Impact of preoperative continuous femoral blockades on morphine consumption and morphine side effects in hip-fracture patients: A randomized, placebo-controlled study

Aurélie Chaudet a, Guillaume Bouhours a, Emmanuel Rineau a, Jean-François Hamel b, Damien Leblanc a, Vincent Steiger c, Sigismond Lasocki a, *  

a Département d'anesthésie-réanimation, LUNAM université, université d’Angers, CHU d’Angers, 49000 Angers, France  
b Centre de recherche clinique, LUNAM université, université d’Angers, CHU d’Angers, 49000 Angers, France  
c Département de chirurgie osseuse, LUNAM université, université d’Angers, CHU d’Angers, 49000 Angers, France

A R T I C L E   I N F O  
Article history:  
Available online 10 November 2015  

Keywords:  
Hip fracture  
Opioid  
Femoral blockade  
Side effects  
Pain

A B S T R A C T  

Background: Upon arrival at the emergency department, hip-fracture pain relief is usually carried out via systemic opioids. Continuous nerve blocks are efficient in the postoperative period, but have not been evaluated preoperatively. This study compared the reduction in morphine consumption and related side effects of a continuous femoral block with a single shot block in hip-fracture patients.  

Methods: Hip-fracture patients admitted to the emergency department received a femoral nerve catheter, with a single lidocaine injection. They were then randomized to ropivacaine (group R) or saline continuous infusion (placebo, group P) in a double-blind manner. Morphine consumption and side effects were prospectively collected until the 24th postoperative hour.  

Results: Sixty patients were included and 55 analyzed. There were no significant differences between the 2 groups regarding fracture types, delay before surgery (median [Q1–Q3]: 21.3 [14.5–29.4] vs. 20.8 [15.7–36.2] hours for groups R and P, respectively; P = 0.87) and catheter duration (47.5 [39.8–52.4] vs. 42.5 [32.1–50.5] hours, P = 0.29). Total morphine consumption was not significantly decreased in group R (5 [0–14] vs. 8 [4.5–11] mg, P = 0.3) and pain scores were similar (mean ± SD; VAS 29 ± 15 vs. 33 ± 13, P = 0.3). We observed a significant reduction in morphine adverse effects (31% versus 69% for groups R and P, respectively; P < 0.01), mainly nausea (31% versus 55%, P = 0.05). One morphine side effect could be avoided for every 5 patients treated.  

Conclusion: Preoperative continuous femoral blockades using ropivacaine reduce morphine side effects (mainly nausea) in hip-fracture patients without reducing morphine consumption.  

© 2015 Société française d’anesthésie et de réanimation (Sfar). Published by Elsevier Masson SAS. All rights reserved.

1. Introduction

Hip fractures are very common, with an incidence of around 1.6 million cases/year worldwide [1]. This high incidence is expected to rapidly increase in the coming decades, driven by population aging [2,3]. Hip-fracture patients are in severe pain upon arrival at the emergency department (ED) [4,5]. Effective pain management is thus a primary goal and should be continued throughout the perioperative period [5]. Indeed, patients who experience greater pain are at a higher risk for delirium, prolonged hospital stays and poorer health-related quality of life [6]. Pain management is usually based on systemic opioids that have many side effects [7], particularly among frail, elderly populations [8,9]. A possible alternative for the latter is regional analgesia [6,10].  

Femoral nerve blocks have been proposed for acute pain control in hip surgery [5]. The literature concerning this block is limited to a few descriptive studies and fewer randomized studies, where it is used as a single shot analgesia in the preoperative period [6,11,12] or as a single shot and/or continuous blockade in the postoperative period [13–15]. In these studies, femoral blockades appear to reduce morphine consumption and/or side effects. However, the delay for surgery may be prolonged in hip-fracture patients [16].
and a single shot block (which lasts for only a few hours) may be insufficient for patients who must wait more than 24 hours for their surgery. The use of a continuous femoral blockade on ED admission and prolonged to the postoperative period may thus reduce morphine consumption and side effects in these patients.

