AN OPEN STUDY OF ROPIVACAINE IN EXTRADURAL ANAESTHESIA

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SUMMARY
Ropivacaine 0.5%, 0.75% and 1.0% was investigated in an open study of extradural anaesthesia in three groups of 15 patients undergoing urological or orthopaedic surgery. Following a test dose of 3 ml of 1.0% lignocaine with 1:200000 adrenaline, ropivacaine 20 ml was given in incremental doses over 4 min via a lumbar extradural catheter. The onset time for analgesia was short in all groups: T12 was blocked 4–6 min after the end of the injection of ropivacaine. The maximum segmental level was significantly higher in the 0.75% and the 1.0% groups (T2) than in the 0.5% group (T5). Complete motor block was obtained in seven, four and nine patients in the 0.5%, 0.75% and 1.0% groups, respectively. Duration of analgesia increased with increasing concentration of ropivacaine: mean duration of analgesia was 203 and 266 min at T10 and 253 and 314 min at L5 for the 0.5 and 1% solutions, respectively. Mean duration of complete motor block was 94 and 192 min for the same solutions. Analgesia was satisfactory for surgery in all patients except for one in the 0.75% group. Hypotension was experienced by three, seven and three patients in the 0.5%, 0.75% and 1.0% groups, respectively. Bradycardia occurred in seven patients and was associated with hypotension in five. Backache was experienced after operation by four patients, and three patients complained of a brief mild headache. No late adverse events were seen.

KEY WORDS

Ropivacaine is a new amino-amide local anaesthetic with a chemical formula similar to that of bupivacaine and mepivacaine. Animal studies have shown that it is an effective, long-acting agent, devoid of serious adverse effects when used for infiltration anaesthesia, and peripheral and central neural block [1]. Additionally, in vitro [2] and in vivo [3] animal experiments have suggested that ropivacaine may be approximately 50% less cardiotoxic than bupivacaine and possess a greater safety margin between convulsant and lethal doses.

The present multicentre study was designed to evaluate the efficacy and clinical characteristics of three concentrations of ropivacaine used for extradural anaesthesia in man.

PATIENTS AND METHODS
Following Ethics Committee approval, informed written consent was obtained from 45 ASA I–II patients undergoing routine urological or orthopaedic surgery or extracorporeal shock wave lithotripsy.

The majority of patients were premedicated with diazepam 10 mg orally and Hartmann's solution 500 ml was administered to every patient via an i.v. forearm cannula before extradural block. An extradural cannula was inserted via a 16-gauge Tuohy needle in the L2–3 or L3–4 space, using a midline approach. With the patient lying supine a test dose of 3 ml of 1% lignocaine with 1:200000 adrenaline was injected via the catheter followed, after 4 min, by 20 ml of one of the ropivacaine solutions.

At each hospital, the first five patients received
FIG. 1. Segmental spread of analgesia (mean 1.96 x SEM). Assessments were performed at 5-min intervals during the first 30 min, but to assist clarity only 15-min assessments are shown. The results for the three groups are “staggered” to obviate overlap. —— = 0.5% Ropivacaine (n = 15); —— = 0.75% ropivacaine (n = 15); —— = 1.0% ropivacaine (n = 15).

0.5% ropivacaine, the next five received 0.75% ropivacaine, and the last five patients were given 1% ropivacaine. Injections were performed by two investigators in each institution.

The levels of sensory analgesia were tested segmentally with a blunt 27-gauge needle 2 and 5 min after the end of the injection of ropivacaine and, thereafter, at 5-min intervals for 30 min and at 15-min intervals until 1 h after injection. Subsequently, the sensory levels were determined at 30-min intervals until block was judged to have worn off completely.

Motor block was assessed using a modified Bromage scale [4] (0 = no block; 1 = inability to raise extended legs but able to move knees; 2 = inability to flex knees but able to move feet; 3 = inability to move feet or knees) following each determination of analgesia, and this was continued until full motor power had been restored.

Heart rate and systolic and diastolic arterial pressures were measured using a Dinamap non-invasive arterial pressure monitor at the same times as the sensori-motor block evaluations; the final readings were made 3 h after the extradural injection. Cardiovascular effects, which included any episode of hypotension (defined by a > 30% decrease in pre-block systolic pressure, or a systolic pressure < 90 mmHg), or bradycardia (heart rate of less than 50 beat min⁻¹) were recorded and treated according to standard hospital practice.

The results are expressed as mean (SEM).

Statistical analyses were performed using the Wilcoxon rank sum test and the $\chi^2$ test, and differences between proportions were analysed by the Fisher exact test. $P < 0.05$ was considered significant.

RESULTS

Forty-one males and four females participated in the study. Each concentration of ropivacaine (0.5%, 0.75% and 1.0%) was given to 15 patients. There were no significant differences between these three groups for mean age, weight and height.

All the times given are from the end of ropivacaine injection.

Onset, spread and duration of analgesia (fig. 1)

The data for the ropivacaine groups are shown by mean dermatomal level. Thus onset of analgesia at T12 occurred at 4–6 min and that at L4 at 4.6–6 min. There were no significant differences between the three ropivacaine groups for mean onset time of analgesia at any segmental level.

