PRACA ORYGINALNA

Comparison of spinal anaesthesia with 0.75% ropivacaine and 0.5% bupivacaine for elective caesarean section

Porównanie znieczulenia podpajęczynówkowego z 0,75% ropiwakainą i 0,5% bupiwakainą do planowego cięcia cesarskiego

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ABSTRACT

BACKGROUND

The aim of this study was to compare clinical efficacy and safety of hyperbaric ropivacaine and hyperbaric bupivacaine for spinal anaesthesia for elective cesarean section.

METHODS

A prospective, randomized study was performed in 75 patients with low preoperative risk, scheduled for elective caesarean section, randomly allocated in two groups (ropivacaine – 36 patients, bupivacaine – 39 patients). Spinal anaesthesia was performed in sedentary position, at the L3/L4 level and 2 mls of 0.75% hyperbaric ropivacaine or 0.5% hyperbaric bupivacaine was administered. The influence of the blockade on the function of the cardiovascular and respiratory system, the need for additional medications, side-effects, the quality of the blockade as well as spread and regression were assessed. The evaluation of anaesthesia was performed by both the patients and the surgeons. All data underwent statistical analysis. Statistical significance was noted if p value was below 0,05.

RESULTS

Haemodynamic parameters and respiratory function were similiar in both groups. There were no differences between groups regarding side-effects, the need for additional medication and the quality of the blockade. Spread and regression of motor and sensory blockade and their duration was similar. The evaluation of the anaesthesia by the patients and the surgeons was similar. Both local anaesthetic agents provided sufficient, safe and satisfactory spinal anaesthesia for elective caesarean section.

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Ann.Acad.Med.Siles. 2009, 63, 6, 15-22

ISSN 0208-5607

CONCLUSIONS
Spinal administration of 2 ml of plain hyperbaric 0,75% ropivacaine and hyperbaric 0,5% bupivacaine provides safe anaesthesia for caesarean section, satisfactory analgesia and good surgical conditions. Ropivacaine offers no significant advantage over bupivacaine during spinal anaesthesia for elective caesarean section.

KEY WORDS
bupivacaine, cesarean section, ropivacaine, spinal anaesthesia.

STRESZCZENIE

WSTĘP
Celem badania było porównanie użyteczności klinicznej i bezpieczeństwa hiperbarycznej ropiwakainy i hiperbarycznej bupiwakainy podczas znieczulenia podpajęczynówkowego do planowego cięcia cesarskiego.

MATERIAŁ I METODY
Prospektywne, randomizowane badanie zostało przeprowadzone u 75 pacjentek niskiego ryzyka operacyjnego, zakwalifikowanych do planowego cięcia cesarskiego, które zostały przydzielone losowo do dwóch grup (ropiwakaina, n=36, bupiwakaina, n=39). Znieczulenie podpajęczynówkowe zostało wykonane w pozycji siedzącej. Pacjentkom podano 2 ml hiperbarycznej ropiwakainy w stężeniu 0,75% lub 2 ml hiperbarycznej bupiwakainy w stężeniu 0,5% do przestrzeni podpajęczynówkowej na poziomie L3/L4. Oceniono wpływ blokady na funkcję układu krążenia i układu oddechowego, konieczność zastosowania dodatkowych leków, częstość objawów ubocznych związanych z blokadą, oraz jakość uzyskanej blokady. Znieczulenie zostało ocenione zarówno przez operatorów, jak i przez pacjentki. Dane poddano analizie statystycznej, a znamienność statystyczną przyjęto dla wartości współczynnika $p<0,05$.

WYNIKI
Parametry hemodynamiczne i funkcja układu oddechowego były zbliżone w obu badanych grupach. Nie stwierdzono żadnych istotnych różnic w zakresie częstości występowania objawów ubocznych, konieczności zastosowania dodatkowych leków, a także jakości i charakterystyki (rozprzestrzeniania się i regresji) uzyskanej blokady. Ocena znieczulenia z użyciem obu środków była zbliżona. Oba analgetyki miejscowe zapewniły wystarczającą i bezpieczną analgezję podpajęczynówkową do planowego cięcia cesarskiego.

WNIOSKI
Znieczulenie podpajęczynówkowe z użyciem 2 ml hiperbarycznej 0,75% ropiwakainy i hiperbarycznej 0,5% bupiwakainy zapewnia bezpieczne znieczulenie do cięcia cesarskiego, zadowalającą analgezję i dobre warunki operacyjne. Ropiwakaina nie wykazuje znaczącej przewagi nad bupiwakainą podczas planowego cięcia cesarskiego.

