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REVIEW ARTICLE

Ropivacaine

J. H. McClure

Ropivacaine is a new aminoamide local anaesthetic. It is the monohydrate of the hydrochloride salt of 1-propyl-2′,6′-pipecoloxylidide and is prepared as the pure *S*-enantiomer. It is one of a group of local anaesthetic drugs, the pipecoloxylidides (fig. 1), which were first synthesized in 1957 [3]. Mepivacaine and bupivacaine are both well known members of this group and have been in clinical use for more than 30 years [4, 23, 82]. Mepivacaine has a methyl group, ropivacaine a propyl group and bupivacaine a butyl group on the piperidine nitrogen atom of the molecule.

The pipecoloxylidides are chiral drugs because the molecules possess an asymmetric carbon atom (fig. 1) and they may have a left-(sinister) or right-(rectus) handed configuration. Mepivacaine and bupivacaine are currently produced for clinical use as racemic mixtures of the enantiomers containing equal proportions of the "*S*" and "*R*" forms but ropivacaine is the single "*S*" enantiomer. It has an enantiomeric purity of 99.5% and is prepared by the alkylation of the *S*-enantiomer of dibenzoyl-L-tartaric acid [25].

Differences in three-dimensional structure confer differences in the activity of enantiomers in the complex biological environment of the receptor [15]. This property of the pipecoloxylidides was known in the late 1960s because the different enantiomers had different durations of action at the target receptor in neural tissue [1, 47]. These differences in biological activity, whether measured in terms of desired or adverse effects, are not surprising because individual enantiomers bind to receptors or enzymes which are chiral amino acids with stereoselective properties. There may be differences in the activity of enantiomers of a drug: one may be active, the other partially active or inactive, or at the extreme, one may have an opposite effect to the other.

The clear advantages [22, 65, 72, 79, 80] of the long duration of action and sensory–motor differential block seen with bupivacaine consigned other members of this group of local anaesthetic drugs to the laboratory shelf, although some research work [2, 5] was carried out on the racemic mixture of the propyl homologue.

Historical background

In 1979, Albright published an alarming editorial [7] which associated the long-acting local anaesthetics, bupivacaine and etidocaine with cardiac arrest during regional anaesthesia. Albright reported six cases of presumed accidental intravascular injection of either bupivacaine or etidocaine which caused sudden ventricular arrhythmia occurring at the same time as severe convulsions. There were three cases of attempted brachial plexus block with 0.5 % bupivacaine, one i.v. regional anaesthetic with 0.5 % bupivacaine and chloroprocaine, one caudal extradural anaesthetic with etidocaine and, interestingly, only one case in this initial report was caused by 0.75 % bupivacaine used extradurally for Caesarean section. It was clear that there was a problem and there was a *paucity of experimental or clinical data delineating the effects of bupivacaine (and etidocaine) on the cardiovascular system above the convulsive threshold* at that time. Subsequently, sporadic cases of maternal death resulting from accidental i.v. injection of 0.75 % bupivacaine at the time of

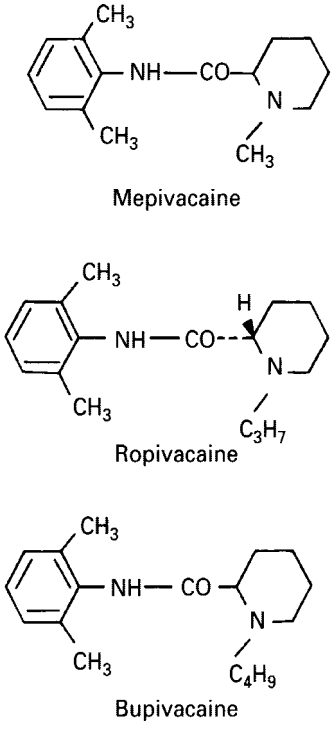

Figure 1 The pipecoloxylididles group of local anaesthetic drugs. The position of the asymmetric carbon atom is illustrated for ropivacaine.

