Comparison of plain and hyperbaric solutions of ropivacaine for spinal anaesthesia


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Background. Preliminary work has shown that ropivacaine provides spinal anaesthesia of shorter duration than bupivacaine, and may be of particular use in the day-case setting. However, there are few data comparing the actions of plain and hyperbaric solutions of this drug.

Methods. Forty ASA grade I–II patients undergoing elective perineal surgery under spinal anaesthesia were randomized to receive 3 ml ropivacaine 5 mg ml\(^{-1}\), either in plain solution or with glucose 50 mg ml\(^{-1}\). The extent and duration of sensory and motor block, pulse rate, blood pressure, and time to mobilization were recorded.

Results. Two patients (one per group) were withdrawn because of total block failure. There were significant differences in median time to onset of sensory block at T10 (plain 10 min; hyperbaric 5 min; \(P<0.01\)), median maximum extent (plain T8; hyperbaric T4; \(P<0.05\)), and median duration of sensory block at T10 (plain 25 min; hyperbaric 115 min; \(P<0.001\)). However, median times to complete regression of both sensory (270 vs 240 min; \(P<0.05\)) and motor (180 vs 120 min; \(P<0.001\)) block were longer in the plain group. Patients therefore mobilized sooner in the hyperbaric group (218 [\(n=16\)] vs 286 min [\(n=17\]; \(P<0.01\]). All the hyperbaric blocks were adequate for surgery, but three patients receiving plain ropivacaine required general anaesthesia.

Conclusion. Addition of glucose 50 mg ml\(^{-1}\) to ropivacaine 5 mg ml\(^{-1}\) increases the speed of onset, block reliability, duration of useful block for perineal surgery, and speed of recovery. Plain solutions are less reliable for surgery above a dermatomal level of L1.


Keywords: anaesthetics local, ropivacaine; anaesthetic techniques, subarachnoid

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Ropivacaine has been studied relatively little in intrathecal use. Early studies comparing two doses (15 vs 22.5 mg) of glucose-free (plain) ropivacaine found that intrathecal injection produced a sensory block of very variable extent, a proportion of the patients in both studies requiring general anaesthesia because of inadequate distribution of block, mainly, but not exclusively, in the patients receiving 15 mg.\(^{12}\) Since then, other studies have shown that plain ropivacaine can produce satisfactory analgesia for surgery,\(^{3-5}\) but doubt remains about its reliability, as is the case with other agents in plain solution.\(^{6,7}\) However, two recent studies of hyperbaric ropivacaine (15 mg) have shown that it produces predictable and reliable anaesthesia for surgery,\(^{8,9}\) and with a duration that is shorter than that of bupivacaine. The aim of this prospective, randomized, double-blinded study was to make a direct comparison between plain and hyperbaric solutions of ropivacaine in patients receiving subarachnoid block for elective surgery.

Methods
Forty ASA grade I–II patients who were to undergo elective perineal (gynaecological or urological) surgery under spinal anaesthesia gave written informed consent to take part in the study, which was approved by the local research ethics board. The Board of Management and Trustees of the British Journal of Anaesthesia 2004

Declaration of interest. Dr Fettes and Dr Luck have had salaries paid by AstraZeneca. Professor Wildsmith has also received consultancy payments from AstraZeneca. AstraZeneca provided the ropivacaine for the study.
committee. Patients were pre-medicated with oral temazepam 0–20 mg at the discretion of the responsible clinical anaesthetist and, in the anaesthetic room, monitoring with pulse oximetry, ECG, and non-invasive blood pressure was initiated, and venous access secured.

Lumbar puncture was performed with a 25-swg Whitacre needle using a midline approach at the second or third lumbar interspace with the patient in the left lateral position. The patients were randomized (shuffled, then numbered, opaque envelopes) to receive 3 ml ropivacaine 5 mg ml⁻¹ (15 mg) injected over 10–15 s in either plain solution or with glucose 50 mg ml⁻¹. The solution was prepared aseptically by the anaesthetist administering the block, immediately before injection, by mixing ropivacaine 10 mg ml⁻¹ with an equal volume of either glucose 100 mg ml⁻¹ or sodium chloride 9 mg ml⁻¹ to give solutions with densities (at 37°C) of 1.01949 and 0.99953 g ml⁻¹ respectively.10 The patient was turned supine immediately at the end of injection, the time of which was defined as ‘zero’.

