

GUIDELINES FOR DRUG PRESCRIBING AND MONITORING

B. THERAPEUTIC GUIDELINES

1. LOCAL ANAESTHETIC (LA) AGENTS - STRUCTURAL CLASS & ALLERGY:

Local anaesthetics are grouped into two categories depending on their chemical structure: aminoamides and aminoesters. Esters are less stable in solution and are broken down in plasma by hydrolysis. Amides are very stable and are broken down in the liver.

True hypersensitivity (IgE mediated reaction) to LAs is rare and accounts for <1% of all reported adverse reactions. Allergic reactions have primarily been reported with **ester-type LAs**, possibly due to their similarity in structure with para-aminobenzoic acid (PABA), which is known to be allergenic in nature. Cross sensitivity among members of the ester group and structurally related compounds (paraben preservatives) has been documented. Hypersensitivity to amide-type LAs is extremely rare and may be due to the preservative (metabisulfite, methylparaben or other substances that are structurally similar to PABA) or to accidental intravascular injection of an epinephrine-containing local anesthetic, however a few reports are present in the literature^{3,4}. These reports suggest that cross-reactivity exists among LA agents belonging to the amide group.

Most untoward effects allegedly ascribed as allergic reactions may be attributed to other factors such as acute toxicity, psychomotor reactions, the presence of preservatives (methylparaben and metabisulfite) or systemic epinephrine administration instead of the drug itself. Differentiating between allergic and adverse reactions is often difficult because of the similarity of the symptoms. Thus many patients are conservatively labeled as “allergic” to all “-caine” drugs even when the signs and symptoms are consistent with adverse reactions. In a patient presenting with a history of allergy to local anesthetic the first step is to ascertain the signs and symptoms of the reaction (See Table 1).

It is suggested that the best option for patients having a true allergic reaction to an LA of one class is the use of an LA from the other class. As well, preservative-containing solutions should be avoided.

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Table 1: Adverse reactions to local anesthetics (taken from Adriani et al⁷)

Nonallergic symptoms	
Transient CNS excitation - agitation, disorientation, nausea, apprehension, slurred speech, tremors, convulsions - followed by CNS depression - lethargy, respiratory depression, myocardial depression, hypotension	Due to inadvertent intravascular injection of local anesthetic
syncope, tachycardia	Psychomotor reactions secondary to patient apprehension - occur because of increased vasovagal activity and elevated levels of endogenous catecholamines
Tachycardia, palpitations, diaphoresis, apprehension, nervousness, pallor, hypertension, headache, nausea	Toxic reaction to epinephrine used concomitantly with local anesthetic
Allergic symptoms	
Inflammation, burning, edema, erythematous macules, papules, exudation, crusting, urticaria, pruritis, wheals	Contact dermatitis (most frequent allergic reaction)
Severe hypotension, bronchospasm, dyspnea, asthma, general urticaria, laryngeal and/or pharyngeal edema	Anaphylaxis (rare, but life threatening)

Alternate therapies: In the rare instance that hypersensitivity to both ester and amide local anesthetics occurs, then alternative therapies including diphenhydramine, benzyl alcohol, opioids, or general anesthesia can be used.

Diphenhydramine 0.5 to 1.0% and benzyl alcohol 0.9% are alternative anesthetic choices in patients with true allergies to the amides and/or ester-type anesthetics. Some clinical trials have determined that 1% diphenhydramine is approximately equivalent to 1% lidocaine. Although diphenhydramine is an effective local anesthetic, its injection is more painful than lidocaine and can cause tissue irritation and even skin necrosis. Thus, its role for local anesthesia is extremely specific and limited to those patients who have true allergies to ester or amide anesthetics, which are quite rare. Benzyl alcohol 0.9% with epinephrine (1:100,000) is as effective as lidocaine and superior to diphenhydramine as an LA. However, the duration of action is short, and about 30 percent of patients need additional anesthetic injection during the procedure.⁷

Pregnancy: Safe use of local anesthetics during pregnancy prior to labor has not been established with respect to adverse effects on fetal development. Careful consideration should be given to this fact before administering these drugs in pregnant women. Local anesthetics generally cross the placenta rapidly, and when used for epidural, paracervical, pudendal, or caudal block anesthesia, can cause varying degrees of maternal, fetal, and neonatal toxicity. The incidence and degree of toxicity depend on the procedure performed, the type and amount of drug used, and the technique of drug administration. Adverse reactions in the parturient, fetus, and neonate involve alterations of the CNS, peripheral vascular tone, and cardiac function.⁷

In addition to differences in structural class, the LAs vary in regard to potency, onset time duration and toxicity. The following tables provide information on these differences (see Table 2 and 3).