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Key words

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extradural anaesthesia for Caesarean section were reported [48]. In the UK there were five deaths after i.v. regional anaesthesia performed by trainee casualty officers. Malfunction of an automatic tourniquet and the drug, bupivacaine, were common factors in these deaths [31]. Albright subsequently presented his findings to the United States Food and Drug Administration (FDA) which issued urgent recommendations about bupivacaine which contained the specific statement that 0.75 % bupivacaine was no longer recommended for obstetric anaesthesia. This sequence of events provided the impetus to develop a new local anaesthetic drug. It was possible that a drug of a lower lipid solubility compared with bupivacaine was less cardiotoxic.

The high lipid solubility of bupivacaine confers benefit by reducing absorption from the intended site of action, for example the extradural space. However, this property is not relevant if this site is bypassed when the drug is injected directly into the circulation. When a large dose of bupivacaine is injected rapidly into a vein, it is transported to the heart and brain and there is a high concentration of free drug available to cross the lipoprotein membrane of conducting tissue by first-pass extraction [74, 75]. After accidental i.v. injection, the mass of plasma protein (α_1-acid glycoprotein and albumin) in the volume of blood exposed to the drug is quickly saturated leaving a significant mass of unbound drug available for diffusion into conducting tissue of the heart and brain.

The FDA recommendations, while initially seeming illogical, in that it was the drug and not the concentration that was potentially cardiotoxic, achieved their objective. Appropriate measures, including slow or fractionated administration of a high dose of local anaesthetic drug, to detect potential systemic toxicity, have reduced the risk significantly.

Physiochemical properties

The physiochemical properties of lignocaine, ropivacaine and bupivacaine are summarized in table 1. The relative lipid solubility of ropivacaine, as measured by partitioning studies between N heptane and buffer and relative mean uptake into rat sciatic nerves, shows ropivacaine to be intermediate between lignocaine and bupivacaine. Plasma protein binding of ropivacaine is marginally less than that of bupivacaine but the pK_a is identical.

Preclinical studies

PRIMARY PHARMACODYNAMICS

Rosenberg and Heinonen in 1983 [63], using isolated sheathed vagus and phrenic nerves of rats, showed that ropivacaine at low concentration (25–50 μmol litre^{-1}) produced a profound and rapid block of both Aδ and C fibres and was more potent than similar low concentrations of bupivacaine in blocking these fibres. At higher concentrations, ropivacaine and bupivacaine had similar blocking activity. A study comparing higher doses of drug on isolated sheathed rabbit vagus nerve [11] found that A fibre block was 16 % greater with bupivacaine than similar concentrations (100, 150 and 200 μmol litre^{-1}) of ropivacaine. The degree of C fibre block was similar with both drugs at these concentrations.

Wildsmith and colleagues [83], using desheathed rabbit vagus nerves, found that ropivacaine blocked C fibres faster than A fibres and was a potent producer of frequency- (or use-) dependent block, that is block which only occurs when the fibre is stimulated. Low pK_a and high lipid solubility of a local anaesthetic drug favoured A over C fibre block whereas the reverse was true for high pK_a and low lipid solubility. Frequency-dependent block is considered to be related to lipid solubility and the molecular weight of the local anaesthetic drug. The lower lipid solubility of ropivacaine compared with bupivacaine is presumed to retard penetration of myelin sheaths.

This greater degree of differential block with ropivacaine at low concentration and the property of producing frequency-dependent block were considered to offer considerable clinical advantages in providing analgesia with minimal motor block.

Infiltration anaesthesia

Subcutaneous administration of ropivacaine 1 ml (0.25–0.5 %) has been shown to reduce cutaneous blood flow in pigs, as assessed by the laser Doppler method [43]. Bupivacaine in similar concentrations increased cutaneous blood flow. The addition of adrenaline 5 μg ml^{-1} to both ropivacaine and bupivacaine solutions reduced blood flow. Ropivacaine (0.25 ml of 0.25–0.75 %) has been shown to be two to three times longer acting than similar doses of bupivacaine when administered intradermally in the guinea pig [5]. The duration of effect of both drugs was increased further by the addition of adrenaline

Table 1 Physical properties of lignocaine, ropivacaine and bupivacaine. Data derived from Rosenberg, Kytta and Alila [64]