Thereafter an investigator, blinded to the solution administered, assessed the upper and lower extent of sensory block (analgesia to pinprick with the short bevel end of a 27-swg dental needle: caudal limit of sensory block assessment, S2), and the degree of motor block (modified Bromage scale: 0=full leg movement; 1= inability to raise extended leg, can bend knee; 2=inability to bend knee, can flex ankle; 3=no movement) and recorded the pulse rate and blood pressure 2, 5, 10, 15, 20, 25, and 30 min after injection. The patients were then transferred to the operating room and, if they wished, received sedation with a target-controlled infusion of propofol titrated to maintain verbal contact throughout. Because of this, and to avoid any interference, assessments were not made during surgery, but were continued at 30 min intervals thereafter until the block had regressed completely. I.V. fluid was administered only to replace operative blood loss, hypotension (>30% decrease in systolic pressure from baseline) being treated with i.v. ephedrine 6 mg.

Once sensory block had regressed fully, patients were encouraged to mobilize under supervision. Bladder catheterization was performed when surgically indicated, but time to micturition was recorded in all other patients. Patients were visited or telephoned 24 h and 3–7 days later to identify any sequelae.

**Statistical analysis**

The sample size was chosen to show a difference in extent of sensory block of 2 dermatomes (SD 1 dermatome) between the groups, based on an α risk of 0.05 and a β risk of 0.10, using data from a previous study.5 Data are presented as median [range], mean (SD) or frequencies as appropriate. Block characteristics were compared using the two-tailed Mann–Whitney U-test. A P value of <0.05 was considered statistically significant. Data were analysed using a standard computer based statistics package (Number Cruncher Statistical Systems [version 2001], Cork, Ireland).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics and types of surgery performed. Data are median (range), mean (SD) or frequencies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Plain (n=19)</strong></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>60 (50–73)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167 (8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71 (14)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>7/12</td>
</tr>
<tr>
<td>ASA I/II</td>
<td>4/15</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>40 [09–90]</td>
</tr>
<tr>
<td>Surgical specialty</td>
<td></td>
</tr>
<tr>
<td>Gynaecology</td>
<td>11</td>
</tr>
<tr>
<td>Urology</td>
<td>8</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Table 2</th>
<th>Block characteristics. Data are median [range]; (*n=15, †n=16, ‡n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset to T10 (min)</td>
<td>10 [2–25]</td>
</tr>
<tr>
<td>Median maximum block (dermatome)</td>
<td>T8 [T2–T2]</td>
</tr>
<tr>
<td>Time to maximum block (min)</td>
<td>25 [15–150]</td>
</tr>
<tr>
<td>Duration at T10 (min)</td>
<td>25 [0–206]**</td>
</tr>
<tr>
<td>Sensory regression (min)</td>
<td>270 [150–390]</td>
</tr>
<tr>
<td>Motor regression (min)</td>
<td>180 [90–270]</td>
</tr>
<tr>
<td>Time to mobilize (min)</td>
<td>286 [101–403]**</td>
</tr>
</tbody>
</table>

**Results**

The groups were comparable with respect to age, height, weight, sex, and ASA status (Table 1). After recruitment, randomization, and lumbar puncture, one patient in each group was withdrawn because of total block failure (no muscle weakness or loss of sensation) and given a general anaesthetic, so leaving 19 patients in each group. There was no difference in the type of surgery, although its duration was somewhat longer in the plain group (Table 1).

Hyperbaric ropivacaine produced a more rapid onset of more extensive, but less variable sensory block, which, nonetheless, ultimately regressed more quickly. The onset of analgesia to pinprick at T10 was more rapid, and the maximum block height (median T4 vs T8) was greater, but less variable (Table 2; Fig. 1). Median time to maximum block height was the same in both groups, but the range was considerably greater with the plain solution (Table 2). The onset of lower limb motor block was slightly faster in the hyperbaric group, but the maximum degree obtained was the same in both groups (Fig. 1). Median time to regression of sensory block to T10 (an indicator of useful duration for surgery) was longer in the hyperbaric group, but median times to complete regression of both sensory and motor block were longer in the plain group (Table 2; Figs 2 and 3). Patients therefore mobilized sooner in the hyperbaric group (Table 2), although the data for mobilization time were incomplete because of surgical constraints. While all hyperbaric blocks were adequate for surgery, three patients (Fig. 1) who received plain ropivacaine required general.
anaesthesia: two blocks were not extensive enough; and the third became inadequate 30 min after the start of surgery.

Cardiovascular changes were unremarkable throughout, and similar in the two groups, as were the volumes of fluid and doses of ephedrine administered. There were no major sequelae.