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Table 2: Injectable Formulations

	Drug	Potency (Equianesthetic Concentration)	Onset of Action	Duration of Action	Routes of Administration	Preparations available in RQHR (PF = preservative free)	Comments
AMIDES	Bupivacaine (Marcaine®, Sensorcaine®)	High (0.25)	moderate-slow (4-10 min)	1.5 - 8.5 hours	infiltration, nerve block, epidural, intrathecal/spinal,	0.25% inj 0.25% PF inj 0.25% w epi 1:200,00 PF inj 0.5% inj 0.5% PF inj 0.5% w epi 1:200,000 PF inj 0.75% spinal inj	- less effect on motor nerves than other LAs
	Lidocaine (Xylocaine®)	Intermediate (1)	intermediate	intermediate	topical, infiltration, IV regional, nerve block, epidural, intrathecal/spinal	0.5% inj 1% inj 1% PF inj 1% w epi 1:100,000 inj 1% w epi 1:200,000 inj 2% inj 2% PF inj 2% w epi 1;100,000 inj 2% w epi 1:200,000 PF inj	- most commonly used drug
	Mepivacaine (Carbocaine®, Polocaine®)	Intermediate (1)	intermediate (7-15 min epidural)	intermediate (2-2.5 hours)	infiltration, nerve block, epidural, intrathecal/spinal	1% inj 2% PF inj	- similar to lidocaine, but less toxic
	Prilocaine (Citanest®)	Intermediate (1)	intermediate	intermediate	infiltration, nerve block	NOT available in RQHR	- for dental use only
	Ropivacaine (Naropin®)	High (0.3)	moderate-slow (3-15 min)	long (3-15 hours)	infiltration, nerve block, epidural	0.5% PF inj	- use in labor and birth - decreased CNS toxicity and cardiotoxicity
ESTER	Drug	Potency (Equianesthetic Concentration)	Onset of Action	Duration of Action	Routes of Administration	Preparations available in RQHR (PF = preservative free)	Comments
	Chlorprocaine (Nesacaine®)	Low (2)	rapid	short	Infiltration, nerve block, epidural	2% PF inj	- low toxicity with rapid but short action
	Tetracaine (Pontocaine®)	High (0.25)	slow	long	Topical, nerve block, intrathecal/spinal	0.5% eye drop NO IV available in RQHR	IV is non-formulary and NOT available in RQHR

NOTE: Procaine (Novocaine®) is no longer available for human use in Canada.

* Products containing epinephrine also include sodium bisulfite or metabisulfite as a stabilizer. People with sulfite allergies may react to these products therefore a local anesthetic without epinephrine should be used.

Table 3: Topical Formulations

A M I D E S	Drug	Potency (Equianesthetic Concentration)	Onset of Action	Duration of Action	Routes of Administration	Preparations available in RQHR	Comments
	Dibucaine* (Nupercainal®)		intermediate (~15 min)	long (2-4 hours)	topical	0.5% cream 1% ointment	- topical and rectal use
	Lidocaine (Xylocaine®)	Intermediate (1)	intermediate	intermediate	topical, infiltration, IV regional, nerve block, epidural, intrathecal/spinal	2% viscous 2% topical jelly 4% topical solution 5% ointment Endotrach spray	- most commonly used drug
	Lidocaine & prilocaine * (EMLA®)		slow (1-2 hrs post application)	up to 5 hours	topical	2.5%/2.5% cream	- use in children pre- venipuncture
E S T E R S	Drug	Potency (Equianesthetic Concentration)	Onset of Action	Duration of Action	Routes of Administration	Preparations available in RQHR	Comments
	Benzocaine / Antipyrine* (Auralgan®)		rapid ~1 min	short 15-20min	Topical	Ear drops	- antipyrine is a wax softener
	Benzocaine/ cetylpyridium* (Cepacol®)		rapid ~1 min	short 15-20min	Topical	Lozenges	- cetylpyridium is an antiseptic
	Cocaine*	High	rapid (1 min)	short (≥30 min)	Topical use only*		
	Proparacaine* (Alcaine®)		rapid (20 sec)	short (15-20 min)	Topical	0.5% eye drop	
	Tetracaine (Pontocaine®)	High (0.25)	slow	long	Topical, nerve block, intrathecal/spinal	0.5% eye drop	IV is non-formulary and NOT available in RQHR
	Tetracaine/ Lidocaine/ Epinephrine* (LET®)			20-30min	Topical	available	

*topical use only – indicated for topical anesthesia of ear, nose and throat only due to its abuse potential as well as its potential to cause unexpected rapid and severe adverse reactions

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