	Lignocaine	Ropivacaine	Bupivacaine
Molecular weight (base)	234	274	288
pK_a	7.7	8.1	8.1
Partition coefficient (N heptane/buffer)	1	2.9	10
Mean uptake ratio (rat sciatic nerve)	1	1.8	3.3
Protein binding	65	94	95

5 μg ml^{-1}. An *in vitro* study on ring segments of the femoral artery and vein of dogs [54] confirmed that ropivacaine has a vasoconstrictive effect but this effect may be minimal with the doses used in clinical practice. No difference was found in skin blood flow or surgical bleeding when comparing 0.25 % ropivacaine and bupivacaine given s.c. before skin incision in pigs [30]. However, the addition of adrenaline 5 μg ml^{-1} decreased blood flow by 50 % when added to each drug.

Peripheral nerve block

Animal studies have shown that 0.5–1 % ropivacaine consistently produces effective sensory and motor anaesthesia in sciatic nerve and brachial plexus block. Neither increasing the concentration above 0.75 % nor adding adrenaline were found to significantly improve the duration of motor or sensory anaesthesia in peripheral nerve block. Onset time and duration of block were shorter with ropivacaine than equal concentrations of bupivacaine in the rat [28].

Central blocks

In extradural and spinal anaesthesia in the guinea pig, mouse and dog, ropivacaine and bupivacaine were found to be equipotent in terms of sensory block but the duration of motor block was shorter with ropivacaine [5, 28].

SECONDARY PHARMACODYNAMICS

In vivo *studies*

The toxic effects of local anaesthetics on the brain and heart provided the initial stimulus to develop ropivacaine and much of the early animal research involved assessment of the potential of this new drug to cause cardiotoxicity. Central nervous system (CNS) toxicity is related directly to the anaesthetic potency of local anaesthetic drugs and similar doses of ropivacaine and bupivacaine have been found to cause convulsions in conscious dogs [26, 27]. Early work showed little difference between the cardiotoxic effect of a bolus dose of ropivacaine or bupivacaine in sheep [66, 67] but at supraconvulsant doses in dogs [26] ropivacaine was less arrhythmogenic than bupivacaine. This reduced cardiotoxic potential with ropivacaine was confirmed subsequently in sheep and the ratio of fatal doses was 1: 2: 9 for bupivacaine:ropivacaine:lignocaine [55].

The effect of local anaesthetic on the electrophysiology of the heart has been defined further. The maximal rate of increase in the cardiac action potential (*V*max) is largely dependent on sodium ion influx via the sodium channels. All local anaesthetic drugs are known to depress *V*max in a dose-dependent manner depending on the membrane potential and rate of stimulation. Bupivacaine depresses *V*max considerably more than lignocaine and results in slowed conduction of the cardiac action potential which is manifest by prolongation of the PR and QRS intervals of the electrocardiograph [62]. This results in re-entrant phenomena and ventricular arrhythmia [37]. When bupivacaine is bound to cardiac muscle, recovery from block is slow. The sodium channels are blocked in a "fast-in, slow-out" manner which causes difficulty in resuscitation when ventricular fibrillation has occurred. Studies suggest that the cardiotoxicity of bupivacaine results from its high lipid solubility and that the "*R*" enantiomer is more toxic than the "*S*" enantiomer [77].

Ropivacaine is intermediate in its depressant effect on *V*max in guinea pig papillary muscle between bupivacaine (highest) and lignocaine (lowest) and recovery from block is slower with bupivacaine [8]. Moller and Covino, in two studies [50, 51], confirmed that ropivacaine was intermediate between bupivacaine and lignocaine in decreasing *V*max in isolated rabbit Purkinje fibres. Exogenous progesterone had no additional effect on depression of *V*max with ropivacaine in contrast with the effect of bupivacaine where depression of *V*max was increased [51]. This was considered to reflect the increased susceptibility to cardiotoxicity with bupivacaine seen in pregnancy.

A favourable cardiotoxic profile of ropivacaine compared with bupivacaine was confirmed in pigs [61]. An electrophysiological toxicity ratio, based on the inverse of the amount of local anaesthetic agent required to prolong the QRS interval to the same degree, was determined as 1:6.7:15 for lignocaine, ropivacaine and bupivacaine.

