Review Article

Understanding the Pharmacological Properties of Commonly Used Drugs in Day Care Procedures: What is in it for an Anesthetist?

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Abstract: Anaesthesia is an ever evolving branch. In order to understand the function of an anaesthetic drug, it is imperative to assess the pharmacodynamic and pharmacokinetic properties of the inducing agent. Levobupivacaine is one such local anaesthetic drug that is commonly used in day care operative procedures. The success of the surgery mainly depends on the safety and efficacy of the drug, that is usually dose responsive. Levobupivacaine is about 97% bound to plasma proteins. Half life of levobupivacaine is 3.3 hours. The volume of distribution is estimated at 66.91 ± 18.23. It is found to have stable effect on the central nervous system, respiratory system, autonomic nervous system as well as it provides hemodynamic stability as well. The most common adverse drug reactions reported are: hypotension (31%), nausea (21%), vomiting (14%), headache (9%), procedural pain (8%), dizziness (6%). It is concluded that levobupivacaine can be used safely as a anaesthetic drug.

Keywords: Pharmacology, Pharmacodynamics, Anaesthesia, Adverse Reaction.

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INTRODUCTION

Levobupivacaine is an amino-amide local anaesthetic drug belonging to the family of n-alkyl substitute picecloxyxilide. Its molecular structure is 2– piperidinecarboxamide 1–Butyl–N–(2,6–dimethyl phenyl)–hydrochloride monohydrate. Its pKa is 8.1. Levobupivacaine is a non-pyrogenic, colourless solution (pH 4.0 - 6.5) with a water solubility of 0.0977 mg/mL (Albrecht, E. et al., 2019).

Pharmacokinetics

Levobupivacaine is about 97% bound to plasma proteins. Half life of levobupivacaine is 3.3 hours. Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine or feces (Bajwa, S. J. & Kaur, J. 2013).

Absorption

The plasma concentration of levobupivacaine following therapeutic administration depends on dose and route of administration, because absorption from the site of administration is affected by the vascularity of the tissue.

Distribution

The volume of distribution is estimated at 66.91 ± 18.23 L (after intravenous administration of 40 mg in healthy volunteers) (Leone, S. et al., 2008). Clearance of levobupivacaine is 39.06 ±13.29 L/h [after intravenous administration of 40 mg in healthy volunteers].

Biotransformation and Excretion

Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine and faeces. In CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. Levobupivacaine appears to undergo further transformation to glucuronide and sulfate conjugates (Burlacu, C. L. & Buggy, D. J. 2008). Metabolic inversion of levobupivacaine to R (+) - bupivacaine was not evident in both in vitro and in vivo.
Mechanism of Action

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves; and small nerves are blocked more easily than larger ones. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibers. Specifically, the drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. It blocks nerve conduction in sensory and motor nerves mainly by interacting with voltage-sensitive sodium channels on the cell membrane. It also interferes with impulse transmission and conduction in other tissues (Rachel, H. & Foster, A. M. 2000).

Onset and duration of action

It depends upon the particular drug’s pKa and on lipophilic of its base and cation species. Levobupivacaine is long acting with a dose-dependent duration of anaesthesia. The onset of action is more than 15 minutes with various anesthetic techniques. In studies of surgical anesthesia in adults, levobupivacaine provided sensory block for up to 9 hours after epidural administration of less than 202.5 mg, 6.5 hours after intrathecal 15 mg, and 17 hours after brachial plexus block with 2 mg/kg (El-Soudy, E. M. et al., 2019).

Clinical effects of levobupivacaine(Abrahams, M. S. 2009)

It is relatively free of adverse effects if administered in appropriated doses. The clinical effects are following:

1. Central nervous system

CNS is more susceptible to levobupivacaine. The initial symptoms involve feeling of light headedness and dizziness followed by visual and auditory disturbances. Disorientation and occasional feeling of drowsiness may occur. Objective signs are usually excitatory in nature which includes shivering, muscular twitching and tremors; initially involving muscles of the face (perioral numbness) and part of extremities. At still higher doses cardiovascular or respiratory arrest may occur. Acidosis increases the risk of CNS toxicity from, since an elevation of PaCO₂ enhances cerebral blood flow, so that more anaesthetic is delivered rapidly to the brain.

2. Cardiovascular system

It depresses rapid phases of depolarization (Vmax) in purkinje fibres and ventricular musculature to a greater extent than lignocaine. It also decreases the rate of recovery from a dependent block than that of lignocaine. This leads to incomplete restoration of Vmax between action potential at high rates, in contrast to complete recovery by lignocaine.

3. Respiratory system

Respiratory depression may be caused if excessive plasma level is reached which in turn results in depression of medullary respiratory center. Respiratory depression may also be caused by paralysis of respiratory muscles as may occur in high spinal or total spinal anaesthesia.

4. Autonomic nervous system

Myelinated preganglionic β fibres have a faster conduction time and are more sensitive to the action of local anaesthetic including levobupivacaine. Involvement of preganglionic sympathetic fibres is the cause of widespread vasodilation and consequent hypotension that occurs in epidural and paravertebral block. When used for conduction blockade all local anaesthetic particularly levobupivacaine produces higher incidence of sensory blockade than motor fibres.

Dosage

Maximal dose is 2 mg/kg body weight (25-30 mL 0.5% solution) (Williams, S. R. et al., 2003).

Availability

Levobupivacaine is available in following concentration: 0.25% and 0.5% 0.25% and 0.5% in isotonic solution 0.125% - 0.75% used for nerve block and epidural anaesthesia or analgesia. 0.5% or 0.75% plus 80% of dextrose to make solution hyperbaric for subarachnoid block (Ilham, C. et al., 2014).

Adverse effects

Levobupivacaine produces the same adverse effects as seen with racemic bupivacaine and other local anaesthetics (Abdelhamid, B.M. 2018).

- The most common adverse drug reactions reported are: hypotension (31%), nausea (21%), vomiting (14%), headache (9%), procedural pain (8%), dizziness (6%).
- The cardiac toxicity, neurological injury after peripheral nerve block and unwanted CNS effects, may be lower than bupivacaine.
- Allergic type reactions are rare and range in severity from urticaria to anaphylactoid-like reaction.

REFERENCES:


