était similaire entre les groupes (douleur : P = 0,24, mobilité : P = 0,65 et capacité de marcher : P = 0,44).

Conclusion : *De la ropivacaïne à 0,1 % combinée à 0,5 μg·mL^{-1} de sufentanil, utilisée comme analgésie postopératoire après une ATH, réduit efficacement la douleur et, comparé à 0,75 et 1 μg·mL^{-1} de sufentanil, réduit la consommation de sufentanil sans compromettre la satisfaction des patients, les scores à l'EVA et les effets fonctionnels.*

CONTINUOUS epidural infusion of ropivacaine 0.1% with sufentanil 1 μg·mL^{-1} has proved highly effective in preventing pain after total hip replacement (THR), and appears to achieve the aim of avoiding motor block of the legs.[1,2]

For postoperative thoracic epidural analgesia after major abdominal surgery, the combination of ropivacaine 0.2% with 0.75 μg·mL^{-1} sufentanil provided the best analgesia with the fewest side effects compared to plain ropivacaine 0.2%, and ropivacaine 0.2% combined with 0.5, and 1 μg·mL^{-1} sufentanil.[3] The best concentration of sufentanil to be added to ropivacaine 0.1% for postoperative lumbar epidural analgesia in order to achieve good analgesia with minimal side effects remains unclear.

This randomized, double-blinded pilot study was designed to evaluate the clinical effectiveness of ropivacaine 0.1% combined with various concentrations of sufentanil, and to evaluate if the functional outcome of the arthroplasty is influenced by the different ropivacaine/sufentanil mixtures.

Methods

After obtaining Institutional Ethics Committee approval and written informed consent, 36 patients were enrolled. Eligible patients were those scheduled for elective THR, aged 30–75 yr, ASA physical status I–III, weighing 50–100 kg and being 150–190 cm tall. They had to be capable of operating an *iv* patient-controlled analgesia (PCA) device. Exclusion criteria were any contraindications to epidural anesthesia, allergy to local anesthetics or opioids, history of opioid dependency, postoperative intensive care unit stay, and communication difficulties that would prevent reliable postoperative assessment. Oral premedication consisting of 7.5–15 mg of midazolam was given one hour preoperatively. After the administration of at least 500 mL of isotonic saline solution over 15 min, an epidural catheter was inserted 3–5 cm into the epidural space at L3–5 via an 18-gauge Tuohy needle with the bevel placed in a cephalad direction and the patient in the lateral position. With the catheter secured and the patient in the supine position, a 3-mL test dose of ropivacaine 0.75% was given over 15 sec through the catheter after aspiration for cerebrospinal fluid or blood was negative. Five minutes later, a further 12 mL of ropivacaine 0.75% were administered over five minutes. If sensory block to pinprick did not reach T10 within 30 min after injection, an additional 5-mL top-up dose of ropivacaine 0.75% was administered. Patients were sedated with propofol or, if desired by the patient, general anesthesia was induced with thiopentone, cisatracurium, isoflurane, and oxygen in nitrous oxide and a maximal dose of fentanyl 100 μg. During surgery, additional doses (3–5 mL) of 0.75% ropivacaine could be given via the epidural catheter after two hours; if required, based on clinical signs. No additional doses of fentanyl were allowed.

Randomization was based on a computer-generated code prepared at a remote site and sealed in sequentially numbered, opaque envelopes. On arrival in the recovery room (time 0) patients were randomly allocated to three groups. A continuous epidural infusion with either 0.1% ropivacaine and 0.5 μg·mL^{-1} sufentanil (R+S0.5), 0.1% ropivacaine and 0.75 μg·mL^{-1} sufentanil (R+S0.75), or 0.1% ropivacaine and 1 μg·mL^{-1} sufentanil (R+S1) was commenced. The infusion rate in mL was calculated as follows: (height in cm - 100) × 0.1.[1,2] All patients had access to an *iv* PCA device with piritramide, an opioid used commonly in Europe with approximately 0.7 times the potency of morphine, with 1.5-mg bolus doses, a six-minute lockout time, and a 45-mg dose limit over 45 hr (Multifuse®, B. Braun Melsungen AG, Melsungen, Germany).

