diovascular changes, such as depression of conduction and diastolic function, were less pronounced with ropivacaine than with bupivacaine.

1. Cederholm I. Preliminary risk-benefit analysis of ropivacaine in labour and following surgery. *Drug Safety* 1997; **16:** 391–402.
2. Knudsen K, *et al.* Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. *Br J Anaesth* 1997; **78:** 507–14.

Interactions

For interactions associated with local anaesthetics, see p.1851.

Giving ropivacaine with general anaesthetics, opioid analgesics, or drugs structurally related to amide-type local anaesthetics (e.g. certain antiarrhythmics) may result in potentiation of adverse effects.

The metabolism of ropivacaine is mediated by the cytochrome P450 isoenzyme CYP1A2 and the potential exists for interactions between ropivacaine and other drugs that inhibit or act as a substrate for this isoenzyme. Prolonged use of ropivacaine should be avoided in patients treated with potent CYP1A2 inhibitors, such as fluvoxamine. Plasma concentrations of ropivacaine may be reduced by enzyme-inducing drugs such as rifampicin.

Pharmacokinetics

Ropivacaine is about 94% bound to plasma proteins. The terminal elimination half-life has been reported to be 1.8 hours. It is extensively metabolised in the liver, predominantly by aromatic hydroxylation which is mediated by the cytochrome P450 isoenzyme CYP1A2; the isoenzyme CYP3A4 plays a minor role in the metabolism of ropivacaine. The metabolites are excreted mainly in the urine; about 1% of a dose is excreted as unchanged drug. Some metabolites also have a local anaesthetic effect but less than that of ropivacaine. Ropivacaine crosses the placenta.

See also under Local Anaesthetics, p.1852.

Uses and Administration

Ropivacaine hydrochloride is a local anaesthetic of the amide type with actions and uses similar to those described on p.1852. It is a long-acting local anaesthetic, although onset and duration of action are dependent upon the site of injection; the presence of a vasoconstrictor such as adrenaline has no effect. Ropivacaine is used for epidural block, peripheral nerve block, and infiltration anaesthesia and field block, but is contra-indicated for obstetric paracervical block and for use in intravenous regional anaesthesia (Bier's block). (Local anaesthetic techniques are discussed on p.1853.) At high doses ropivacaine produces surgical anaesthesia, whereas at lower doses it is used for the management of acute pain such as labour pain (p.7) and in postoperative analgesia (p.4).

Like bupivacaine (p.1854), ropivacaine has a differential blocking effect on nerve fibres and, at the lowest concentration used, there is good differentiation between sensory and motor block. The onset and duration of sensory block produced by ropivacaine is generally similar to that obtained with bupivacaine but the motor block is often slower in onset, shorter in duration, and less intense.

Ropivacaine hydrochloride is given in concentrations of 0.2 to 1%. The dosage depends on the site of injection and the procedure used, as well as the status of the patient. The dose of ropivacaine should be reduced in the elderly, and in acutely ill or debilitated patients. A test dose of lidocaine with adrenaline should be given before starting epidural block with ropivacaine to detect inadvertent intravascular administration.