The cardiotoxicity of ropivacaine is not enhanced by pregnancy in sheep [68]. Early work [52] found that pregnancy enhanced the cardiotoxic effects of bupivacaine, but this has since been refuted [69]. Greater doses of ropivacaine (12.9 ± 0.8 mg kg^{-1}) compared with bupivacaine (8.5 ± 1.2 mg kg^{-1}) are required to produce circulatory collapse in pregnant ewes. Pregnancy did not appear to alter plasma protein binding by both drugs.

Bupivacaine has also been found to be more cardiotoxic than equivalent doses of lignocaine or ropivacaine in the isolated perfused rabbit heart (Langendorff preparation) [60]. Bupivacaine produced more severe arrhythmias than those observed with ropivacaine; lignocaine was devoid of arrhythmogenicity. The development of ECG disturbances and severe myocardial depression was more rapid with bupivacaine than ropivacaine.

Ropivacaine administered by i.v. infusion was found to be less toxic than bupivacaine in human volunteers. Mild CNS symptoms and minor cardiovascular toxicity, as measured by changes in conductivity and contractability, occurred at lower dosage and lower plasma concentration with bupivacaine compared with ropivacaine [70].

PHARMACOKINETICS

The pharmacokinetics of ropivacaine and bupivacaine after i.v. and extradural administration have been determined in the dog and Rhesus monkey [9, 40]. The effect of adrenaline on extradural administration has also been evaluated. The concentration of ropivacaine decreases more rapidly than bupi-

vacaine during the elimination phase after i.v. infusion. Mean clearance (*Cl*) for ropivacaine in the dog was 41.1 ± 8.2 ml min^{-1} kg^{-1} compared with 32.3 ± 4.8 ml min^{-1} kg^{-1} for bupivacaine, although this difference was not statistically significant. After extradural administration the pharmacokinetic profiles of the two drugs were similar. Peak arterial ropivacaine concentration (C_P max) after extradural injection was higher for ropivacaine than bupivacaine with the 0.25 % concentration. The addition of adrenaline to either drug administered extradurally did not decrease C_P max consistently. The pharmacokinetic profiles of ropivacaine and bupivacaine in humans after extradural administration are similar to those determined in animal studies [38, 78].

The pharmacokinetic characteristics of ropivacaine after i.v. infusion have been determined in human volunteers [46]. Clearance (0.82 ± 0.16 litre min^{-1}) was found to be higher than the previously determined value for bupivacaine (0.58 litre min^{-1}). Plasma binding of ropivacaine averaged 94 ± 1 % (slightly lower than bupivacaine) and volume of distribution at steady state (V^{ss}) based on blood drug concentration was 59 ± 7 litre (cf. bupivacaine 73 litre). The terminal elimination half-life was 111 ± 62 min which is less than that determined previously for bupivacaine [75]. The higher clearance of ropivacaine compared with bupivacaine may offer an advantage in terms of systemic toxicity.

Human volunteer and clinical studies

The potency of ropivacaine in terms of sensory and motor block has now been determined in clinical use. A large number of open and double-blind studies have been performed on human volunteers and patients to determine the efficacy and degree of differential block with ropivacaine compared with bupivacaine in peripheral and central neural block.

Infiltration anaesthesia

Studies have been performed in human volunteers to determine the effect of ropivacaine compared with bupivacaine on cutaneous blood flow after intradermal injection of 0.1 ml of drug. Both bupivacaine and lignocaine produce vasodilatation in human skin, but a low concentration (0.25 %) of ropivacaine decreases skin blood flow [18]. Adrenaline 5 μg ml^{-1} reduces flow maximally when used alone but ropivacaine diminishes and does not accentuate the vasoconstrictive effect of adrenaline [19]. Plain solutions of ropivacaine produce a significantly longer duration of dermal analgesia than plain solutions of bupivacaine. Adrenaline significantly increases duration with both drugs [16]. The intradermal administration of small doses of local anaesthetic drug provides an interesting experimental model but this cutaneous vasoconstriction is observed with low doses and is not considered to be clinically important.