Wound pain at rest and on movement was assessed by using a 100-mm visual analogue scale (VAS) ranging from 0 (no pain) to 100 (worst pain imaginable). Sensory block was assessed bilaterally by using analgesia to pinprick with a short-bevelled 27-gauge needle, and motor block was assessed according to a modified Bromage scale (0 = no motor block, 1 = inability to flex the hip, 2 = inability to flex the knee and hip, 3 = inability to flex the ankle, knee and hip). All postoperative assessments at eight, 20, 32, and 44 hr were performed by the same anesthesiologist blinded to group assignment. The quality of pain management was judged by the patients and recorded at the last assessment on a four-point scale (1 = poor, 2 = fair, 3 = good, 4 = excellent). Monitoring at each assessment point included noninvasive blood pressure, heart rate, and respiratory rate.

TABLE I Postel-Merle-d`Aubigné (PMA) score[4]

Pain	Pain is intense and permanent	0
	Pain is severe even at night	1
	Pain is severe when walking; prevents any activity	2
	Pain is tolerable with limited activity	3
	Pain is mild when walking; it disappears with rest	4
	Pain is mild and inconstant; normal activity	5
	No pain	6
Mobility	Ankylosis with bad position of the hip	0
	No movement; pain or slight deformity	1
	Flexion < 40°	2
	Flexion 40 - 60°	3
	Flexion 60 - 80°; patient can reach his foot	4
	Flexion 80 - 90°; abduction of at least 15°	5
	Flexion of more than 90°; abduction to 30°	6
Ability to walk	None	0
	Only with crutches	1
	Only with canes	2
	With one cane, less than one hour; very difficult without cane	3
	A long time with a cane; short time without cane and with limp	4
	Without cane but with slight limp	5
	Normal	6

Hypotension was defined as systolic blood pressure < 80 mmHg or > 30% decrease compared with baseline; hypertension was defined as blood pressure > 180 mmHg systolic or 110 mmHg diastolic; bradycardia was defined as heart rate < 50 beats·min^{-1}; and tachycardia was defined as heart rate > 120 beats·min^{-1}.[8,9] Bradypnea was defined as a respiratory rate < 12 breaths·min^{-1} and tachypnea was defined as a respiratory rate > 20 breaths·min^{-1}. Sedation was recorded on a four-point scale (0 = no signs of sedation, 1 = mild sedation, 2 = moderate sedation, 3 = severe sedation). The incidence of pruritus, nausea and vomiting was recorded. Patients who experienced nausea received 10 mg *iv* metoclopramide, patients with vomiting 8 mg *iv* ondansetron. Hypotension was treated with 500 mL of crystalloid infusion.

Postel-Merle-d`Aubigné scoring system (PMA score; Table I), an orthopedic score to assess the functional outcome of hip arthroplasties, was assessed preoperatively, three weeks after surgery, and three months after surgery by an orthopedic surgeon blinded to group assignment.[4,5]

Statistical analysis was performed using the SPSS 11.0 statistical package (SPSS Inc., Chicago, IL, USA). This study was designed as a pilot dose-response study with small-dose ropivacaine combined with different sufentanil concentrations. Ten patients per group were selected as it was thought that clinical differences could be detected with this sample size, especially based on previous data on piritramide consumption under similar circumstances.[1] The primary efficacy variable was area under the curve (AUC) in mg x time based on the piritramide consumption over 44 hr postoperatively. The AUC, based on the repeated measurements up to 44 hr, was calculated using the trapezoidal rule (Stata Corporation, College Station, TX, USA). Post hoc power analysis, based on the primary efficacy variable, was performed using nQuery® 4.0 (Statistical Solutions, Sangus, MA, USA). Repeated-measurement analysis of variance was performed where appropriate. PMA scores were analyzed using multivariate regression analysis. Demographic data and adverse events are presented descriptively. Patient satisfaction was analyzed using two-tailed χ^2-test. Significance was determined at the $P < 0.05$ level. Unless indicated, data are presented as mean ± SD.

