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Local anaesthesia outside the operating room

手術室外的局部麻醉法

An increasing number of minor surgical procedures are performed under local anaesthesia in clinical settings outside the operating room, where monitoring and resuscitation equipment—as well as personnel skilled in resuscitation—may not be readily available. Serious adverse effects and even fatalities may result from the use of local anaesthetic agents, arising from a variety of causes such as systemic toxicity, allergy, vasovagal syncope, and reaction to additives present in the local anaesthetic. This article briefly reviews the pharmacology of local anaesthetic agents, and describes various techniques commonly used for local anaesthesia, with special emphasis on safety. Clinical features of toxicity, and its differential diagnosis and management, are also discussed.

在手術室外以局部麻醉進行的小手術日益增多，這時可能沒有監測和復甦設備以及熟練的復甦人員。使用局部麻醉劑可能會產生嚴重的不利結果甚至不幸，發生的原因可能為系統中毒、過敏、血管迷走神經昏厥、以及對出現在局部麻醉中的添加劑產生反應。本文簡要回顧了局部麻醉劑的藥理學，描述了通常用於局部麻醉的各種技術，特別強調安全性。我們還討論了毒性的臨床特徵，以及各種診斷和處置方法。

Key words:
Ambulatory surgical procedures;
Anesthetics, local;
Drug toxicity;
Pharmacology;
Safety

關鍵詞：
流動外科手術程序；
局部麻醉；
藥物毒性；
藥理學；
安全

HKMJ 2002;8:106-13

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Introduction

Since the introduction of cocaine into clinical practice by Koller in 1884, the history of surgery has changed dramatically. Pain-free surgery can now be accomplished under local anaesthesia, with improved patient comfort and cooperation. Local anaesthesia is defined as the reversible loss of sensation in a relatively small or circumscribed area of the body, achieved by topical application or injection of agents that either depress the excitation of nerve endings or inhibit the conduction of impulses along a peripheral nerve.[1] While there are many ways of producing local anaesthesia, such as topical application of ice or vapo-coolant ethyl chloride,[2] local anaesthetics (LAs) are by far the most commonly used.

Traditionally, surgery is performed in the operating room, where monitoring and resuscitation equipment, as well as personnel trained in resuscitation, are readily available. However, because of the increased safety of surgery and anaesthesia, and socio-economic factors, an increasing number of minor surgical procedures are being performed under local anaesthesia outside the operating room.[3,4] Since potential fatal complications can occur with the use of LAs, a good understanding of LA pharmacology is the key to safe use of these agents. This article reviews the pharmacology, toxicity, and clinical aspects of LAs applicable to settings outside the operating room.

Pharmacology of local anaesthetics

Classification and metabolism

Local anaesthetic agents contain a hydrophobic aromatic ring, which is connected to a hydrophilic secondary or tertiary amine by an intermediate alkyl chain made up of either an amide or ester bond. This linkage to the aromatic ring forms the basis for classifying LAs into amino-esters (eg cocaine, procaine, chloroprocaine,

amethocaine) and amino-amides (eg lignocaine, bupivacaine, etidocaine, ropivacaine), and is also an important determinant of biodegradation. The amino-ester compounds are readily hydrolysed in plasma by pseudocholinesterase to para-aminobenzoic acid (PABA), whereas the amino-amide compounds are more slowly metabolised by the hepatic microsomal enzymes to inactive metabolites.

Physicochemical properties

All LAs are weak bases. In solution there exists a chemical equilibrium between the non-ionised form (B) and the ionised form (BH^+). At a specific pH (pK_a), the concentration of the non-ionised form is equal to the concentration of the ionised form of the LA, and their relationship is defined as:

$$\frac{[BH^+]}{[B]} = 10^{(pKa-pH)}$$

Mechanism of action

There is increasing evidence that LAs impair sodium ion flux across the neuronal membrane by blocking the sodium channels. This results in the inhibition of the rate and amplitude of depolarisation of the neuronal membrane.[5] After injection of an LA, the non-ionised form of the LA is released into the relatively alkaline pH of the tissues.

$$B + H^+ \Leftrightarrow BH^+$$

This non-ionised form (B) then diffuses through the nerve sheath and the neuronal membrane to reach the axoplasm, where it becomes partially ionised. It is this ionised form (BH^+) that blocks the sodium channel (Fig).

Local anaesthetics with a low pK_a are absorbed faster into nerve tissues, and thus have a more rapid onset in action. In contrast, LAs with a high pK_a, although they diffuse into the nerve tissues much more slowly, produce more effective blockade and have a longer duration of action, because they also diffuse out slowly. Local anaesthetics are less effective when injected into tissues which are relatively acidic (eg abscesses) because of reduced availability of the non-ionised form.

