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BRIEF COMMUNICATION

Ropivacaine: A Novel Local Anaesthetic Drug to Use in Otorhinolaryngology Practice

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Abstract Ropivacaine is a long-acting amide local anaesthetic agent which has a significant vasoconstrictive property, long duration of action, least central nervous system and cardiac complications due to the pure (S)-enantiomer property by reversible inhibition of sodium ion influx in nerve fibres. By using additives the duration of analgesia may be prolonged. Ropivacaine has been used routinely in our otorhinolaryngology procedures since 2010 (10 years). The present article details the clinical applications of ropivacaine and its current place as a local anaesthetic in otorhinolaryngology practice.

Keywords Anaesthesia · Regional anaesthetic · Ropivacaine · ENT surgeries

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Introduction

Ropivacaine is a versatile local anaesthetic drug to use in otorhinolaryngology practice, compared to other routinely used drugs like bupivacaine and lidocaine for local infiltration and nerve blocks. By itself it has a significant vasoconstrictive property, long duration of action and in case of overdose central nervous system (CNS) & cardiac complications of ropivacaine are the least because of its pure (S)-enantiomer property. By using additives the duration of analgesia may be prolonged. Ropivacaine has been used routinely in our otorhinolaryngology procedures since 2010 (10 years).

About Ropivacaine

Ropivacaine (1′-propyl-2,6-pipecolo-xylide hydrochloride monohydrate) is a long-lasting local anaesthetic belonging to the amide group family of injectable local anaesthetics. Ropivacaine, a pure *S* (–) enantiomer of the mepivacaine family, is an optically active isomer [1].

Ropivacaine was evaluated in clinical trials starting in 1990 and introduced clinically in 1996. Ropivacaine may also be similar acting like bupivacaine, with useful drug concentrations ranging from 0.2 to 1%. Ropivacaine has been developed and presented as alternative, long-acting local anaesthetics with the desirable blocking properties of racemic bupivacaine and lidocaine but a greater margin of safety due to their reduced toxic potential as compared to other two drugs. Low pKa (acid dissociation constant—stronger acid) and high lipid solubility of local anaesthetic drug favoured Group Aδ over Group C nerve fibre block [2] whereas the reverse was true for high pKa (weak acid) and low lipid solubility. Ropivacaine, being less lipophilic

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has the theoretical advantage of a stronger differential in sensory/motor blocks than bupivacaine and lidocaine, especially when low concentrations are used with good preservation of motor function and least CNS and cardiac toxicity.

In view of potential side effects of bupivacaine–epinephrine or lidocaine–epinephrine combination, ropivacaine is a more appropriate choice, for local anaesthesia pain relief in otolaryngology.

Mechanism of Action

Ropivacaine acts by blocking electrical conduction in peripheral nerves. Peripheral nerves are tubular structures that contain millions of axons bundled into fascicles, which in aggregate comprises an individual nerve. Each axon is composed of a phospholipid bilayer cell membrane, which is impermeable to sodium in the resting state. Sodium is therefore the major extracellular cation and potassium [3] is the major intracellular cation, accounting for the electric gradient from inside to outside the cell of − 70 to − 90 mV. The ropivacaine binds to protein receptors in the transport channel, thereby preventing sodium influx, cell membrane depolarization and propagation of electrical nerve conduction.

Pharmacodynamics

Ropivacaine is less lipophilic than bupivacaine, together with its stereoselective properties which contributes to significant higher threshold for cardiotoxicity and CNS toxicity than bupivacaine in animals and healthy volunteers [4–6].

Ropivacaine has been shown to inhibit platelet aggregation in plasma at concentrations of 3.75 and 1.88 mg/mL (0.375% and 0.188%) [7]. Like other anaesthetics, ropivacaine has antibacterial activity in vitro, inhibiting the growth of *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* [8, 9].

Pharmacokinetics

Ropivacaine is bound to plasma proteins to an extent of 94%, mainly to α1-acid glycoprotein [10]. Ropivacaine is metabolised extensively in the liver and kidney is the main excretory organ for ropivacaine, accounting for 86% [11–13].

Duration of action

Ropivacaine significantly prolongs the duration of nerve block and local infiltration. Ropivacaine is a long acting amide anaesthetic. Duration of action lasts for 5 to 8 h. The duration of action of a local anaesthetic is a function of the degree of protein binding of the drug. The higher the degree of protein binding [11], the greater the affinity of the drug for the protein receptor in the transport channel and the longer the drug remains bound to the receptor.

Clinically, the duration of the infiltration or block can be extended by adding epinephrine in concentration 1:40,000 to the local anaesthetic solution to cause vasoconstriction of capacitance vessels and venules to delay drug washout.