TABLE II Demographic data

	Group R+S0.5 (n = 11)	*Group R+S0.75 (n = 10)*	*Group R+S1 (n = 11)*
Age (yr)	63 ± 11	65 ± 12	67 ± 6
Height (cm)	170 ± 4	170 ± 7	168 ± 5
Weight (kg)	76 ± 12	76 ± 11	70 ± 10
Gender (M/F)	4/7	7/3	4/7
ASA physical status (I/II/III)	1/6/4	1/7/2	2/6/3
Anesthetic technique (EDA/general anesthesia and EDA)	9/2	8/2	10/1
Catheter insertion level (L3-4/L4-5)	9/2	7/3	7/4
Duration of surgery (min)	115 ± 24	114 ± 18	108 ± 29
Time from end of surgery until start of analgesia (min)	29 ± 5	30 ± 3	27 ± 5

Data are presented as mean ± SD, or number of subjects. Group R+S0.5 = epidural infusion of ropivacaine 0.1% with 0.5 μg·mL^{-1} sufentanil; Group R+S0.75 = ropivacaine 0.1% with 0.75 μg·mL^{-1}sufentanil; Group R+S1 = ropivacaine 0.1% with 1 μg·mL^{-1} sufentanil. EDA = epidural anesthesia.

TABLE III Postel-Merle-d`Aubigné (PMA) scoring data

	Group R+S0.5 n = 11	*Group R+S0.75 n = 10*	*Group R+S1 n = 11*
Pain			
Preoperatively	2.1 ± 1.1	1.5 ± 1.1	1.7 ± 1.2
After three weeks	5.0 ± 1.1	4.6 ± 0.7	5.1 ± 1.0
After three months	5.6 ± 0.9	5.9 ± 0.7	5.6 ± 0.7
Mobility			
Preoperatively	5.2 ± 1.0	5.2 ± 1.5	5.4 ± 1.0
After three weeks	5.2 ± 0.7	5.2 ± 1.2	5.6 ± 0.7
After three months	5.9 ± 0.3	5.8 ± 0.5	5.9 ± 0.4
Ability to walk			
Preoperatively	3.1 ± 1.3	2.1 ± 1.1	3.0 ± 1.4
After three weeks	1.0 ± 0.0	1.9 ± 1.6	1.0 ± 0.0
After three months	4.8 ± 1.9	5.5 ± 0.7	4.6 ± 1.8

Data are presented as mean ± SD. Group R+S0.5 = epidural infusion of ropivacaine 0.1% with 0.5 $\mu g \cdot mL^{-1}$ sufentanil; Group R+S0.75 = ropivacaine 0.1% with 0.75 $\mu g \cdot mL^{-1}$sufentanil; Group R+S1 = ropivacaine 0.1% with 1 $\mu g \cdot mL^{-1}$ sufentanil.

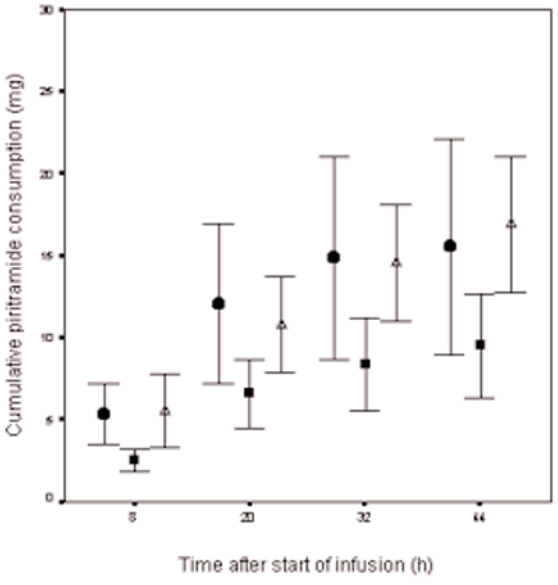

FIGURE 1 Cumulative piritramide consumption over a 44-hr period after total hip replacement. Data are presented as mean ± SE.• Group R+S0.5, ■ Group R+S0.75, Δ Group R+S1.