SŁOWA KLUCZOWE
bupiwakaina, ropiwakaina, cesarskie cięcie, znieczulenie podpajęczynówkowe.

INTRODUCTION

An increasing number of caesarean sections is performed worldwide. In such countries as Brazil, Chile or Mexico, these figures may be as high as 30 – 50% [1]. In the United States and UK caesarean section is performed to terminate 23% of all pregnancies and a steady increase by 1% each year is observed [1]. Spinal anaesthesia is probably the most popular technique of anaesthesia for caesarean section woldwide.

Ropivacaine is a popular local anaesthetic agent, not recommended for spinal anaesthesia by the manufacturer. It is however very easy to confirm that this agent is widely used for spinal anaesthesia [2-8]. Both hyperbaric and isobaric solutions were already investigated and ropivacaine was usually compared with bupivacaine and levobupivacaine. Due to the fact, that only isobaric ropivacaine is available on the market, glucose is usually added to achieve hyperbaric solutions [3, 4].

Ropivacaine is thought to be less toxic than bupivacaine for the central nervous and circulatory system [9, 10]. These properties are of particular importance during caesarean section and therefore the aim of this study was to establish whether plain hyperbaric ropivacaine is superior to bupivacaine for spinal anaesthesia during elective caesarean section when equipotent concentrations are used. The results of this study may also guide pharmaceutical companies, whether there is a need for a standard, spinal hyperbaric solution of ropivacaine.

METHODS

This prospective, single-blind study was performed in pregnant women scheduled for elective caesarean section. 75 ASA I or II patients were randomized in the anaesthetic room by the computer-generated random numbers to receive either 2 mls of hyperbaric plain 0.75% ropivacaine (n= 36, group R) or 2 mls of hyperbaric plain 0.5% bupivacaine (n=39, group B). The study was accepted by the local Ethical Committee and all patients signed informed consent to participate. Patients without contraindications for spinal anaesthesia were qualified when their age was between 18 and 40 years and their height was between 150 – 180 cm. Exclusion during the study was planned if general anaesthesia was needed. The patients were blinded to group assignment.

Patients in group B received standard hyperbaric solution of 0.5% bupivacaine (0,5% Marcaine Spinal Heavy, Astra-Zeneca, Sweden). Patients in group R received a solution prepared from standard isobaric solution of 1% ropivacaine (Naropin, Astra-Zeneca, Sweden). Hyperbaric 0.75% ropivacaine solution was obtained "ex tempore" by adding 1.6 ml of 40% dextrose and 0.4 ml of normal saline to 6 ml of 1% isobaric ropivacaine. From 8 mls of this solution, 2 mls were drawn and used to perform spinal anaesthesia.

All patients were administered 10 – 15 mL/kg of crystalloid solutions 30 minutes before the blockade. Spinal anaesthesia was performed in a sitting position at the L3-L4 level. Pencil-Point 26G spinal needle was used. After intrathecal injection, patients were positioned immediately on their back with the table tilted 15^{o} to the left side. Supplemental oxygen was administered via face mask before the delivery in all patients and also later if the oxygen saturation was lower than 93%.

Once the patient was returned to the supine position, sensation was assessed by ice-cold test. Sensory blockade was assessed as 0 - if there was a comparable feeling of cold in the upper extremity and the place of the planned surgical incision, 1 – when a feeling of cold was less and 2 – if there was no feeling of cold in the region of further surgical incision. During the procedure, this scale was modified as follows: 0 – significant pain, 1 – feeling of touch or minor discomfort and 2 – complete lack of sensation in the operated area. Surgical procedure was started 10 minutes following the spinal injection to allow for recording of observations. Repeated assessments of sensory blockade were made every minute during the first 10 minutes after spinal injection of the local anaesthetic and in 5-minute intervals during the procedure and after the procedure until the complete regression of the blockade was noted. Spread of the blockade up to the Th9 level was considered satisfactory for caesarean section.