The maximum safe dosage of local anaesthetics when injected is generally increased when used in combination with a vasoconstriction agent. Serum concentration increases at a slower rate when blood flow is diminished at the site of treatment as the anaesthetic is sequestered. This same process will increase the duration of analgesic effect when administered along with a vasoconstrictor [14]. Addition of buprenorphine 3 μg/kg, tramadol 1–1.5 mg/kg, clonidine (1–2 μg/kg) or dexamethasone (4–10 mg) to ropivacaine prolonged the duration of action and hence pain relief (Table 1).

The time of onset of the ropivacaine can be shortened by increasing the concentration of the drug. The higher the concentration, more molecules shall be available for diffusion, protein receptor binding and hence faster the onset of drug action.

Adverse Effects and Toxicity

Ropivacaine is an amide-linked local anaesthetic. Allergic reactions to amide-linked local anaesthetics are rare. Cardiotoxicity include myocardial depression and cardiac arrhythmias. Central nervous system toxicity includes confusion, hyperactivity, dizziness, tinnitus, seizures, coma, and respiratory arrest. Cardiovascular and CNS toxicity is least to ropivacaine among all available local anesthetics [10, 15, 16].

Ropivacaine is available in strengths of 0.2%, 0.5%, 0.75% and 1% as 30 ml vials or ampules.

Our Experience with Ropivacaine

For Nose and Sinuses

Most of the nasal and sinus surgeries in our ENT practice are performed under local anaesthesia as day-care procedures. A solution of 0.5% ropivacaine with epinephrine in the ratio 1:40,000 (20 ml of 0.5% ropivacaine with 0.5 ml of epinephrine 1:1000) is used for sinus blocks and infiltration of septum. We also use it for rhinoplasty cases for local nerve block and postoperative pain relief [17, 18].

Table 1 Dosage: Maximum recommended doses [14] in comparison with other commonly used drugs Lidocaine and Bupivacaine

Anaesthetic route of administration	Maximum single dose without vasoconstrictor (mg/kg)	Maximum single dose with vasoconstrictor (mg/kg)	Onset of action (min)	Duration of action in isolation (min) [with vasoconstrictor, if available]
Lidocaine infiltration	3 mg/kg per dose, not to exceed 300 mg per dose,	7 mg/kg per dose—not to exceed 500 mg per dose	1–3 min	1/2–2 h [2 to 4 h with epinephrine]
Bupivacaine infiltration	2.5 mg/kg per dose—not to exceed 175 mg per dose	3 mg/kg per dose—not to exceed 225 mg per dose	2–7 min	2–3 h [3–7 h with epinephrine]
Ropivacaine infiltration	3 mg/kg per dose—not to exceed 225 mg per dose	4 mg/kg per dose—not to exceed 225 mg per dose	3–7 min	3–4 h [5–8 h with epinephrine]

For External and Middle Ear

We use a solution of 0.5% ropivacaine with epinephrine in the ratio 1:40,000 (20 ml of 0.5% ropivacaine with 0.5 ml of epinephrine 1:1000) for all external and middle ear surgeries, performed under local anaesthesia.

We get excellent surgical field, good patient cooperation during surgery and long duration postoperative pain relief [19, 20].

For Adenotonsillectomy

When adenotonsillectomy was performed under general anaesthesia, we inject 0.5% ropivacaine into both pillars of tonsillar fossa and nasopharynx in the adenoids bed [21].

When combined with epinephrine, the patient gets transient tachycardia and elevated blood pressure at the time of infiltration but this subsides within few minutes. So in cardiac patients we reduce the concentration of epinephrine.

The postoperative analgesia lasted for 5 to 8 h (till the patient gets discharged, being done as day care procedure) in all patients. Patients treated with ropivacaine and clonidine [22] fared far better in terms of pain relief up to postoperative day 3 in tonsillectomy and uvulopalatal surgeries [23] for snoring/Obstructive sleep apnea.

Ropivacaine has been used in our otorhinolaryngology procedures since 2010 (10 years). We haven't come across any complication due to over dosage or toxicity. We use 0.5% solution in all otorhinolaryngology procedures, around 20 ml per case even though the maximum toxic dose as mentioned in literature is 30–40 ml for a patient of 50 kg weight [24].

Conclusion

In conclusion, ropivacaine appears to be safest of all injectable local anaesthetics and is clearly effective for the management of preoperative and postoperative pain relief for longest duration. Ropivacaine is superior to the lidocaine and bupivacaine in ENT practice when compared in the duration of action and safety. It can be used as a routine drug for all otorhinolaryngology surgeries.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from individual participant included in the study.

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