This randomized, double-blind, placebo-controlled study was performed in hip-fracture patients to compare morphine consumption and adverse event rates (from ED admission to 24 hours postoperatively) associated with continuous femoral blockades with those of a single shot femoral block.

2. Methods

We conducted this prospective, randomized, double-blinded, placebo-controlled study in a single centre, the Angers University Hospital (a tertiary university hospital), in France. The study was approved by the local ethics committee (“Comité de protection des personnes Ouest II”) and was conducted in accordance with the Declaration of Helsinki. All patients gave and signed an informed consent form. The study was registered at www.clinicaltrials.gov (NCT01052974).

2.1. Patients

Between March 2009 and April 2010, all patients admitted to the ED of the Angers University Hospital with a clinical suspicion of hip fracture (before the X-ray) were eligible and screened, provided one of the study investigators was available. The inclusion criteria were the ability to provide a written informed consent and a mini-mental test score (MMS) [17] higher than 16/30, as required by the local ethics committee for obtaining a valid “informed consent”. Exclusion criteria were: patient refusal, any contraindications for regional analgesia (i.e., treatment with clopidogrel or anticoagulation therapy, local infection at the puncture site, history of homolateral vascular surgery), known allergy to local anesthetic medications, severe renal or hepatic failure, regular narcotic use and use of class III antiarrhythmic drugs.

2.2. Study design

Patients were screened and included in the ED just after their admission. They were then transferred to the emergency theatre recovery room, which is located inside the ED. A femoral perineural catheter was inserted by one of the study investigators under sonographic guidance and/or neurostimulation (using a final current intensity of less than 0.8 mA) under aseptic conditions. Thirty minutes after the injection of 20 mL of lidocaine 20 mg/mL with adrenaline 0.0125 mg/mL, the catheter position was verified by a cold test before performing a hip X-ray. Regional analgesia was expected to reduce the pain linked to patient mobilization for the X-ray, justifying the insertion of a perineural catheter in the placebo group.

Patients were then randomized in two parallel groups (the ropivacaine group [R] or the placebo group [P]) with a 1:1 allocation ratio, using a randomization list electronically generated by the independent statistician. The randomization list was kept in the possession of the independent research pharmacy that prepared the study medications. Patients were secondarily excluded in case of absence of hip fracture when X-rayed.

The perineural catheters for patients in the R group were perfused with ropivacaine 2 mg/mL (Naropeine®, AstraZeneca Polybag®, France) at a constant rate of 8 mL/h, using an elastomeric pump of 400 mL capacity (Easyypump®, B. Braun, France). In the P group, catheters were similarly perfused, using a saline solution. These perfusions were prepared and initiated by a research nurse who was not involved in patient care following the lidocaine bolus. The patient and all the staff involved in his/her care or in data collection were blinded to the solution used. Treatment was administered for a maximum of 4 days preoperatively and for 24 hours postoperatively.

The study drug was stopped and catheters removed in case of perioperative complications related to femoral catheters (i.e. signs of overdose of local anaesthetic drugs, ineffective analgesia after a cold test, catheter displacement, catheter puncture site inflammation), a delay of more than 4 days before surgery or hospitalization in intensive care.

2.3. Anaesthesia and analgesia protocols

Surgery was performed under standardized general anaesthesia. For induction, 0.15 mg/kg of sufentanil, 1 mg/kg of propofol (or 0.2 mg/kg of etomidate for patients > 70 years old) and atracurium as necessary were used. Anaesthesia maintenance and sufentanil reinjections were left at the discretion of the anaesthetist in charge. Paracetamol was administered before the end of surgery and intravenous morphine titration was performed in the postoperative period according to a written protocol (i.e., a 2 mg bolus every 5 min for patients aged < 80 and 1 mg every 5 min for patients > 80 years old, until Visual Analog Scales [VAS] for pain were < 30/100).