- For **surgical anaesthesia**, doses of ropivacaine hydrochloride for *lumbar epidural block* are 75 to 150 mg (15 to 30 mL) as a 0.5% solution, or 112.5 to 187.5 mg (15 to 25 mL) as a 0.75% solution, or 150 to 200 mg (15 to 20 mL) as a 1% solution; for caesarean section, doses are 100 to 150 mg (20 to 30 mL) as a 0.5% solution or 112.5 to 150 mg (15 to 20 mL) as a 0.75% solution. Doses for *thoracic epidural block* to establish a block for postoperative pain relief are 25 to 75 mg (5 to 15 mL) as a 0.5% solution or 37.5 to 112.5 mg (5 to 15 mL) as a 0.75% solution; the actual dose used depends on the level of the injection.
- For *peripheral nerve block* of major nerves such as the brachial plexus, typical doses are 175 to 250 mg (35 to 50 mL) as a 0.5% solution; 225 to 300 mg (30 to 40 mL) as a 0.75% solution has also been recommended for brachial plexus block.
- For *infiltration anaesthesia* and *field block* up to 200 mg (40 mL) as a 0.5% solution or up to 225 mg (30 mL) as a 0.75% solution may be used.
- In the management of **acute pain** ropivacaine hydrochloride is used as a 0.2% solution for epidural block (0.5% solutions may be used for infiltration). Doses for *lumbar epidural block* are 20 to 40 mg (10 to 20 mL) as an initial bolus followed by 20 to 30 mg (10 to 15 mL) at intervals of not less than 30 minutes. Alternatively, 12 to 20 mg (6 to 10 mL) per hour may be given as a continuous epidural infusion; if additional pain relief is required, doses of up to 28 mg (14 mL) per hour may be given. Doses for *thoracic epidural block* are 12 to 28 mg (6 to 14 mL) per hour as a continuous infusion.
- For *infiltration anaesthesia* doses are 2 to 200 mg (1 to 100 mL) as a 0.2% solution or 5 to 200 mg (1 to 40 mL) as a 0.5% solution.
- In neonates, infants, and children aged up to 12 years, ropivacaine hydrochloride may be used for the management of peri- and postoperative pain. A 0.2% solution is given in a dose of 2 mg/kg (1 mL/kg) to achieve a *caudal epidural block*.

◊ References.

1. Markham A, Faulds D. Ropivacaine: a review of its pharmacology and therapeutic use in regional anaesthesia. *Drugs* 1996; **52:** 429–49.
2. McClure JH. Ropivacaine. *Br J Anaesth* 1996; **76:** 300–307.
3. Morton C. Ropivacaine. *Br J Hosp Med* 1997; **58:** 97–100.
4. Stienstra R. The place of ropivacaine in anesthesia. *Acta Anaesthesiol Belg* 2003; **54:** 141–8.
5. Zink W, Graf BM. Benefit-risk assessment of ropivacaine in the management of postoperative pain. *Drug Safety* 2004; **27:** 1093–1114.
6. Simpson D, *et al.* Ropivacaine: a review of its use in regional anaesthesia and acute pain management. *Drugs* 2005; **65:** 2675–2717.

Preparations

USP 31: Ropivacaine Hydrochloride Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Naropin; ***Austral.:*** Naropin; ***Austria:*** Naropin; ***Belg.:*** Naropin; ***Braz.:*** Naropin; Ropi; ***Canad.:*** Naropin; ***Chile:*** Naropin; ***Cz.:*** Naropin; ***Denm.:*** Naropin; ***Fin.:*** Naropin; ***Fr.:*** Naropeine; ***Ger.:*** Naropin; ***Gr.:*** Naropeine; ***Hong Kong:*** Naropin; ***Hung.:*** Naropin; ***Indon.:*** Naropin; ***Irl.:*** Naropin; ***Israel:*** Narop; ***Ital.:*** Naropina; ***Malaysia:*** Naropin; ***Mex.:*** Naropin; ***Neth.:*** Naropin; ***Norw.:*** Naropin; ***NZ:*** Naropin; ***Philipp.:*** Naropin; ***Pol.:*** Naropin; ***Port.:*** Naropeine; ***Rus.:*** Naropin (Наропин); ***S.Afr.:*** Naropin; ***Singapore:*** Naropin; ***Spain:*** Naropin; ***Swed.:*** Narop; ***Switz.:*** Naropin; ***Thai.:*** Naropin†; ***Turk.:*** Naropin; ***UK:*** Naropin; ***USA:*** Naropin; ***Venez.:*** Naropin†.

Multi-ingredient: ***Austral.:*** Naropin with Fentanyl; ***NZ:*** Naropin with Fentanyl.

Tetracaine *(BAN, rINN)*

Amethocaine; Tetracaína; Tétracaïne; Tetracainum; Tetrakaiini; Tetrakain. 2-Dimethylaminoethyl 4-butylaminobenzoate.

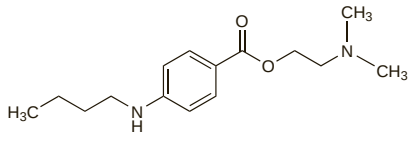
Тетракаин

$C_{15}H_{24}N_2O_2$ = 264.4.