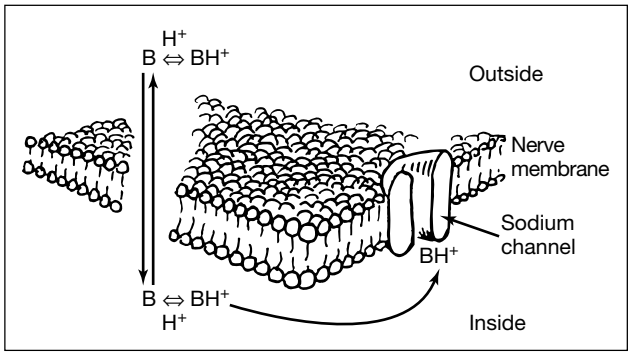

Fig. Local anaesthetics exist in non-ionised (B) and ionised (BH^+) forms in physiological solution

The non-ionised form (B) readily diffuses across the cell membrane and re-ionises to form BH^+ within the cell, which then binds to sodium channels to impair sodium influx across the neural membrane

Preparation

Most LAs are bases that are almost insoluble in water. Solubility is greatly enhanced by their preparation as the hydrochloride salt, which is usually dissolved in modified isotonic Ringer solutions. Dilute preparations of LAs are usually acidic (pH 4.0-5.5), and contain a reducing agent (eg sodium metabisulphite) to enhance the stability of added vasoconstrictors. Methylparaben is also added to multidose vials of lignocaine as a preservative.

Pharmacological profile

The pharmacological activity of an LA is determined by its physicochemical properties. These include lipid solubility, protein binding, and pK_a, which determine LA potency, duration of action, and onset time, respectively. Table 1 summarises the pharmacological profiles of LAs commonly used in Hong Kong.

The effect of an injected LA is terminated mainly by absorption to the systemic circulation, which is dependent on local blood flow.[5] Agents with high protein binding, such as bupivacaine, bind to the local tissue, and hence have a longer duration of action. Most LAs, except cocaine and to a certain extent ropivacaine, produce some degree of vasodilatation, and hence are rapidly absorbed after local injection. Consequently, vasoconstrictors are frequently added to reduce systemic absorption, which may result in reduced systemic toxicity and an increase in the margin of safety (see below).

Factors affecting anaesthetic activity

Dosage of local anaesthetic solutions

As the dose of LA is increased, the quality of anaesthesia, ie the onset, depth, and duration of nerve blockade, is improved.[6] This can be achieved either by using a large volume of a less concentrated LA solution, or a small volume of a more concentrated LA solution. However, with the same dosage, larger volumes produce greater spread after epidural injection.[7]

Site of injection

The site of injection can influence the onset time and duration of nerve blockade of an LA. For example, bupivacaine, when used for intercostal nerve block, has an onset time of approximately 5 minutes and duration of effect of approximately 4 hours, and when used for brachial plexus block has an onset time of approximately 30 minutes and duration of around 10 hours.[6] These differences can partly be explained by differences in anatomy, and variable rate of vascular uptake from the site of injection.

Addition of vasoconstrictors

Vasoconstrictors are frequently added to LA solutions to decrease systemic absorption and thus increase the depth and duration of nerve blockade. In addition, vasoconstrictors, by sequestering LAs in tissues, can enhance LA potency and prolong the duration of nerve blockade. Adrenaline

Table 1. Pharmacological profile of local anaesthetics available in Hong Kong[2]

Agent	Concentration (%)	Onset of action with infiltration	Onset of action with nerve block (mins)	Duration of action with nerve block (mins)	Maximum single dose without adrenaline	Maximum single dose with adrenaline
Lignocaine	1-2	Fast	4-10	60-120	4.5 mg/kg	7.0 mg/kg
Bupivacaine	0.25-0.5	Moderate	8-12	240-480	2.5 mg/kg	2.5 mg/kg
Ropivacaine*	0.2-1.0	Fast-moderate	8-12	240-480	150-200 mg†	ND‡
Cocaine§	1-4	-	-	-	3 mg/kg	-

* Data from Mather and Chang[19]
† Manufacturer's (AstraZeneca, Södertälje, Sweden) quoted maximum dose
‡ ND data not available
§ Cocaine is indicated only for topical anaesthesia of mucosal membranes