In addition, patients received a standardized analgesia protocol (preoperatively and later in the ward) consisting of the systematic administration of 15 mg/kg intravenous paracetamol every 6 hours and 0.1 mg/kg of subcutaneous morphine if VASs were > 30/100.

2.4. Study parameters

Demographic, clinical and biological characteristics were recorded. The type of fracture (extra or intracapsular), surgery information (type, delay and duration) and the doses of anaesthetic drugs were recorded. Pain evaluation assessed via VASs, morphine consumption and the presence of morphine-related adverse effects (nausea, vomiting, pruritus, respiratory depression, urine retention) were prospectively collected every 6 hours and after each patient’s mobilization (i.e. standing up, X-ray, physiotherapy…). Nausea and/or vomiting were treated using intravenous ondansetron (Zophren®, GlaxoSmithKline, France). Respiratory depression was defined as a respiratory rate of less than 10/min, and was treated by close surveillance together with naloxone (Narcion®, SERR, France), if necessary. Urine retention was recorded only in case of bladder catheterization. We recorded these adverse events when they required treatment, and, for analysis, pooled all these “clinically relevant” events together.

Finally, mortality was assessed at 1 and 6 months.

2.5. Statistical analysis

Data were analysed using Stata version 12.1 (StataCorp LP, Texas, USA). Data are presented as medians [Q1–Q3] or means (SD) as appropriate for continuous variables, and as percentages for categorical variables.

We hypothesized that continuous femoral blockades using ropivacaine would reduce morphine consumption and morphine side effects during the pre- and postoperative periods (i.e. until the 24th postoperative hour). The primary endpoints were total morphine consumption from ED admission until 24 hours post-surgery and the prevalence of morphine side effects during the same period, because lowering the rate of side effects is the primary goal of reducing morphine consumption. Secondary endpoints were median pain scores during this period, as well as mortality during hospitalization and at 1 and 6 months.
To detect an effect-size of 1 on total morphine consumption and morphine side effects, we estimated that the sample size necessary to show a statistical difference with a power of 90% and an alpha risk of 2.5% (bonferroni adjustment to obtain a global alpha risk of 5% with two primary endpoints) was 50 patients (25 per group). We decided to include 60 patients (30 per group) to compensate for the post randomization exclusion of patients.

Due to non-normal data distributions, comparisons between the two groups (R and P) were made using a Mann-Whitney test for continuous variables and a Fisher’s exact test for categorical ones. Analysis was performed according to a modified intention to treat design (mITT): patients who had protocol violations (receiving ropivacaine boluses instead of lidocaine [n = 2]) or who did not have hip fractures (n = 3) were not included in the analysis (Fig. 1). However, patients for whom the catheter had been removed before the end of the study (i.e. the 24th postoperative hour) were taken into account in the analysis.

3. Results

3.1. Demographic data

From March 2009 to April 2010, among the 342 patients admitted with a clinical suspicion of hip fracture, 60 were included and randomized. Among these 60 patients, five were subsequently excluded (3 because of absence of hip fracture when X-rayed [one had a fracture of the acetabulum, one had hip arthritis, and the remaining patient had chronic pain and a depressive syndrome without a fracture] and 2 because of protocol violations during the initial perineural blockade [use of ropivacaine instead of lidocaine]). Fig. 1 depicts the flow chart for the study.

Demographic data for the 55 patients (the mean age was 82 [11] years old; 46 [84%] patients were women) are presented in Table 1. There were no significant differences between the 2 groups for patient characteristics, fracture and surgery type, delay before surgery, catheter duration and mobilization. The median delay between admission and surgery was 21 [15–31] hours for the entire study population.

3.2. Perineural catheter

A perineural catheter was successfully inserted in all patients. However, the catheter was removed before 24 hours post-surgery in 7 (13%) patients: 5 in group P and 2 in group R. These catheters were removed before surgery in 2 cases (2 patients in group P, 11 and 24 hours after insertion), during surgery in 3 cases (2 in group P and 1 in group R), and during mobilization in the postoperative period in 2 cases (42 and 52 hours after insertion, one in each group). The median catheter duration was 24 [16–42] hours for these 7 patients and 47 [38–51] hours for all patients.