Time required to achieve analgesia was counted from the moment when the anaesthetic agent was injected until the moment when surgical analgesia was obtained. Regression of the blockade was noted, when the patient regained a normal feeling of pain or cold (0

level of the sensory blockade). Time between the injection of the local anaesthetic and the full regression of the sensory blockade was regarded as the time of sensory blockade.
Motor blockade was assessed with the use of the Bromage scale in 5-minute intervals during the procedure, starting from the moment when local anaesthetic was injected intrathecally, until the complete regression of the motor blockade was noted (0 level in the Bromage scale). Time between the injection of the local anaesthetic and the full regression of the motor blockade was regarded as the time of motor blockade.
Parameters of the cardiovascular system (heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure) and saturation before anaesthesia and in the early postoperative period were analyzed. Measurements were made before the blockade and in the 5-minute intervals. In addition, Holter ECG monitoring (Aspel, HolCARD-24W) was used from the moment when the patient arrived in the operating theatre to register minimal and maximal heart rate in the whole observational period for each patient. Haemodynamic observation for the purpose of the study was terminated when the full regression of the blockade was noted.
Each newborn was assessed by the paediatrician with the use of the Apgar score – one minute, five minutes, and ten minutes after the delivery.
All patients received 1 mg of midazolam iv after delivery. Ephedrine was given intravenously when systolic blood pressure dropped below 80 mmHg and atropine was used if the heart rate dropped below 55 beats/min. In cases when the patient experienced minor pain, discomfort or required additional sedation, intravenous injection of ketamine 0.25 mg/kg was given. The use of all interventional drugs as well as the incidents of nausea and/or vomiting were noted.
Before the beginning of the study, power analysis for the duration of the sensory blockade was performed on the basis of the results of the first 20 patients studied (10 patients in each group). It was calculated that to detect 20% difference between groups it should be at least 30 patients studied in each group to achieve power>0.8 and significance level of 0.05.
Data are expressed as mean and standard deviation. Data were compared using t-test or Mann-Whitney test and the Wilcoxon test, when appropriate. Statistica 6.0 statistical software was used. For all calculations $p<0.05$ was considered statistically significant.

RESULTS

Patients in both study groups were not different regarding their initial demographic data (table 1). Mean time of the procedure was 50.5 ± 22.0 min. in group R and 52.7 ± 20.4 min. in group B. There were no exclusions during the study and no patients were converted to general anaesthesia. It was,however not possible to analyze Holter monitoring in all patients due to technical errors during recording – analysis was possible in 31 patients (86%) in group R and in 37 patients (95%) in group B.

Table 1. Demographic data.

	Group R (n=36)		Group B (n=39)	
Age (years)	25.4	± 4.4	27.3	± 4.6
Weight (kg)	79.5	± 13.6	76.2	± 12.8
Height (cm)	165.5	± 5.5	164.2	± 6.2
BMI	29.0	± 4.3	28.3	± 4.5

Haemodynamic parameters were similar in both groups before the intrathecal injection of the study drug and during the procedure (figure 1 and 2).
Mean minimal and maximal heart rate values were similar in patients receiving ropivacaine and bupivacaine. Mean minimal heart rate was 63.9 ± 10.1 beats/min. for group R and 63.5 ± 9.2 beats/min. for group B. Mean maximal heart rate was 113 ± 15 beats/min. for group R and 117 ± 16 beats/min. for group B. According to the study protocol, it was necessary to administer atropine due to bradycardia in two patients in group R (5.1%) and in one patient in group B (2.6%). Ephedrine was given due to the drop of systolic blood pressure in five patients in group R (13.9%) and in two patients in group B (5.1%). All differences were not statistically significant.
Four patients in group R (11.1%) and none in group B were given 0.25 mg/kg ketamine ($p=0.12$), but only in one case it was due to insufficient analgesia. Nausea and/or vomiting were registered in one patient in group R (2.8%) and in four patients in group B