Discussion

This study has confirmed, in a direct, blinded comparison between two randomized groups of patients, findings only inferred previously by comparing the results of unrelated studies, namely that a hyperbaric solution of ropivacaine produces a more consistent block than a plain one. Addition of glucose led to a more rapid spread to a higher median level and with less variation in maximum sensory and motor block. However, the useful duration was longer and more consistent, but complete regression occurred sooner so that patients mobilized earlier. Similar observations on the effect of adding glucose have been made with other local anaesthetics.7,11 The increase in density produced by the addition of glucose would appear to result in a more even distribution of the local anaesthetic, gravity presumably encouraging spread of the bolus of drug ‘down’ the slopes of the lumbar curve when the patient is placed supine after injection.12 Usually, glucose-free solutions are marginally hypobaric, and have been found previously to be ‘unpredictable’,6 perhaps because gravity does not encourage their spread in the supine position. Spread is likely to be more dependent on other factors such as the currents produced by injection and simple diffusion. This may mean that more of the injected drug stays closer to the point of injection, making the block less useful for surgery, yet prolonging significantly sacral nerve block and so delaying recovery.

This study provides further evidence that hyperbaric ropivacaine, in a dose of 15 mg, produces predictable and reliable spinal anaesthesia for a variety of surgical procedures of relatively short duration. Duration of surgery was longer in the patients in this study, who received the plain solution, but two of the three blocks that were inadequate for surgery were related to inadequate spread, rather than regression before surgery ended. Even then, the regression was from a fairly low initial level (Fig. 1). Two previous studies of our own, using 3 ml ropivacaine 5 mg ml−1 in either glucose 10 mg ml−1 or glucose 50 mg ml−1, produced a block that was predictable, and adequate for surgery in all patients.8,9 Similar findings have also been obtained by others using somewhat different protocols (e.g. larger doses) for spinal anaesthesia for Caesarean section.13,14 One study compared plain and hyperbaric solutions of ropivacaine, and the other hyperbaric solutions of ropivacaine and bupivacaine, but in both studies hyperbaric ropivacaine provided adequate spinal block for the procedure. In the comparison of the different solutions of ropivacaine, the hyperbaric preparation produced a higher, more consistent block with faster onset and recovery, whereas there was a failure rate with the plain solution,13 something noted by others also.12,5 While the addition of glucose to a local anaesthetic solution improves predictability, all users of spinal anaesthesia must be aware that considerable variation in both total spread and duration of action still occurs. Figure 2 shows the differences between the two groups by plotting median spread against time, but it is important to recognize that there is, at every time interval, a similar degree of variation to that shown for maximum observed spread in Figure 1. For the clinician, the key data are not so much the figures for ‘average’ spread and duration, but their minima and maxima. Minimum figures for spread and duration indicate the guaranteed clinical utility of a particular technique. The maximum spread figure indicates the likelihood of complications such as hypotension, and that for maximum duration the potential need for close observation. While variability in
spread can be minimized by adding glucose, the variation in duration is very much a patient-specific factor. The average duration can be influenced by drug and dose choices, but the variability remains. This variability is even evident between studies. In a previous study the median duration of 15 mg ropivacaine 5 mg ml\(^{-1}\) (with glucose 50 mg ml\(^{-1}\)) at T10 was 56 [range 28–145] min, whereas it was 115 [50–180] in our study.

Although this study was not performed in the day-case setting, the suitability of hyperbaric ropivacaine for ambulatory surgery should be considered. McDonald and colleagues, using sub-clinical doses of ropivacaine in volunteers, concluded that it was less potent than bupivacaine and offered no advantage for use in outpatient anaesthesia. However, what they found was that ropivacaine produced sensory block of similar onset and extent as bupivacaine, but that it was associated with less motor block and faster regression of both sensory and motor block, findings similar to those reported here.\(^{15}\) Subsequently, clinically relevant doses of hyperbaric ropivacaine have been shown, as in this study, to provide predictable and reliable anaesthesia for elective surgery, albeit of a shorter duration than equal doses of bupivacaine.\(^9\) The standard agent for short duration spinal anaesthesia has been lidocaine, but continuing concerns about the high incidence of transient neurological symptoms limit its use.\(^{16,17}\)

In summary, hyperbaric ropivacaine produced more predictable and reliable sensory and motor block, with faster onset, than a plain solution. In addition, although the duration of useful block for surgery was increased, so was the speed of recovery from both sensory and motor block. Patients therefore mobilized more quickly after spinal

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**Fig 3** Proportions (%) of patients with each Bromage score (0, 1, 2, or 3) over time in two groups of patients: (A) ropivacaine with 50 mg ml\(^{-1}\) glucose; (B) plain ropivacaine.
anaesthesia with hyperbaric ropivacaine, something that may be particularly useful for ambulatory surgery and any operation when a long duration of block is unnecessary or undesirable, although it should be noted that the drug is unlicensed for this indication at present. Plain solutions of ropivacaine are associated with a less favourable pattern of block such that we advocate that they should not be used for surgery at or above the dermatomal level of the inguinal ligament, that is L1.

Acknowledgement
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