Table 1: Study population characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 29)</th>
<th>Ropivacaine (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>80.1 [12.0]</td>
<td>85.0 [10.3]</td>
</tr>
<tr>
<td>Female</td>
<td>24 (83)</td>
<td>22 (85)</td>
</tr>
<tr>
<td>ASA class 3–4</td>
<td>9 (31)</td>
<td>6 (23)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.6 [13.4]</td>
<td>60.9 [13.0]</td>
</tr>
<tr>
<td>Fracture type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>15 (52)</td>
<td>18 (69)</td>
</tr>
<tr>
<td>I</td>
<td>14 (48)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>Surgery type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FP</td>
<td>12 (41)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>DHS</td>
<td>7 (24)</td>
<td>12 (46)</td>
</tr>
<tr>
<td>PFNA</td>
<td>9 (31)</td>
<td>6 (23)</td>
</tr>
<tr>
<td>THP</td>
<td>1 (4)</td>
<td>0</td>
</tr>
<tr>
<td>Delay before surgery (h)</td>
<td>20.8 [15.7–36.2]</td>
<td>21.3 [14.5–29.4]</td>
</tr>
<tr>
<td>Catheter duration (h)</td>
<td>42.5 [32.1–50.5]</td>
<td>47.5 [39.8–52.4]</td>
</tr>
<tr>
<td>Mobilizations (n/patient)</td>
<td>4 [2.5–7]</td>
<td>5 [3–6.3]</td>
</tr>
</tbody>
</table>

Data are presented as means (SD), medians [Q1–Q3] or numbers (%); ASA: American Society of Anesthesiologists physical status; MMS: mini-mental score; I: intracapsular; E: extracapsular; FP: femoral prosthesis; DHS: dynamic hip screw; PFNA: proximal femoral nail antrotation; THP: total hip prosthesis.
complication was observed during catheter insertion or during follow up.

3.3. Pain assessment

Fig. 2 shows pain assessment using VASs during catheter perfusion. There was a significant decrease in pain scores after catheter insertion (and lidocaine bolus) in each group (VAS 50 [30–80] versus 23 [0–40] for group R, \( P = 0.003 \) and 50 [30–60] versus 20 [5–45] for group P, \( P < 0.001 \)). There was no significant difference between the two groups at any point in time, despite a tendency for lower pain scores in group R versus P.

3.4. Total morphine consumption

Total morphine consumption (i.e., from ED admission to the 24th postoperative hour) was lower in group R compared to group P, without reaching statistical significance (median 5 [0–14] versus 8 [4.5–11] mg, \( P = 0.3 \) (Fig. 3). The mean difference in morphine consumption between groups R and P, adjusted for the main confounding factors, was −4.8 [95% CI: −12.6–2.9] mg. Preoperative morphine consumption in the 33 patients with extracapsular fractures was significantly reduced in group R compared to group P (median 0 [0–2.8] mg versus 4 [1–6] mg, \( n = 0.03 \)).
Table 2
Main outcomes: total morphine consumption, pain and side effects.

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=29)</th>
<th>Ropivacaine (n=26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative sufentanil (µg)</td>
<td>25 [22.5–35]</td>
<td>25 [20–30]</td>
<td>0.75</td>
</tr>
<tr>
<td>Total morphine (mg)</td>
<td>8 [4.5–11]</td>
<td>5 [0–14]</td>
<td>0.3</td>
</tr>
<tr>
<td>VAS (100)</td>
<td>33 ± 13</td>
<td>29 ± 15</td>
<td>0.3</td>
</tr>
<tr>
<td>Patients with one or more side effects</td>
<td>20 (69)</td>
<td>8 (31)</td>
<td>0.002</td>
</tr>
<tr>
<td>Nausea</td>
<td>17 (59)</td>
<td>8 (31)</td>
<td>0.03</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8 (28)</td>
<td>5 (19)</td>
<td>0.46</td>
</tr>
<tr>
<td>Agitation or mental confusion</td>
<td>6 (21)</td>
<td>5 (19)</td>
<td>0.89</td>
</tr>
<tr>
<td>Sedation</td>
<td>2 (7)</td>
<td>2 (8)</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>1 (4)</td>
<td>4 (15)</td>
<td>0.46</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1 (3)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Hospital length of stay (days)</td>
<td>9.5 [8–13.8]</td>
<td>11 [9–12.8]</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Data are presented as medians [Q1–Q3] or numbers (%); side effects were assessed every 6 hours until the 24th postoperative hour; one patient can have many side effects.

