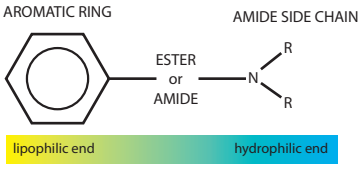
# LOCAL ANAESTHETICS




**Physiochemical characteristics and clinical relevance** Local anaesthetics are weak bases and exist predominantly in the ionised form at neutral pH as their pKa exceeds 7.4. They fall into two groupings ester or amide, which describes the linkage between aromatic lipophilic group and the hydrophilic amide group that each possess. Individual structures confer different physiochemical and clinical characteristics. Potency is closely correlated to lipid solubility (more so in vitro - but still significantly in vivo). The duration of action is closely associated with the extent of protien binding. Local anaesthetics with limited protien binding have a short duration of action and conversely those with more extensive protien binding have a longer duration of action. The onset of action is closely related to the pKa. Local anaesthetics are weak bases and exist mainly in the ionised form at normal pH. Those with a high pKa have a greater fraction present in the ionised form, which is unable to penetrate the phospholipid membrane, resulting in a slow onset of action. Conversely, a low pKa reflects a higher proportion in the un-ionised form and therefore a faster onset of action as more is available to cross the phospholipid membrane. A cororally of this characteristic is the decreased efficacy of local anaesthetics in bacterially infected tissues which, due to CO2 production are acidic and therfore exacerbates the difference between pKa and pH (in addition there is increased vasodilation and blood flow which decreases the anaesthetic efficacy). The intrinsic vasodilator activity varies between drugs and influences both the potency and the duration of action. In general local anaesthetics cause vasodilation in low concentrations (lignocaine>bupivacaine>ropivacaine) and vasoconstriction in higher doses.

**Local anaesthetic toxicity** can be caused by excessive amounts of the drug (max doses shown below), by rapid absorption and/or by impaired metabolism (such as patients with cardiac failure and liver disease). Perhaps more commonly it is seen after accidental intravascular injection. Systemic toxicity of local anaesthetics is concentration dependent, with CNS toxicity occuring a lower concentrations than cardiac toxicity.

| Lignocaine blood concentration µg/mL | 0 | 5 | 10 | 15 | 20 | 25 |
|---|---|---|---|---|---|---|
| | Therapeutic range | Mild CNS excitation | Severe CNS excitation | CNS Inhibition | Cardiac depression | |
| Symptoms | sedation<br>antiarrhythmic effects | tinnitis<br>altered sound perception<br>lightheadedness<br>circumoral numbeness<br>paresthesias | agitation<br>confusion<br>muscle twitching<br>tremors<br>seizures | unconsciousness<br>central cardiorespiratory<br>-depression | impaired cardiac conduction<br>decreased contractility<br>cardiac arrest | |

More potent local anaesthetics, such as bupivacaine and ropivacaine also produce systemic toxicity but at lower levels. Bupivacaine has extremely high potency at cardiac $Na^+$ channels such that the cardaic symptoms occur prior to CNS symptoms. It appears that the R (+) enantiomer of local anaesthetics has greater affinity for the cardiac $Na^+$ channels which has lead to the development of S (-) enantiomer drugs levobupivacaine and ropivacaine. Other toxicity issues include anaphylaxis which is gerenally rare, transient neurological syndrome associated with intrathecal lignocaine and methemoglobinaemia which is associated with prilocaine.

**Prevention and management** Prevention involves ensuring the patient is not overdosed by using the reference values, using with caution in patients with congestive cardiac failure and liver failure, and being aware of the vascularity and risk of direct intravascular injection. Management of the situation if toxicity is suspected, involves stopping the injection immediately and prepare to treat the reaction. Aggressive resuscitation is indicated in most cases following ACLS protocols. Benzodiazepines are the drugs of choice for seizure control. Phenytoin is not effective and should be avoided. Propofol can be used to control seizures but has the risk of potentiating cardiovascular toxicity. In severe reactions, monitor the cardiovascular system (CVS) and support the patient with intravenous fluids and vasoactives as required. Small boluses doses of adrenaline are preferred. Vasopressin is not recommended. Amiodarone is the drug of choice for ventricular arrhythmias due to local anesthetic toxicity.

| | Bupivacaine | Lignocaine |
|---|---|---|
| Classification of local anaesthetic (amide / ester) | Amide | Amide |
| Relative potency (lipid solubility) | 8 times more potent | 1 |
| Toxic dose<br>Toxic dose with adrenaline | 2mg/kg<br>2mg/kg | 3mg/kg<br>7mg/kg |
| Toxic plasma concentration | >1.5 mcg/kg | >5 mcg/kg |
| Protien binding (duration of action) | 95% | 70% |
| Elimination half time | 160 minutes | 100 minutes |
| pKa (onset of action)<br>% un-ionised at physiological pH 7.4 | 8.1<br>15% | 7.9<br>25% |

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