Results

We enrolled 36 patients during an 18-month period. Two patients were withdrawn because the epidural catheter could not be placed. Two patients did not complete the protocol as their epidural catheter was removed after accidental disconnection. The data of 32

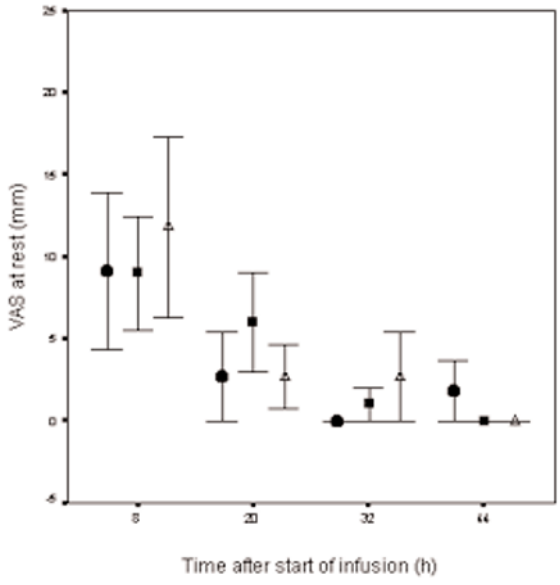

FIGURE 2 Pain at rest over a 44-hr period after total hip replacement. Data are presented as mean ± SE.•Group R+S0.5, ■ Group R+S0.75, Δ Group R+S1.

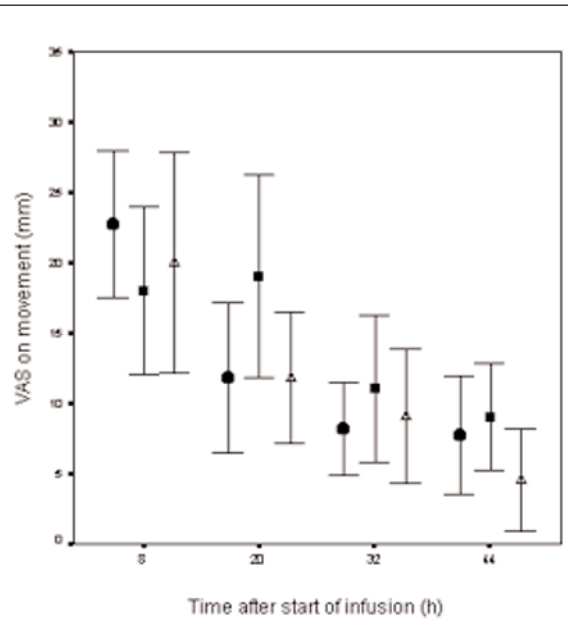

FIGURE 3 Pain on movement over a 44-hr period after total hip replacement. Data are presented as mean ± SE. • Group R+S0.5, ■ Group R+S0.75, Δ Group R+S1.

patients were eligible for statistical analysis (11 in Group R+S0.5, ten in Group R+S0.75, 11 in Group R+S1).

The demographic characteristics of the three groups were similar (Table II).

Motor block resolved rapidly in all groups. One patient in Group R+S0.5 and one patient in Group R+S0.75 showed a Bromage grade 1 motor block after 20 hr and eight hours of epidural infusion, respectively.

After eight hours of epidural infusion, sensory block had regressed completely in all patients.

