Single shot spinal anesthesia with very low hyperbaric bupivacaine dose (3.75 mg) for hip fracture repair surgery in the elderly. A randomized, double blinded study☆

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Abstract

Purpose: Single shot spinal anesthesia is used worldwide for hip fracture repair surgery in the elderly. Arterial hypotension is a frequent adverse effect. We hypothesized that lowering local anesthetics dose could decrease the incidence of arterial hypotension, while maintaining quality of surgical anesthesia.

Methods: In a randomized double blinded study, 66 patients over the age of 65 years, with hip fracture needing surgical repair, were assigned to B0.5 group 7.5 mg hyperbaric bupivacaine 5 mg/ml (control group), and B0.25 group 3.75 mg hyperbaric bupivacaine 2.5 mg/ml (study group). Sensory and motor block level, and hemodynamic parameters including blood pressure, heart rate and vasopressor dose administration were registered, along with rescue anesthesia needs, the feasibility of surgery, its duration, and regression time of sensory anesthesia to T12.

Results: After exclusions, 61 patients were included in the final analysis. Arterial hypotension incidence was lower in the B0.25 group (at the 5, 10, and 15 min determinations), and a lower amount of vasopressor drugs was needed (mean accumulated ephedrine dose 1.6 mg vs. 8.7 mg in the B0.5 group, p < 0.002). Sensory block regression time to T12 was shorter in the B0.25 group, mean 78.6 ± 23.6 (95% CI 51.7–110.2) min vs. 125.5 ± 37.9 (95% CI 101.7–169.4) min in the B0.5 group, p = 0.033. All but one patient in the B0.25 group were operated on under the anesthetic procedure first intended. No rescue anesthesia was needed.


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PALABRAS CLAVE
Anestesia subaracnoidea; Efectos adversos; Anciano; Cirugía de la fractura de cadera; Bupivacaina

Conclusion: Lowering bupivacaine dose for single shot spinal anesthesia for hip fracture repair surgery in elderly patients was effective in decreasing the occurrence of arterial hypotension and vasopressor use, while intraoperative quality remained.

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Introduction

Hip fracture in the elderly due to osteopenia is one of the most prevalent trauma diseases in developed countries, with increasing frequency in the past years. The disease has been related with frailty that consists of a reduction in the physiological reserve due to environmental and genetic factors, in turn associated with delirium and falls. The rate of mortality after hip fracture is high, ranging from 5% to 8% during the first admission, and from 14% to 36% during the first year, being higher for some subtypes of patients, such as cardiac or the very old ones. In addition, costs incurred by hip fractures are high, in the range of those of myocardial infarction or strokes.

Surgery is indicated in most of the patients, and single shot spinal anesthesia (SSA) is the technique chosen most of the times. Although generally safe, complications or adverse events have been described and are frequent. Apart from technical-procedural failures, arterial hypotension due to decrease in the systemic vascular resistance as a consequence of sympathetic block is the most frequent hemodynamic complaint. Arterial hypotension is especially dangerous in the aged, and has been linked to age-related changes and concomitant diseases. The higher the sensory (analgesic) level and the older the patient, the most frequent the arterial hypotension is. These pathophysiological considerations, added to the reduced physiological and cardiac reserve, and together with the associated diseases that these patients suffer from, can lead to an imbalance in arterial pressure regulation. However, the long-term impact of intraoperative and immediate postoperative events is unclear, and needs additional investigation.

In order to avoid this complication, several preventive measures have been proposed, such as volume preload (hidration) before the block is established, or positioning...
the patient lying on the lateral decubitus during the anesthetic puncture. However, all these strategies have not been enough to avoid hypotensive episodes, albeit can minimize it.

With the same purpose, different regional anesthetic techniques and general anesthesia have been compared. Notwithstanding, there is not enough evidence about the risk/benefit superiority of these techniques when compared to SSA.

Our hypothesis was that for SSA in this type of surgery and patients, lower than normal doses of local anesthetics can be sufficient. Thus, by decreasing the dose, arterial hypotension incidence might be reduced, without decreasing the quality and safety required for hip fracture repair surgery in elderly patients.

Materials and methods

A randomized, double blinded study was designed. The study was approved by the Ethics Committee of the Hospital General Universitario de Valencia (Valencia, Spain). Informed consent was requested and obtained from all patients or relatives.