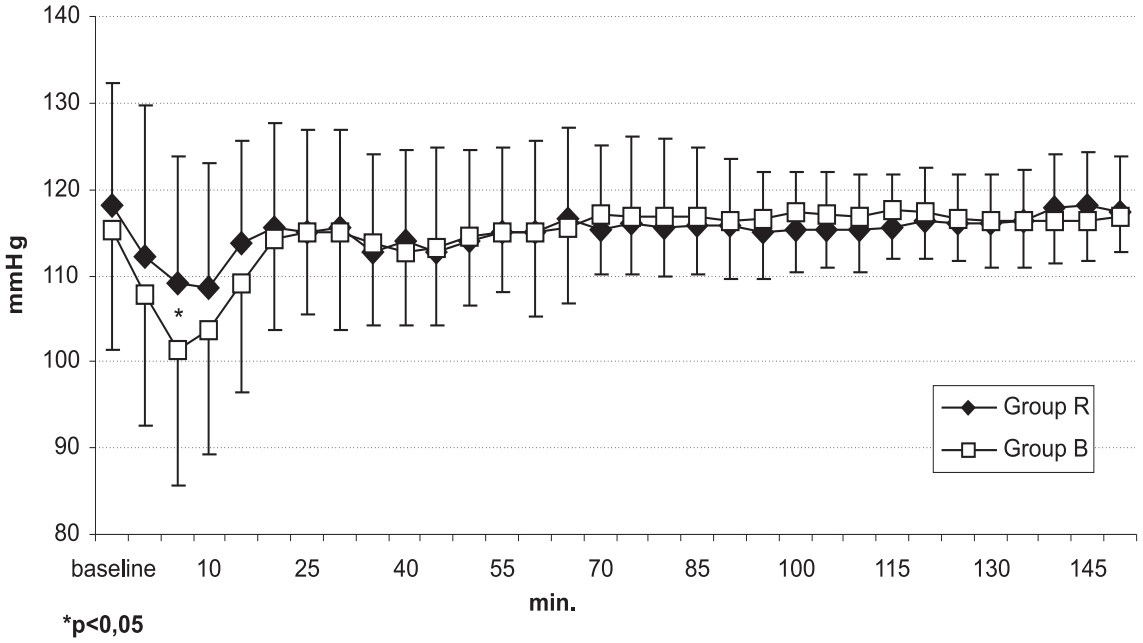

Figure 1. Values of systolic blood pressure.

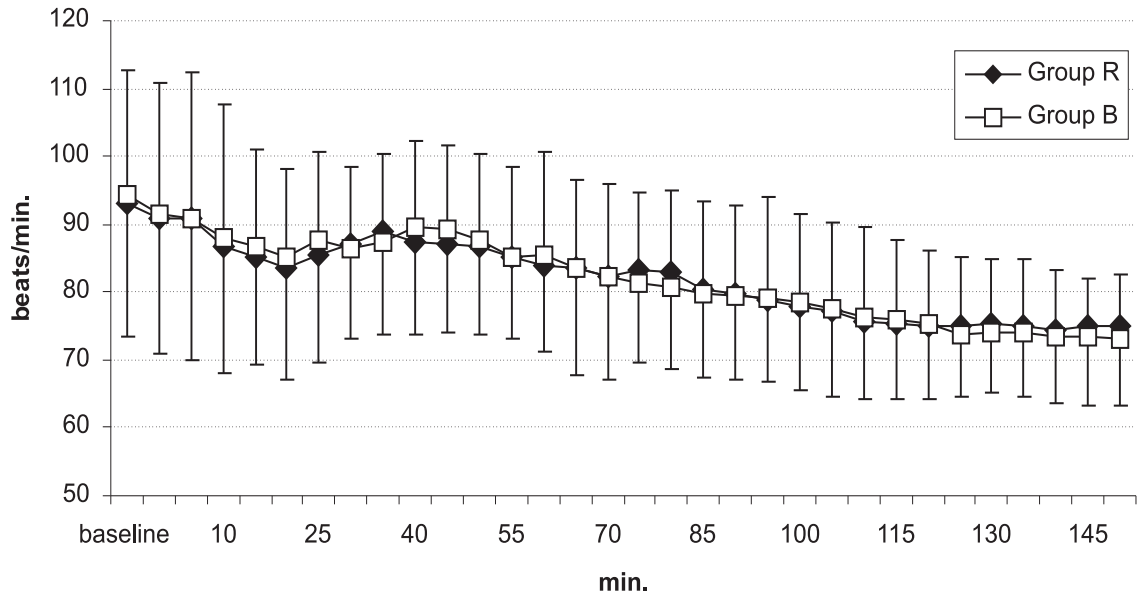

Figure 2. Values of heart rate.

(10.8%), but this difference was also not significant (p=0.24). Apgar score was found to be similar in both groups.

Time required to achieve full sensory blockade and the duration of the sensory blockade was similar in both groups. The same was also true for the motor blockade (table 2).

Spread and regression of the sensory and motor blockade was not significantly different in both study groups. Percentages of patients who achieved complete sensory and motor blockade in consecutive time points during the observational period are shown in figure 3 (for sensory blockade) and figure 4 (for motor blockade).

Table 2. Parameters of sensory and motor blockade.