There was no statistical difference between groups regarding *iv* PCA use. All groups had a minimal piritramide consumption over the study period (Figure 1). The AUC for opioid rescue medication in Group R+S0.5 was 469 ± 620 mg x time, Group R+S0.75, 433 ± 511 mg x time, and Group R+S1, 461 ± 391 mg x time ($P = 0.99$). Post hoc power analysis indicated that if the total sample size across the three groups was 8600, a one-way analysis of variance would have 80% power to detect at the 0.05 level a difference characterized by a variance of means of 231.

The VAS scores at rest and on movement are presented in Figures 2 and 3. There was no statistical difference between groups (VAS at rest: $P = 0.55$, VAS on movement: $P = 0.63$).

Orthopedic PMA scoring data are presented in Table III. There was no difference between groups regarding orthopedic functional outcome (pain: $P = 0.24$, mobility: $P = 0.65$, and ability to walk: $P = 0.44$).

All patients rated quality of pain treatment as excellent or good (Group R+S0.5: nine excellent, two good; Group R+S0.75: six excellent, four good; Group R+S1: ten excellent, one good; $P = 0.22$).

Side effects were of a mild nature and did not change patient care. In Group R+S0.5 one patient experienced nausea after 32 hr of epidural infusion. One patient of Group R+S0.5 and Group R+S1 experienced pruritus after 32 hr of epidural infusion. One patient in Group R+S0.75 suffered from nausea and vomiting at the 20 hr assessment point, another patient in Group R+S0.75 was mildly sedated 32 hr and 44 hr postoperatively. One further patient in Group R+S0.75 experienced hypotension at the first two assessment points. In Group R+S1 one patient had hypotension after 44 hr of epidural infusion, and two patients eight hours postoperatively.

Discussion

In this study the continuous epidural infusion of ropivacaine 0.1% with 0.5, 0.75, and 1 $\mu g \cdot mL^{-1}$ sufentanil proved highly effective in preventing pain after THR while avoiding motor block of the legs. All three study groups consumed only minimal opioid rescue medication over the 44-hr study period.

We did not examine the use of plain ropivacaine 0.1% for postoperative analgesia after THR in a control group, since it did not prove effective in a previous study.[1] The plain ropivacaine 0.1% group consumed a sixfold higher amount of opioid rescue medication after THR than the group receiving the epidural combination of ropivacaine 0.1% with sufentanil 1 $\mu g \cdot mL^{-1}$.[1] Theoretical advantages for adding lipophilic drugs to epidural local anesthetics have been postulated.[6,7] Our results support this theory as the addition of just 0.5 $\mu g \cdot mL^{-1}$ sufentanil resulted in effective postoperative pain therapy compared with previously published data on plain ropivacaine.[1]

Not only efficacy, but also tolerance (side effects) is one of the primary reasons for conducting a dose-response study. We did not consider side effects as a primary efficacy variable in our study because, based on previously published data on ropivacaine with 1 $\mu g \cdot mL^{-1}$ sufentanil,[1,2] and based on the cerebrospinal and plasma pharmacokinetics of sufentanil after epidural administration,[8] we did not expect patients to experience severe side effects.

The PMA scoring system is an established orthopedic scoring system to assess functional outcome after THR.[9,10] We found no difference between groups regarding PMA scores. This is most likely due to the fact that all three study groups received an effective postoperative pain therapy. Postoperative pain is thought to be an important predictor for poor functional outcome after THR.[11] Our study groups had low VAS scores at rest and on movement throughout the study period.

Recent data support continuous psoas compartment block,[12] or recommend extended femoral nerve sheath block[13] for postoperative pain therapy after THR. Our study was not designed to address the risk/benefit discussion between central and peripheral blockades.

In view of our preliminary results we recommend the continuous epidural infusion of ropivacaine 0.1% with 0.5 $\mu g \cdot mL^{-1}$ sufentanil for postoperative epidural analgesia after THR as it provides good pain relief. Compared with 0.75 and 1 $\mu g \cdot mL^{-1}$ sufentanil, it reduces sufentanil consumption without compromise in pain control, patient satisfaction, and functional outcome.

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