We included consecutive patients scheduled for hip fracture repair surgery by means of bone osteosynthesis that was operated on in the first 36 h after admission.

Exclusion criteria were contraindications of SSA, age under 65 years, coagulopathies, American Society of Anesthesiologists (ASA) physical status IV/V, moderate to severe aortic stenosis, non-corrected preoperative anemia, treatment with warfarin, and the use of osteosynthesis plates of more than 4 screws (i.e. meaning no diaphyseal fracture extension).

Patients were randomized by a computer-generated list of randomized numbers into two groups: B0.5 group (hyperbaric bupivacaine 5 mg/ml, control group) 7.5 mg, and B0.25 group (hyperbaric bupivacaine 2.5 mg/ml, study group) 3.75 mg. Both drugs were prepared in the same volume (1.5 ml) outside the operating room by an assistant not involved in the procedure. To prepare the 0.25% hyperbaric drug, 0.5% hyperbaric bupivacaine was diluted with saline. Density at room temperature of this dilution remained in the hyperbaric range (data not showed, mean density >1.009900 mg/ml). The anesthesiologist in the operating room was blinded for the drug selected. Allocation was by closed envelopes.

We registered patients’ characteristics (age, gender, weight, high, and ASA physical status), concomitant diseases, existing chronic arterial hypertension and antihypertensive drug therapy.

Patients were moved to the operating room without premedication. For bed-trolley shifting only small midazolam plus fentanyl boluses were administered. 500 ml lactated Ringer were perfused intravenously in the operating room. Monitoring consisted of non-invasive arterial pressure, continuous ECG and SaO2. Systolic (SAP), mean (MAP) diastolic (DAP) arterial pressures, and heart rate (HR) were registered at time 0 (basal, calculated as the mean of three measurements after entering the operating room) 2, 5, 10, 15, 20 and 30 min after spinal injection, and every 5 min throughout the procedure. Lumbar puncture was performed in the lateral decubitus on the operating side. A 25 G pencil point needle was used, by a median or paramedian access, at the L3–L4 or L2–L3 interspinous spaces. Spinal anesthesia procedure was standardized (bevel orientation to the dependent side, injection in 30's, no barbotage, local anesthetic at room temperature). Patients were turned supine in 1–2 min, and then shifted to the orthopedic table. All patients received supplementary oxygen 2–3 L/min by nasal prongs. A warm-air blanket was used to avoid hypothermia. If needed, 1–2 mg iv midazolam boluses were used for sedation, as were 5–20 mg iv ketamine if supplementary analgesia needed before surgery started. If spinal analgesia was not sufficient for surgery, large midazolam (up to 0.1 mg/kg), ketamine (up 1 mg/kg), and/or fentanyl (up to 1–2 μg/kg) iv doses were selected, and the case excluded from calculations. If the previous approach was not sufficient, total iv anesthesia with propofol and remifentanil was administered, and a laryngeal mask inserted.

The blinded anesthesiologist in the operating room performed the clinical evaluations. The time to achieve sensory block adequate for surgery, and its evolution at the times stated before and until T12 recovery, were registered. This was evaluated by pinprick with a plastic pin bilaterally. Motor block was evaluated by the surgeon by means of a “working score” that consisted of grading the quality of motor block for surgical conditions, and included both evaluation of the resistance to fracture closed reduction in the operating table, and the presence of limb movements at the start of the procedure. Motor blockade was scored as: (1) permits surgery and there are no limb movements (or minimal), (2) permits surgery, but there are moderate movements of the limbs, and (3) surgery is not possible due to limb movements or excessive muscle tension impeding or hampering bone fracture reduction. This score was selected instead of the standard Bromage score, because during the surgical procedures both legs were closely fixed to the operating table, and the patients were unable to move it.

Arterial hypotension was defined as a decrease in SAP in a single determination <90 mmHg, or <100 mmHg if the patient suffered from hypertensive disease or its basal SAP was >160 mmHg.

Use of vasopressor drugs was registered until 30 min, in two periods, as was the total accumulated dose administered. Ephedrine 5–10 mg boluses repeated every 3–5 min was the drug chosen for hypotension treatment. Phenylephrine 50–100 μg boluses was used if hypotension was associated with HR >110 bpm.

Data on rescue analgesia were registered, as were the time to sensory block regression to T12, and total duration of the surgical procedure (until the end of wound closure).

Blood losses and blood transfusion requirements were registered as well.

Patients were followed for the first year after the surgical procedure. Complications and death (if this was the case, together with the cause of death) were registered and grouped depending on the organ system affected.

The primary outcome was the decrease in the incidence of arterial hypotension. Secondary outcomes were use of vasopressors, surgery feasibility and duration of sensory block.
Statistical analysis

Sample size was calculated considering our preliminary data (pilot study), and data from other authors\(^1\)\(^2\) (incidence of arterial hypotension after SSA 40–60%). To obtain a 30% difference (incidence of systolic arterial pressure decrease in the study group with respect to the control group), with an alpha error of 0.8 and a probability of 0.05, 30 patients per group were needed. We decided to include 34 patients per group to balance for withdrawals.

Chi-square test (Fisher’s exact test or Pearson’s test), t-test for independent samples (with Levene’s test), and one-way analysis of variance (ANOVA, with the Bonferroni correction) were used as appropriate. The statistical package SPSS 11.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. Values of \(p < 0.05\) were considered significant.

Results

Fig. 1 shows the flow diagram for enrollment of the patients.

There were no differences between groups in the demographic data (Table 1), including type of surgery. There were no significant differences in the number of patients previously diagnosed of arterial hypertension, under angiotensin converting enzyme inhibitors (ACEI’s) therapy, neither in those treated with two or more antihypertensive drugs. No cases were canceled due to arterial hypertension. There were no patients excluded due to the use of rescue anesthetic drugs.

We found statistical differences in the hemodynamic determinations after spinal drug administration (Table 2). SAP significantly decreased in the B0.5 group vs. B0.25 at 5, 10 and 15 min measurements (\(p < 0.05\)) and MAP at 5 min measurement. Arterial pressures were significantly lower related to the basal determination in the B0.5 group.

Regarding the characteristics of the SSA, we found statistically significant differences in sensory block. The metameric sensory block level was higher in the B0.5 group, reaching significance at 10 min, 15 min, 20 min and 30 min after local anesthetic injection (Table 3). Motor blockade allowed surgery in all patients (scores 1 and 2 in the motor block score, no between group differences). Sensory block permitted surgery in all patients in the B0.5 group. Two patients in the B0.25 group needed additional iv analgesia (low dose midazolam and fentanyl) to surgery to be started, but not afterwards. One patient in the B0.25 group needed delayed iv analgesia due to prolonged surgery (low midazolam and ketamine doses, total duration 130 min).

The partial and accumulated amount of vasopressor drugs injected, as well as sensory block regression time, and surgical procedure duration are shown in Table 4.

Table 1 Characteristics of the patients included, type of surgery, arterial hypertension antecedents, ACEIs therapy, and number of antihypertensive drugs taken. B0.5 group: 0.5% hyperbaric bupivacaine; B0.25 group: 0.25% hyperbaric bupivacaine.

<table>
<thead>
<tr>
<th></th>
<th>B0.5 (n=30)</th>
<th>B0.25 (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>80.3 (8.4)</td>
<td>79.5 (6.5)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>8/22</td>
<td>6/25</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.6 (13.8)</td>
<td>60.0 (15.1)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.8 (13.8)</td>
<td>157.4 (9.3)</td>
</tr>
<tr>
<td>ASA (I/II/III)</td>
<td>1/11/18</td>
<td>1/7/23</td>
</tr>
<tr>
<td>Surgical procedure(^a)</td>
<td>21/1/3/5</td>
<td>19/4/4/4</td>
</tr>
<tr>
<td>Associated medical diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Hypotyroidism</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>AHT/ACEI’s</td>
<td>14/6</td>
<td>19/10</td>
</tr>
<tr>
<td>Number of antihypertensive drugs (1/2/3)</td>
<td>7/7/1</td>
<td>12/4/3</td>
</tr>
</tbody>
</table>

Data as mean (SD) or number of patients. \(p=ns.\)

Chi-square (Pearson’s or Fisher’s tests).

\(^a\) Type of surgical procedure: screw-plate/haemiprosthesis/ cannulated screws/other. AHT, chronic arterial hypertensive disease; ACEI’s, patients receiving angiotensin conversor enzyme inhibitors.