3.5. Side effects

We observed a significant decrease in morphine side effects in group R patients (Table 2), with side effects in only 8 (31%) compared to 20 (68%) patients in group P (P = 0.002). Among all the adverse effects collected, 68% were nausea and vomiting, 2% urinary retention, 6% sedation and respiratory depression, and 13% “other” (mainly agitation/confusion). Among these different side effects, nausea was the only one significantly reduced in the R group (Table 2). This reduction in morphine side effects is considerable: one side effect is avoided for every 5 (95% CI, 2 to 32) patients treated.

3.6. Patient outcomes

No deaths were observed during hospitalization or during the first postoperative month. Three (5.4%) patients deceased by month 6 (one from pulmonary embolism, one from gallbladder cancer and one from unknown causes). Two of them were treated with ropivacaine and one with placebo.

4. Discussion

Our study shows that a continuous femoral blockade reduces morphine side effects (mainly nausea) in the perioperative period in hip-fracture patients, without significantly reducing morphine consumption. To our knowledge, there is no other study aimed at evaluating continuous femoral blockades, inserted for pre- and postoperative pain relief, in hip-fracture patients. In these patients, multimodal pain management is recommended because inadequate pain relief contributes to delayed recovery [18]. Most published studies are focused on postoperative pain relief, using pharmacological management and/or nerve blockades [6]. In certain studies, nerve blockades have been associated with a reduction in pain compared with systemic opioids [19]. In addition, the use of nerve blockades reduces the incidence of delirium in hip fracture [6] or hip replacement surgery patients [20].

Concerning the preoperative period, very few data are available. Lugert et al. [21] report that femoral blockades at ED admission were superior to systemic opioids for pain control. Foss et al. [11] demonstrated that a fascia iliaca compartment blockade significantly reduces pain and morphine consumption. In our study, using femoral blockades, we also observed a significant decrease in VAS pain scores after the first bolus of lidocaine. However, regarding the whole perioperative period, we only observed a significant reduction in morphine side effects. This may be due to a lack of power concerning morphine consumption, since the observed morphine consumptions were relatively low in both groups. Indeed, for ethical reasons, patients in group P received a single shot femoral block with lidocaine, which should have reduced the need for morphine, especially during mobilization for the X-ray. A reduction in morphine side effects is usually found when a continuous blockade is used in the postoperative period [22]. Indeed, compared to intravenous patient-controlled analgesia with morphine and continuous epidural analgesia, continuous femoral blockade has been shown to reduce morphine side effects, without reducing pain relief or supplemental analgesia requirement, in hip surgery [19]. In addition, the reduction of morphine side effects may be the only benefit (and goal) of multimodal analgesia [23].

It must be emphasized that we did not use non-steroidal anti-inflammatory drugs, despite their known impact on the reduction of morphine adverse effects when used in combination with other treatments [24]. However, these drugs are also associated with an increased risk of renal insufficiency among the elderly [9,25] and it was not our standard of care to use them in this patient population. We only added paracetamol to morphine, which does not reduce morphine adverse effects [26,27].