CAS — 94-24-6.

ATC — C05AD02; D04AB06; N01BA03; S01HA03.

ATC Vet — QC05AD02; QD04AB06; QN01BA03; QS01HA03.



Pharmacopoeias. In *US*.

USP 31 (Tetracaine). A white or light yellow waxy solid. M.p. 41° to 46°. Very slightly soluble in water; soluble 1 in 5 of alcohol and 1 in 2 of chloroform or of ether; soluble in benzene. Store in airtight containers. Protect from light.

Tetracaine Hydrochloride *(BANM, rINNM)*

Amethocaine Hydrochloride; Dicainum; Hidrocloruro de tetracaína; Tétracaïne, chlorhydrate de; Tetracaini hydrochloridum; Tetracainii Chloridum; Tetrakaiinihydrokloridi; Tetrakain Hidroklorür; Tetrakain hydrochlorid; Tetrakainhidroklorid; Tetrakainhydroklorid; Tetrakaino hidrochloridas; Tetrakainy chlorowodorek.

Тетракаина Гидрохлорид

$C_{15}H_{24}N_2O_2$,HCl = 300.8.

CAS — 136-47-0.

ATC — C05AD02; D04AB06; N01BA03; S01HA03.

ATC Vet — QC05AD02; QD04AB06; QN01BA03; QS01HA03.

NOTE. TET is a code approved by the BP 2008 for use on single unit doses of eye drops containing tetracaine hydrochloride where the individual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Tetracaine Hydrochloride). A white or almost white, slightly hygroscopic, polymorphic, crystalline powder. Freely soluble in water; soluble in alcohol. A 1% solution in water has a pH of 4.5 to 6.5. Store in airtight containers. Protect from light.

USP 31 (Tetracaine Hydrochloride). A fine, white, odourless, hygroscopic, polymorphic, crystalline powder. Very soluble in water; soluble in alcohol; insoluble in ether and in benzene. Its solutions are neutral to litmus. Store in airtight containers. Protect from light.

Adverse Effects and Treatment

As for Local Anaesthetics in general, p.1850.

Tetracaine has high systemic toxicity. Absorption of tetracaine from mucous membranes is rapid and adverse reactions can occur abruptly without the appearance of prodromal signs or convulsions; fatalities have occurred.

A stinging sensation may occur when tetracaine is used in the eye. Mild erythema at the site of application is frequently seen with topical use; slight oedema or pruritus occur less commonly. Blistering of the skin may occur.

Urethral stricture. There has been a report[1] of a sudden increase in the incidence of urethral stricture after transurethral surgery, which may have been due to an increase in the concentration of tetracaine hydrochloride in the lubricant gel from 0.1 to 3%.

1. Pansadoro V. Role of local anaesthetics in urethral strictures after transurethral surgery. *Lancet* 1990; **336:** 64.

Precautions

As for Local Anaesthetics in general, p.1851.

Tetracaine should not be applied to inflamed, traumatised, or highly vascular surfaces. It should not be used to provide anaesthesia for bronchoscopy or cystoscopy, as lidocaine is a safer alternative.

Interactions

For interactions associated with local anaesthetics, see p.1851.

Pharmacokinetics

See under Local Anaesthetics, p.1852. Tetracaine is reported to be about 15% bioavailable after application of a 4% gel to intact skin, with a mean absorption and elimination half-life of about 75 minutes.

Uses and Administration

Tetracaine, a para-aminobenzoic acid ester, is a potent local anaesthetic with actions and uses similar to those described on p.1852. It is used for surface anaesthesia and spinal block; its use in other local anaesthetic techniques is restricted by its systemic toxicity.

Tetracaine is generally used as the hydrochloride in solutions and creams, and as the base in gels or ointments.

For *anaesthesia of the eye*, solutions containing 0.5 to 1% tetracaine hydrochloride have been used; ointments have also been used. Instillation of a 0.5% solution produces anaesthesia within 25 seconds that lasts for 15 minutes or longer and is suitable for use before minor surgical procedures.