	Group R (n=36)		Group B (n=39)	
Spread of sensory block (min.)	6.1	± 1.1 (5 – 9)	6.4	± 1.4 (5 – 10)
Duration of sensory block (min.)	129	± 29 (50 – 160)	130	± 24 (68 – 159)
Spread of motor block (min.)	10.4	± 2.2 (9 – 15)	11.2	± 2.6 (8 – 15)
Duration of motor block (min.)	79.2	± 12.5 (45 – 112)	78.4	± 16.6 (37 –105)

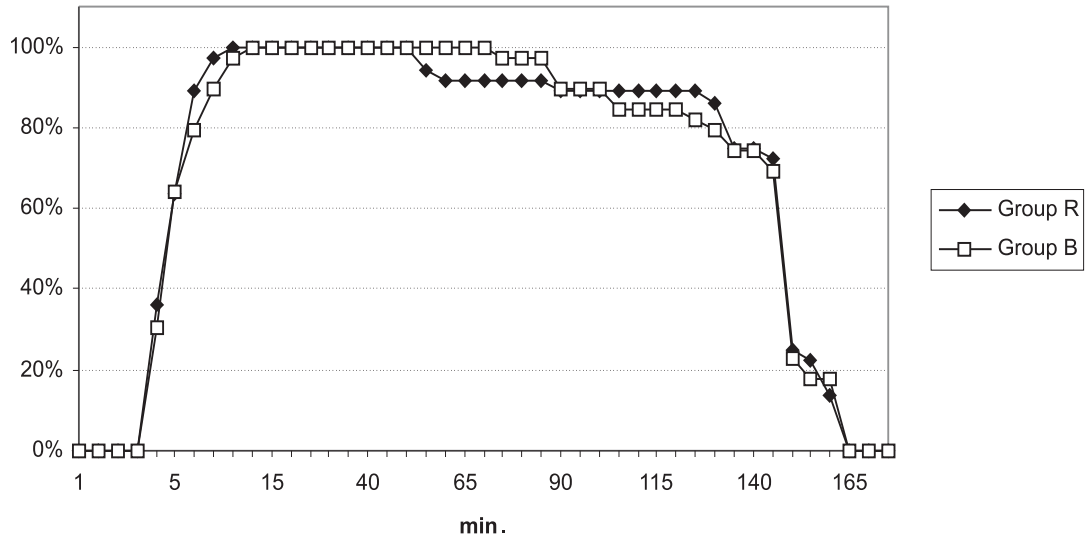

Figure 3. Percentage of patients who achieved complete sensory blockade (grade 2) during the observational period

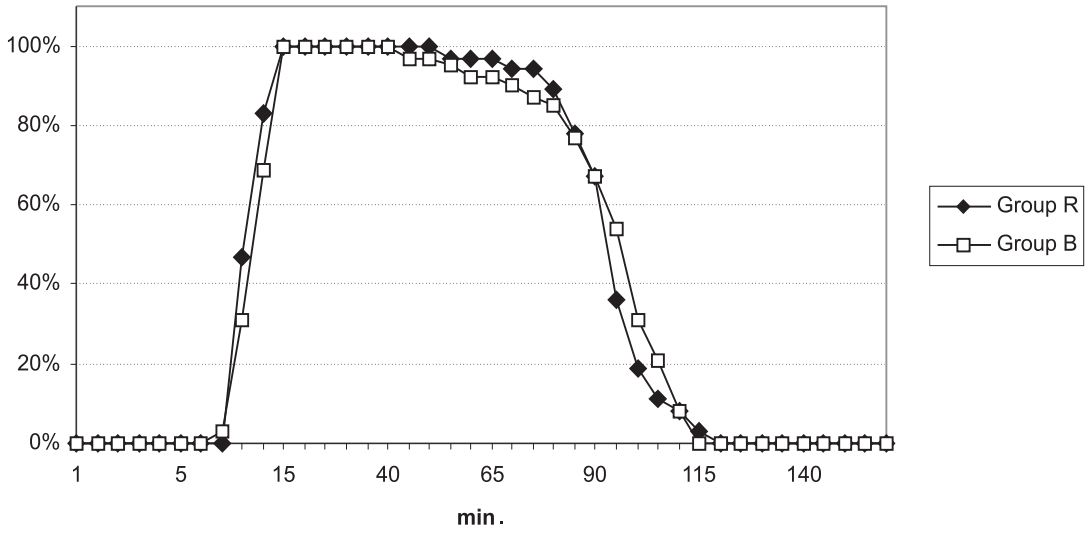

Figure 4. Percentage of patients who achieved complete motor blockade (grade 3) during the observational period.

DISCUSSION

Results of our study suggest that ropivacaine and bupivacaine are comparable when used to provide intrathecal anaesthesia for caesarean section. To be certain that this conclusion is correct, the "material and method" section of our study needs to be looked at.