(epinephrine) is the most commonly used vasoconstrictor, at a concentration of 1:200 000 (5 mg/mL), which provides optimal vasoconstriction with lignocaine,[8] although concentrations ranging from 1 in 80 000 to 1 in 300 000 are also available. Adrenaline also acts as a marker for inadvertent intravascular injection. The effect of adrenaline on the duration of action is most profound with LAs having short-to-moderate duration of action, eg lignocaine.[9] Local anaesthetics which are more potent and longer acting, such as bupivacaine, are influenced less by the addition of adrenaline, particularly when such agents are used for epidural blockade.[10] Other vasoconstrictors, such as noradrenaline (norepinephrine) and phenylephrine, have also been used in conjunction with LA solutions. However, studies were unable to demonstrate superiority of these agents to adrenaline.[11,12]

Use of additives with local anaesthetics

Attempts have been made to modify LA solutions in a number of ways, in order to improve the onset of action or prolong the duration of nerve blockade. Adding sodium bicarbonate (1 mmol/10 mL LA solution) to lignocaine decreases the onset time after epidural injection by increasing the amount of non-ionised drug (because of the more alkaline medium).[13]

Mixtures of local anaesthetics

The advantages of mixing two LAs are, in theory, to allow the use of a smaller amount of any one drug, thus limiting its toxicity, and to combine the rapid onset of one drug with the long duration of the other, eg chloroprocaine mixed with bupivacaine.[14] However, this has not been demonstrated consistently.[15,16] At present there appears to be no significant clinical advantage in using mixtures of LAs.[9]

Toxicity and adverse effects of local anaesthetics

Adverse reactions to LAs include systemic effects, localised reactions, specific adverse effects related to particular LAs, allergy, and addiction. Other toxic reactions may be related to the additives, such as adrenaline and preservatives, rather than the LA itself. Considering the large number of LAs administered worldwide, the frequency of toxic reactions is extremely low. Moreover, most adverse reactions following LA administration are due to inappropriate use, such as overdose and inadvertent intravascular or intrathecal injection.

Systemic toxicity

Injected LAs are absorbed into the systemic circulation, and toxic effects on the central nervous system (CNS) or cardiovascular system (CVS) depend on the plasma level of the drug (Boxes 1 and 2). The rate of change, as well as the absolute plasma level of LA, influences toxicity with more rapid accumulation being more toxic.[17] Hence, doses of LA that are considered safe for local infiltration may become toxic when injected intravascularly.

Most of the data on CNS toxicity are based on lignocaine, and are extrapolated to other LAs. Central nervous system toxicity is directly related to the plasma concentration. It is manifested by initial excitation (muscle twitching, convulsion) followed by depression (coma, respiratory arrest).

Cardiovascular system toxicity includes dose-dependent myocardial depression, severe ventricular arrhythmias, ventricular fibrillation (VF), and asystole. Bupivacaine is more cardiotoxic than lignocaine, since doses that cause irreversible CVS collapse are close to those producing CNS toxicity.[18] Acidosis and hypoxia markedly potentiate the cardiotoxicity of bupivacaine, and pregnant patients are more susceptible. Ropivacaine, a new amino-amide LA agent recently introduced for clinical use in Hong Kong, has a sensory block profile very similar to bupivacaine, but produces less motor blockade and is less cardiotoxic than bupivacaine.[19] Levobupivacaine, the S-enantiomer of bupivacaine, which is not yet available in Hong Kong, also exhibits similar potency but is less toxic.[19]

Box 1. Factors affecting systemic toxicity

- Potency of the local anaesthetic
- Total dose administered
- Addition of exogenous vasoconstrictor
- Vascularity of the tissues
- Rate of systemic uptake
- Patient's acid-base status

Box 2. Signs and symptoms of local anaesthetic toxicity (with increasing plasma concentration)

- Numbness of tongue
- Lightheadedness
- Visual and auditory disturbances
- Muscular twitching
- Unconsciousness
- Convulsions
- Coma
- Respiratory arrest
- Cardiovascular depression

Direct local tissue toxicity

Under experimental conditions, high concentrations of LAs,[20] and various buffers and preservatives added to LAs, are neurotoxic.[21] Under clinical conditions, intraneural injection, by causing pressure effects on the nerve fasicles,[17] may contribute to some of the observed nerve injuries. Full thickness skin necrosis has been reported after subcutaneous infiltration of 1% lignocaine, which is presumably due to the added adrenaline.[22] Nevertheless, commercially available LAs are generally safe for clinical use.