Figure 1 Study flowchart showing exclusion criteria and withdrawals, together with the causes.
Data from the patient’s evolution during the first year after surgery are depicted in Table 5.

Discussion

We have demonstrated lower incidence of arterial hypotension (both absolute and by the surrogate of vasopressor drug requirements) using 3.75 mg hyperbaric bupivacaine 2.5 mg/ml, instead of 7.5 mg hyperbaric bupivacaine 5 mg/ml. Clinical usefulness was maintained, with this dose and concentration, in old patients under hip fracture repair surgery.

Table 5 Postoperative survey at one year. B0.5 group: 0.5% hyperbaric bupivacaine; B0.25 group: 0.25% hyperbaric bupivacaine.

<table>
<thead>
<tr>
<th>Patients evaluated (male/female)</th>
<th>B0.5 (n = 30)</th>
<th>B0.25 (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No contact^a</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None detected</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Exitus^b</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cerebrovascular event</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Surgical wound infection</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonia-respiratory</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

^a Impossible telephone contact and/or living outside the public health system area.
^b Death due to any cause.

Table 4 Vasopressor doses, sensory block level duration, and surgical procedure duration. Drug dose in mg; time to block regression and surgery duration in minutes. B0.5 group: 0.5% hyperbaric bupivacaine; B0.25 group: 0.25% hyperbaric bupivacaine.

<table>
<thead>
<tr>
<th>Group</th>
<th>Ephedrine dose, 1st</th>
<th>Ephedrine dose, 2nd</th>
<th>Cumulated ephedrine dose</th>
<th>Sensory block regression to T12</th>
<th>Surgical procedure duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>B0.5</td>
<td>4.4 (3.4), 0–10</td>
<td>2.3 (3.6), 0–10</td>
<td>8.7 (6.8), 0–20</td>
<td>125.5 (37.9), 70–210</td>
<td>54.8 (11.9), 30–70</td>
</tr>
<tr>
<td>B0.25</td>
<td>0.6 (2.1), 0–10</td>
<td>0.3 (1.2), 0–5</td>
<td>1.6 (4.5), 0–20^</td>
<td>78.6 (23.6), 60–160^</td>
<td>59.3 (23.7), 30–115</td>
</tr>
</tbody>
</table>

Data as mean (SD), range.
^p = 0.002.
^" p = 0.033.
Apart from SSA, arterial hypotension development in the elderly under a surgical procedure can be related to chronic disease decomposition, and in the postoperative period – as a result – with postoperative cognitive disorder and delirium. SSA has arterial hypotension among their recognized adverse effects. To avoid it, some preventive measures have been recommended, such as technical modifications, fluid preload, or prophylactic administration of vasopressors, having all of them its own adverse effects or contraindications.

Several anesthetic techniques can be selected in order to obtain hemodynamic stability. In old patients general anesthesia is not a guarantee of cardiovascular balance. Continuous spinal anesthesia has been used in old patients, but slow incremental sensory block, more incidence of paresthesias, large gauge catheters inserted into the dural sac, are among the drawbacks of this technique. Moreover, some studies reported that the total local anesthetic dose administered is almost the same as in the SSA, with no hemodynamic advantages and additional technical difficulties. Incremental epidural anesthesia has been related with low quality sensory and motor block, and time required to start surgery is longer. In addition, the total local anesthetic volume is higher, and thus the possibility of systemic toxicity. However it remains an option. Combined spinal–epidural anesthesia has disadvantages of being most time consuming, and that in most cases it is unnecessary to use the epidural catheter due to the short duration of surgery. In this kind of surgery, postoperative pain is usually well controlled with NSAIDs and systemic opiates.

Rapid infusion of fluids and prophylactic vasopressors have been proposed as well, but these could have deleterious effects in patients with comorbidities as cardiac diseases or chronic arterial hypertension. A high proportion of old patients sustaining hip fractures have clinical or subclinical cardiac diseases, and opposed to the usual relationship, low body mass index is related with more cardiac events. Ephedrine and the other vasopressors could cause hypertensive crises and tachycardia, as well as coronary vasospasm. Compared with general anesthesia, regional anesthesia, including SSA, has been related with lower incidence of severe complications and mortality as showed in several metaanalyses. Postoperative cognitive disorders and delirium are frequent in in-hospital elderly patients, and increase when submitted to surgical procedures and other circumstances including drugs and general anesthesia.