Ropivacaine (70 ml of 0.25 %) infiltrated into cholecystectomy wounds significantly decreases wound pain and increases the time to the first request for postoperative analgesia compared with saline [36]. However, wound infiltration with 0.25 % ropivacaine or bupivacaine 40 ml was equally effective in the management of post-herniorrhaphy pain [24]. There was no clinically significant difference between ropivacaine and bupivacaine in terms of duration of block or intensity of pain relief.

Peripheral nerve block

In a dose–response study in human volunteers undergoing bilateral ulnar nerve block, it was found that ropivacaine 2 ml was maximally effective at concentrations between 0.5 % and 0.75 % [58]. The profile of action resembled bupivacaine. The addition of adrenaline had no effect on onset time or duration of action of ropivacaine or bupivacaine. Several cases of residual paraesthesia lasting for longer than 1 month were observed with ropivacaine and bupivacaine. This was considered to result from needle trauma as there was no difference between ropivacaine and bupivacaine and there was no correlation with dose [58].

In a pharmacokinetic study bilateral intercostal block (T5–11) was performed in volunteers [44] using a total of 0.25 % plain ropivacaine or bupivacaine 56 ml. There was no difference in maximum plasma concentration ($C_P$max) but this tended to peak (tC_Pmax) earlier with ropivacaine. The terminal half-life ($T_{\frac{1}{2}}^{\beta}$) was significantly shorter with ropivacaine. Sensory and motor block were of shorter duration with ropivacaine (6.0 ± 2.5 h) compared with bupivacaine (10.0 ± 3.0 h).

Brachial plexus block

Hickey and colleagues [32–35] studied ropivacaine in subclavian perivascular brachial plexus block. The addition of adrenaline to 0.5 % ropivacaine was not found to alter the pharmacokinetic properties of ropivacaine absorbed from the brachial plexus sheath. Ropivacaine 0.5 % was comparable with 0.5 % bupivacaine in terms of onset time and duration of effect, and motor block was profound with both drugs.

Lumbar extradural block

Open studies [20, 57, 81] of lumbar extradural administration of ropivacaine in concentrations of 0.5 %, 0.75 % and 1 % showed that ropivacaine was a long-acting local anaesthetic which gave surgical anaesthesia of good quality. Increasing the concentration decreased onset time and increased motor block, as occurs with other local anaesthetic agents [71]. The peak plasma concentration ($C_P$max) of ropivacaine was below the concentration associated with systemic toxicity in animals. Comparison of 0.5 % bupivacaine and ropivacaine showed that bupivacaine had a slightly longer duration of sensory and motor block but spread was similar [14]. Katz, Knarr and Bridenbaugh [39] compared 0.75 % ropivacaine 20 ml with 0.5 % bupivacaine 20 ml and

no major differences were noted except that the time to two dermatome segment regression was of longer duration with 0.75 % ropivacaine compared with 0.5 % bupivacaine. Two studies [56, 85] comparing 1 % ropivacaine and 0.75 % bupivacaine found no difference in terms of onset, extent or duration of motor block but the duration of sensory block was longer and clinical efficacy was better with 1 % ropivacaine compared with 0.75 % bupivacaine. In elective hip surgery, 1 % ropivacaine provided satisfactory anaesthesia more frequently than 0.5 % bupivacaine and the duration of sensory and motor block was significantly longer [84]. The addition of adrenaline 5 $\mu g\ ml^{-1}$ to 0.5 % and 0.75 % ropivacaine or bupivacaine did not appear to confer any advantage in terms of duration of action [17]. There were also no differences in block or cardiovascular effect other than those expected from extradural block itself [41, 42].

Brockway and colleagues [12] compared 0.5 %, 0.75 % and 1 % ropivacaine 15 ml with 0.5 % and 0.75 % bupivacaine 15 ml in 110 patients and found no significant difference in onset, spread or duration of sensory block when similar concentrations were compared. However, ropivacaine produced a slower onset, shorter duration and less intense motor block than the same concentration of bupivacaine. Interestingly, four patients in this study, who were excluded from analysis of extradural block, received accidental i.v. injections which were not detected with a test dose of 1 % lignocaine with adrenaline 3 ml. No patient, including one patient who received a total dose of 112.5 mg of ropivacaine, suffered from harmful systemic toxicity as a slow incremental injection of the main dose was given.