Continuous femoral nerve blockades seem to have a greater effect on pain relief in extracapsular than in intracapsular fractures. This is in accordance with the observation of variable pain levels according to the type of hip surgery [28]. Femoral nerve blocks reduced morphine consumption in extracapsular femoral neck fractures [29]. This is probably due to anatomical considerations, with the femoral nerve being implicated in the sensitivity of the femoral diaphysis, whereas hip innervation involves the lateral cutaneous nerve of the thigh, the femoral nerve and the obturator nerve. All three of these nerves are derived from the lumbar plexus. Local anaesthetic drugs injected around the femoral nerve at the inguinal ligament are expected to spread proximally to the other two nerves. However, the latter may not be sufficient for obtaining analgesia of the proximal part of the femur [30], and may fail to be effective [31]. One may thus propose fascia iliaca continuous blockades for proximal fractures. However, frequent modifications of the psoas compartment render this route uncertain [31]. We may also propose a continuous psoas compartment block by a posterior approach. This block has been used successfully for postoperative analgesia after total hip arthroplasty [14]. Because patients have to lie on the lateral position to perform this block, it is not suitable for hip fractures [32]. Nonetheless, a recent study found that femoral blockades are more efficient than fascia iliaca blockades in hip-fracture patients with regards to morphine consumption [12]. Two meta-analyses also confirmed that femoral blockades are an efficient means for pain management among hip-fracture patients [6,10] and they are largely proposed [5]. The present study confirms the benefit of performing a femoral blockade upon arrival in the ED.

We observed no complications associated with femoral blockades, apart from catheter removal in 7 patients. In 5 patients, such removals were secondary to patient mobilization, either in the operating room or during physiotherapy. These removals should be avoided via improved communication with the medical/paramedical personnel. In the literature, certain authors have proposed tips on how to avoid catheter mobilization: subcutaneous catheter tunnelling [33,34], liquid adhesive/glue [35,36] or use of an anchoring device [37]; but without prospective, randomized evaluations. However, when these systems are used in combination, catheter retention rates are around 95% for periods longer than 60 hours [38]. One or many of these tips may have been used to aid the maintenance of continuous blockades for these patients, who often wait more than 24 hours before surgery [16].

Our study is mainly limited by its size. Despite an a priori calculation for the number of patients required, including a
Bonferroni correction for the double primary endpoint, our study is probably underpowered for the demonstration of statistically significant differences in terms of morphine consumption. Indeed, morphine consumption was quite low (probably thanks to the first lidocaine bolus, which significantly reduced pain in all patients). In addition, morphine consumption may have been low because it was administered by nurses (on patient demand) and not via a patient-controlled analgesia system. In fact, according to the morphine consumptions we observed, 46 patients per group would have been needed to demonstrate a significant difference with an alpha risk of 0.05 and a power of 0.9. However, despite relatively low numbers, we were able to observe an important reduction in morphine side effects, which is the most important goal when using multimodal analgesia [24] and which may be the only benefit of regional anaesthesia [19]. In addition, patients underwent different surgical procedures. However, we decided to include patients prior to X-ray verification of fractures so that all patients could have a perineural catheter insertion (i.e., less pain during mobilization for the X-ray), and were thus unable to stratify randomization on fracture types or on surgical procedures. Another limit may be the relatively high number of patients not included. Indeed, because of the need for informed consent and urgent inclusion, we excluded all patients with a mini–mental test score of less than 16, which is frequent in the concerned, elderly age group. However, in daily practice, these patients may benefit from a continuous blockade due to an increased risk for morphine side effects, such as delirium/confusion. Finally, we did not evaluate the effect of this technique on rehabilitation or functional outcomes; certain studies have found that multimodal analgesia and perioperative pain management allow for early functional re-education and better rehabilitation [18,38,39].

In conclusion, this study demonstrated that continuous femoral blockades using ropivacaine performed at ED admission reduce morphine side effects (mainly nausea), but not morphine consumption or pain intensity, during the perioperative period for hip-fraction patients. One morphine side effect could be avoided for every 5 patients treated.

Disclosure of interest

The authors declare that they have no competing interest. Funding: this work was solely supported by the Angers University Hospital.

Acknowledgements

We would like to thank Dr Elsa Parot-Schinkel for her assistance with the methodology of the study.

References