The most important issue is whether the doses of ropivacaine and bupivacaine used in our study were comparable and the concentrations were equipotent in a setting of spinal anaesthesia. We compared 2 mls of 0.5% hyperbaric bupivacaine (10 mg) with 2 mls of 0.75% hyperbaric ropivacaine (15 mg). It is well known that ropivacaine is less potent than bupivacaine when identical concentrations are used [11-15]. Some authors state that 0.5% bupivacaine is equipotent to 0.75% ropivacaine, others suggest that a concentration of 0.75% is equal to 1% [12]. Gautier et al. [8] think that to achieve a comparable quality of regional anaesthesia, ropivacaine dose should be 50% higher than bupivacaine. Taking all these opinions into account, it seems that 10 mg of 0.5% bupivacaine is equipotent to 15 mg of 0.75 % ropivacaine.

The way the duration of the blockade is assessed is equally important for the conclusions about the comparability of the local anaesthetic agents. Calculating the time of the sensory blockade is not easy, because regression is gradual, usually slow and sometimes both the patient and the investigator are not sure whether the blockade is over or whether there is some residual block still observed. One could ask whether correct criteria for such assessment were used in our study.

Different solutions to this problem may be found in the literature. Most researchers think that blockade is over when analgesia is required to provide patient's comfort or a patient states that pain has reached a certain level on the Visual Analogue Scale (VAS). In our opinion a moment of complete regression of the blockade may not be associated with a perception of pain. Therefore, in our study we decided to register a complete regression of the blockade when there was a full perception of cold on the skin in the previously operated area. This may be a reason why the duration of a blockade in our study was considerably shorter in comparison with the data from the literature.

Interestingly, in our study 10% of patients in the ropivacaine group were given ketamine, while there were no such cases in patients receiving bupivacaine. Does this mean that average quality of the blockade was worse after ropivacaine? In our opinion, such conclusion cannot be justified, because – as it was mentioned in a "results" section - only in one case administration of ketamine was due to insufficient analgesia. All other cases were due to the fact that ketamine was included in our protocol for the situations when additional sedation was needed. Sedation "on demand" is quite popular during regional anaesthesia. The use of propofol for this purpose was described in a paper published by Whiteside et al. [10] – the authors found that 22 patients asked for sedation even if a blockade provided sufficient analgesia.

When subarachnoid "heavy" 5% lignocaine was banned, many researchers tried to prove that bupivacaine is not the only local anaesthetic for central blockade during caesarean section. Most authors compared bupivacaine with ropivacaine [2, 6, 7, 16], ropivacaine with levobupivacaine [17, 18] or bupivacaine with both ropivacaine and levobupivacaine [3, 19, 20]. There are studies comparing the effectiveness of various concentrations of the same agent – bupivacaine [21] and studies comparing hyperbaric and isobaric bupivacaine solutions of bupivacaine [21-23]. It is difficult to compare the results of these studies with our results due to various aims of these studies, wide range of dosing and various concentration, barites and volumes of the local anaesthetic agents.

A few studies are, however, quite similar to our study. Gautier et al. [8] compared spinal ropivacaine and bupivacaine for caesarean section. In this study concentration of ropivacaine was 50% higher than bupivacaine but the doses (and concentrations) were lower and 2.5 μg of sufentanyl was added to this solution [8]. Bupivacaine provided longer duration and more profound blockade.

Probably the most comparable study that could be found in the literature was published by Chung et al. [2]. The authors compared intrathecal administration of plain 12 mg of 0.5% hyperbaric bupivacaine solution with plain 18 mg 0.5% hyperbaric ropivacaine solution in patients scheduled for elective caesarean section. Duration of sensory blockade was significantly shorter after ropivacaine

(163 ± 20 min. vs 189 ± 28 min.). In our study duration of sensory blockade was not only comparable but also much shorter in both study groups (129 ± 29 min. vs 130 ± 23 min., respectively). This could be explained by the fact that much lower volumes and doses of both local anaesthetics were used in our study and the equipotent concentrations were compared.

In conclusion, spinal administration of plain hyperbaric ropivacaine has no advantage over plain hyperbaric bupivacaine for elective caesarean section. We therefore conclude, that a routine use of spinal ropivacaine cannot be recommended in this group of patients.

SOURCE OF SUPPORT

This work was self-funded. Presented in a form of an abstract during the Euroanaesthesia 2006 Meeting in Madrid.

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