In a study of clinical efficacy and kinetics of the lumbar extradural administration of 10 ml of 1 %, 20 ml of 0.5 % ropivacaine and 20 ml of 0.5 % bupivacaine, Morrison and colleagues [53] observed no difference between the groups in terms of onset, duration and spread of sensory block. Motor block produced by 0.5 % ropivacaine was less intense and of shorter duration than that of 0.5 % bupivacaine. The $C_P$max of ropivacaine was significantly greater and the terminal phase $T_{\frac{1}{2}}$ significantly shorter than that of bupivacaine.

Two volunteer studies of lumbar extradural block are considered pivotal in the interpretation of clinical data as they are the only studies which measured motor block in a quantitative manner. The modified Bromage scale [13] is simple to apply in a clinical setting and analyses movement in various muscle groups. It is a qualitative measure of spread and intensity of block. Mechanical measurement of the isometric muscle force (IMF) in a single muscle group is a more valid measurement of intensity of motor block [10, 45, 59, 87], although it is difficult to apply in the clinical situation and hence the importance of these volunteer studies.

In the first study [86] 0.5 %, 0.75 % or 1 % ropivacaine 20 ml was given to 30 volunteers (10 in each group) in a bolus dose. Motor block was assessed by quantitative (IMF in separate muscle groups) and qualitative (modified Bromage scale) methods. Onset of motor block, as assessed by the quantitative method, was significantly slower with 0.5 % ropivacaine and the intensity and duration of motor block increased with increasing dose. Motor block measured by the modified Bromage scale showed only the first part of the regression phase. Full recovery of muscle strength, as assessed by the qualitative method (Bromage scale = 0), was attained 1.5 to 2.5 h earlier than that assessed by the quantitative method.

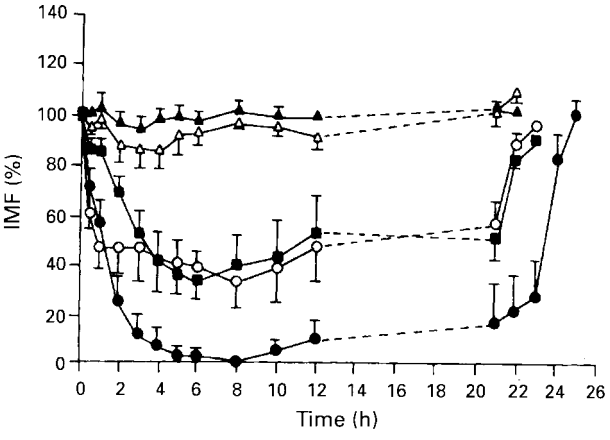

Figure 2 Motor block of the muscles of knee flexion in the 0.1 %(△), 0.2 % (■) and 0.3 % (○) ropivacaine groups, and in the 0.25 % bupivacaine (●) and saline (▲) groups (mean, SEM). IMF = Isometric muscle force. Reprinted with permission from Zaric and colleagues [88].

In the second study [88], volunteers (eight in each group) received a bolus dose of 0.1 %, 0.2 % or 0.3 % ropivacaine 10 ml or 0.25 % bupivacaine 10 ml followed by a continuous infusion of 10 $ml\ h^{-1}$ of the same drug and concentration for 21 h. Similar sensory spread was seen in all groups. Bupivacaine 0.25 % caused motor block of the greatest intensity as assessed quantitatively by IMF in three separate muscle groups. The regression phase of motor block when the infusion was stopped at 21 h was significantly shorter with all three concentrations of ropivacaine than with bupivacaine. This was seen most clearly in the knee flexors (fig. 2) but a similar profile was seen in the abdominal muscles and plantar flexors of the foot. This similar spread of sensory block, the reduced intensity of motor block and quick recovery observed with infusions of 0.2 % and 0.3 % ropivacaine compared with 0.25 % bupivacaine offer distinct advantages in the clinical setting during extradural analgesia for labour or postoperative pain.