The mean maximum cephalad level of analgesia was significantly lower ($P < 0.05$) in the 0.5% group (T5) compared with the 0.75% (T2) and 1.0% (T2) groups. However, the interval before onset of analgesia at the maximum dermatome level (0.5%, 26 (3.3) min; 0.75%, 38 (8.7) min; and 1%, 26 (2.8) min) was not significantly different between the groups.
The cephalad level of analgesia was significantly higher in the 1% group ($P < 0.05$) compared with the 0.5% group at 30–300 min after the end of administration of ropivacaine. The differences between the 0.5% and 0.75% groups were significant ($P < 0.05$) at 150–210 min after injection. There were no significant differences between the 0.75% and 1% groups.

Sensory to block levels above T1 were experienced by four patients in the 0.75% group (two at C5 and one each at C4 and C6) and similarly four patients in the 1% group (one patient at each of levels C2, C3, C6 and C8). No respiratory difficulties were experienced by any of these patients.

At each segment, there was a trend for higher ropivacaine concentrations to increase the duration of analgesia. At segments T8–T12, the effects of 0.75% and 1% ropivacaine were significantly longer than 0.5% ($P < 0.05$); at L2 and S3, 1% ropivacaine was significantly different from both the 0.75% and 0.5% doses. Mean durations for block at T10 were 203, 253 and 266 min and at L5 253, 260 and 314 min for 0.5, 0.75 and 1%, respectively.

Motor block (fig. 2)

No significant differences were found between the three groups with regard to onset or frequencies of various degrees of motor block. However, within each group significantly fewer patients had complete motor block (degree 3) than had degree 1 block ($P < 0.05$). Ropivacaine 1% was associated with significantly longer durations of all degrees of motor block than 0.5%; additionally, 1% ropivacaine produced significantly longer durations for degrees 1 and 2 compared with 0.75%.

Surgery

Surgery was commenced at approximately 45 min after the extradural injection and was of 45 min mean duration in all three groups. Analgesia and muscle relaxation were satisfactory in the majority of patients. Six patients (three in the 0.5% group, three in the 0.75% group) experienced some sensation during the surgical procedures, but only one required supplementation with i.v. opioids and Entonox.

Cardiovascular changes (fig. 3)

No significant differences were observed between the groups in heart rate and mean arterial pressure during the first 30 min after extradural injection.

Significant hypotension requiring administration of i.v. ephedrine and increased i.v. infusion of fluid was noted in three patients in the 0.5% group, seven patients in the 0.75% group and three patients in the 1% group. In five of these patients hypotension was associated also with bradycardia. Three of the patients in the 0.75% group and two in the 1% group had a maximum cephalad level of analgesia above T1 (0.75% C4, C6, C6; 1% C4, C6).

Bradycardia alone was seen in two patients who had maximum sensory levels of T4 (0.75%) and C6 (1%) and responded satisfactorily to i.v. atropine 0.6 mg.
Adverse sequelae

Mild to moderate backache was experienced by four patients on the first day after operation, while three patients complained of mild headache: all made a complete and rapid recovery. Forty-four patients were questioned between days 6 and 14 after operation for late complications: none was reported.

DISCUSSION

The open, non-randomized design of this study was chosen as it represented the first use of this new agent in the extradural space in man. Patients were recruited sequentially to receive greater concentrations of the agent. It was thus hoped that any adverse effects would be noted with the weaker solutions.

The study has demonstrated that ropivacaine in three concentrations (0.5, 0.75 and 1%) is an effective, long-acting local anaesthetic agent when administered in the extradural space in man. The agent behaved in a predictable fashion producing good clinical block at all concentrations tested. The agent was not associated with any significant adverse effects or toxicity.

Onset of block was rapid, with analgesia to T10 occurring within 10 min for all three concentrations. There was no difference in speed of onset between the three concentrations, but the maximum height of block differed; the two stronger solutions produced a block three segments higher than the weaker solution. Given the standard 20-ml volume of the injectate, the cephalad spread of the block was surprising, and higher than would have been expected from experience with other agents [4]. This aspect caused some anxiety before progressing to the 1% solution, but the difference in activity between the 0.75% and 1% solutions did not seem to be as marked as that between 0.5% and 0.75%. This grouping was noted in other areas of the study (e.g. duration of analgesia) and may be a feature of the drug. It could be related to its vasoactivity which, even in high concentration, tends to cause vasoconstriction [5].

The quality of surgical anaesthesia was generally excellent. Increasing the concentration of ropivacaine increased the duration of sensory analgesia with mean times of 203 (0.5%), 253 (0.75%) and 266 (1%) min for block at T10. This represents prolonged sensory analgesia, probably longer than for other available agents.

The agent is capable of producing good motor block, the duration increasing with concentration. Surprisingly, there were no apparent differences between groups for onset times to or frequencies of the three degrees of block although, within each group, significantly fewer patients achieved complete motor block compared with degree 1 block. It must be remembered, however, that these data

![Graph showing relative changes in mean arterial pressure (MAP) during the first 30 min after injection.](image)
are subject to the vagaries of the Bromage scale [4], which is an insensitive measure of the percentage of motor fibres blocked. Good sensory–motor dissociation is obtainable with the lower concentration which may prove to be a useful feature of the agent.

Arterial pressure decreased significantly, but to a similar extent, in all groups up to 30 min after injection. Surgery commenced soon after this time in many patients, so subsequent data were not analysed. Thirteen patients experienced hypotension, five episodes being associated with a block higher than T1. A minor incidence of backache and headache is seen commonly following extradural analgesia as was noted in this study. There were no other, or more major, adverse sequelae.

Ropivacaine would seem to be an efficacious and potent local anaesthetic agent when used for extradural analgesia. The drug might be particularly useful where a long duration of action is required.

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