The use of very low doses of local anesthetics in the SSA technique, as we propose, can prevent or minimize arterial hypotension. General toxicity does not exist. Lower requirements of ephedrine or atropine avoid pro-delirium drugs. This can be extended to the very low request of intraoperative sedatives or opiates.

Asehnoune et al. observed that MAP was more stable in 50 young ambulatory surgery patients after very low SSA bupivacaine doses (4 mg plus 20 μg fentanyl) vs. low (7.5 mg) bupivacaine dose, as defined by authors. Cardiac output was well maintained in both groups.

Spinal injection of 7.5 mg hyperbaric bupivacaine 5 mg/ml posed a high number of patients at risk of arterial hypotension, that this was more intense and of longer duration, as showed by the direct determinations and by vasopressor needs and number of boluses, the time the drugs were needed (in general after a few minutes after block instansion, Table 4), and the accumulated vasopressor drug dosing.

We wish to underline that patients under antihypertensive treatment with ACEIs can suffer from refractory hypotension when under SSA, and this did not occur in our patient population in the low dose group.

We have found only three similar studies in old patients, regarding the total bupivacaine dose. In all three, lipolytic opiates were added to the local anesthetic, and recommended bupivacaine dose was higher than ours. The opiate can increase sympathetic block and can produce respiratory depression due to rostral migration in elderly patients.

Our study has some limitations. The number of patients included could be not sufficient, but hemodynamic changes observed are consistent and suggest that our results can be generalized to most patients of these characteristics and for this type of surgery. The results have been obtained from patients over the age of 65 years, operated on from hip fracture repair and cannot be extrapolated to younger people or other types of surgical procedures, and/or with different duration. Hemodynamic parameters were obtained from noninvasive measurements, and these cannot directly correlate with cardiac output and tissue oxygen transport. Evaluation of sensory block is difficult in some old patients and cannot be obtained from some of them accurately. Although re-diluting local anesthetics increases the hypobaric, this is not the case when diluting only one time hyperbaric bupivacaine with normal saline.

Several studies showed correlation between CSF volume and the cephalad level reached by the local anesthetic (sensory and sympathetic block). Thus, there will be great variability in the CSF volume, the sensory level being not predictable in a particular patient in response to a fixed dose. This suggests that efforts in using fixed – low – doses to minimize vasodilatation after SSA could induce technical failures in a proportion of patients.

In the same way, in – for instance – teaching hospitals with longer lasting surgeries, perhaps a slight increase in the suggested doses will be needed (around 4–5 mg with the same dilution, authors suggestion, unpublished data), as will be if long plates for bone fixation were required. However this is the usual practice of the authors but has not been formally studied.

In our patients needing some sedation-analgesia at the start of the procedure, this was due to slight painful sensation on the non-operative leg due to traction in the orthopedic table, that was short lasting. In our experience, it is important to restate the patient supine rapidly in order to avoid excessive unilaterality of the block.

It is possible to add low amounts of lipolytic opiates, as this prolongs block duration without affecting hemodynamic stability (provided low doses of local anesthetics have been used): but this has not yet been proven with very low doses of bupivacaine, and in old patients as in our study. Additional investigations are warranted addressing these questions.

Because of the advantages of the described procedure, its indication in severely ill patients needing surgery can be suggested. It has been proposed to increase
"aggressive" therapy in these patients, in part due to the great prevalence of the disease and associated surgery. In addition, despite an elevated early and delayed mortality, this old patients group should be managed adequately during surgery, but in the postoperative period as well, applying several evidence-based interventions including analgesia, nutritional status care, early mobilization, and inclusion in rehabilitation programs in a multidisciplinary fashion. All these might improve the short- and medium-term prognosis and quality of life.

We conclude that 3.75 mg hyperbaric bupivacaine 2.5 mg/ml for SSA in patients sustaining hip fracture needing surgery is sufficient for this type of surgical procedure, and presents lower hemodynamic adverse effects compared to the same volume of bupivacaine 5 mg/ml.

Conflict of interest

The authors declare no conflict of interest.

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References