Spinal block

In a safety study, subarachnoid administration of 0.5 % or 0.75 % glucose free (plain) ropivacaine 3 ml were compared [76]. The incidence of complete motor block, as assessed by a qualitative method, was higher with 0.75 % (18 of 20) compared with 0.5 % (10 of 19) ropivacaine. The duration of analgesia was longer with 0.75 % ropivacaine. No unexpected adverse events were registered, although there was a high incidence (11 of 40) of postdural puncture headache in this study of relatively young patients in whom a 26-gauge Quincke point needle was used.

The high proportion of patients not achieving complete motor block with 0.5 % ropivacaine 3 ml may have implications in terms of a "test dose" as the absence of full motor block may not exclude intrathecal placement of a catheter. Ropivacaine is not currently intended for use in spinal anaesthesia and research work has been restricted to safety analysis.

Extradural analgesia in labour

Two studies [49, 73] have been published, at the time of writing, comparing ropivacaine and bupivacaine in extradural analgesia in labour. The first study [49] compared a loading dose of 10 ml of 0.5 % followed by a top-up of 0.25 % ropivacaine or bupivacaine 10 ml. The other study [73] compared a continuous infusion of 0.25 % ropivacaine with 0.25 % bupivacaine 6–12 ml h^{-1} after a loading dose of 10 ml of this concentration. There was no difference in motor block in both studies, as assessed by the modified Bromage scale. This qualitative assessment may not be sensitive enough to detect differences in intensity of motor block in the segmental block required for analgesia in labour. Ropivacaine provided effective pain relief in labour and there was no difference in mode of delivery or neonatal outcome.

Extradural anaesthesia for Caesarean section

Ropivacaine 0.5 % has been compared with 0.5 % bupivacaine in extradural anaesthesia for Caesarean section. In one study [21] a standard dose of ropivacaine or bupivacaine 150 mg (30 ml) was given, and in another study [29] a mean volume of 23.7 ml of ropivacaine and 23.1 ml of bupivacaine was required to achieve an upper sensory level of block to the sixth thoracic dermatome. Both studies showed no difference in the profile of sensory block, but the duration of motor block with ropivacaine was significantly shorter compared with bupivacaine. Neonatal outcome and umbilical cord blood-gas tensions were similar. No detrimental effect has been observed with ropivacaine in extradural anaesthesia for Caesarean section on the uteroplacental or fetal circulations, as assessed by colour Doppler ultrasound [6].

Safety analysis

More than 2500 patients have now received ropivacaine in closely monitored controlled clinical trials evaluating the efficacy and safety of the drug. Details of all adverse events have been recorded and investigated. The reported incidences of serious adverse events that occurred in double-blind studies were lower during surgery, labour and Caesarean section with ropivacaine than with bupivacaine. None of the adverse events was considered to be drug related. Inadvertent i.v. injection of ropivacaine 75–200 mg occurred in five patients. None showed signs of cardiotoxicity. Convulsions occurred in one patient who received ropivacaine 200 mg intravascularly during an axillary brachial plexus block procedure. Prompt appropriate treatment led to full recovery within 2 min [personal communication, Dr Dag Selander].

Conclusions

Ropivacaine is an effective long-acting local anaesthetic and the first produced as a pure enantiomer. The sensory block provided by ropivacaine is similar to that produced by an equivalent dose of bupivacaine in extradural and peripheral nerve block. The motor block produced by ropivacaine is slower in onset, less intense and shorter in duration than that after an equivalent dose of bupivacaine. Motor block intensifies as the dose of ropivacaine is increased in extradural anaesthesia. This, together with its lower toxicity compared with bupivacaine, enables ropivacaine to be used for surgical anaesthesia in concentrations up to 1 %.

Ropivacaine is the first local anaesthetic drug to have been evaluated definitively, at an early stage in its development, as an analgesic for continuous extradural infusion. The profile of block with low doses of ropivacaine in terms of its greater sensory–motor separation and higher clearance than bupivacaine make it suitable for such use, although current experience is limited to 24 h. The clinical place of ropivacaine in extradural analgesia by continuous infusion during labour and the postoperative period has yet to be determined, but research to date suggests that ropivacaine offers distinct advantages over bupivacaine—the current local anaesthetic drug of choice.

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