Allergy

Although reports of allergic reactions, hypersensitivity, or anaphylactic reactions to LA agents appear periodically,[23,24] it is often found that these 'reactions' have been confused with systemic toxicity,[25] vasovagal syncope, or allergy to the preservatives methylparaben or metabisulphite.[26,27] In addition, the majority of LA allergies are associated with the ester agents,[28] and are related to the metabolite PABA. True allergy to amide-type LAs is extremely rare.[1,5] Allergic cross-reactivity between amide and ester agents is weak. Patients sensitive to one ester are likely to be sensitive to the entire group, whereas patients who are allergic to one amide LA may be able to tolerate an alternative amide.[1] In patients with a history of an anaphylactic reaction to LAs, skin testing and subcutaneous challenge tests, with and without preservatives and/or adrenaline, is recommended.[1]

Adverse effects of specific local anaesthetics

Prilocaine, in doses exceeding 600 mg, can cause oxidation of the ferrous form of haemoglobin to the ferric form (methaemoglobin). Methaemoglobin cannot carry oxygen and the skin develops a bluish discolouration, in most cases benign and resolving spontaneously. However, when symptoms of tissue anaemia do occur, it can be promptly treated with intravenous methylene blue.

Cocaine, which causes vasoconstriction and inhibits the reuptake of catecholamines, can cause hypertension, tachycardia, arrhythmia, myocardial ischaemia, and sudden death. Although the maximum recommended dose of cocaine in adults is 1-3 mg/kg,[29] fatalities have been reported following the use of less than 200 mg.[30] Management of cocaine toxicity is mainly supportive, with benzodiazepines for the treatment of convulsions. Although propanolol has been used successfully to treat cocaine-induced cardiac effects,[31] β-blockers should be used with caution because of unopposed α-receptor–mediated effects.[32] Alternatively, a short-acting β-blocker such as esmolol may be considered.[33] Although cocaine is a commonly used 'street drug', it has no known addictive risks if used appropriately on a one-time basis as an LA.[34]

Clinical applications

The choice of an LA depends on the clinical profile of the specific agent, ie the onset time, duration of action and toxicity, and the clinical situation. Bupivacaine, for example, should not be used for intravenous regional anaesthesia (IVRA), and prilocaine should be avoided in patients with low levels of methaemoglobin reductase, or glucose-6 phosphate dehydrogenase deficiency.[35]

Topical anaesthesia

Topical anaesthesia of mucosal membranes can be achieved with a number of agents, eg cocaine and amethocaine. Cocaine, because of its unique properties of both local anaesthesia and vasoconstriction, remains popular among otorhinolaryngologists. Caution must be exercised when combining cocaine with adrenaline, as cumulative toxicity can occur.[36] Alternatives, such as 1 to 2% lignocaine with adrenaline or other vasoconstrictors, may be considered.

Topical anaesthesia of the skin, because of poor penetration by the LA, is more difficult to achieve. A mixture of the crystalline bases of lignocaine and prilocaine, by reducing their melting points, produces a liquid at room temperature, which is called a 'eutectic mixture of local anaesthetics' (EMLA). A eutectic mixture of LAs 1 to 2 g/10 cm^2 of skin is applied under an occlusive dressing. An EMLA patch (AstraZeneca, Södertälje, Sweden) is currently available; this consists of an adhesive disc impregnated with EMLA cream 1 g intended for anaesthesia of 10 cm^2 of skin. When EMLA cream is applied under an occlusive dressing, an anaesthetic depth of 3 mm is achieved after 60 minutes.[37] The depth increases by 1 mm per 30 minutes up to 5 mm at 120 minutes. However, in highly vascular sites, such as the face or damaged skin, the onset is much more rapid.[37] Adverse effects of EMLA are minimal, and include local erythema, pallor, oedema, pruritus, and potentially methaemoglobinaemia attributable to prilocaine.

Local infiltration

This technique involves injection of LA directly into the tissue; pain during injection is therefore common. Several approaches to reducing pain on injection have been suggested: deep intradermal rather than superficial dermal injection, slow injection using a long needle of the smallest possible calibre, administration of the LA solution at body temperature, the LA buffered with sodium bicarbonate in a 10:1 ratio, use of the smallest amount of the lowest concentration, and use of the smallest volume syringe that can provide the desired amount of local anaesthesia.[2]

Field block

When local infiltration of the surgical margin is deemed inappropriate, such as with a contaminated wound, or when it is necessary to avoid tissue distortion (eg the ear), local anaesthesia can be achieved by injecting the LA around the area under consideration.

Tumescent technique

Tumescent anaesthesia is the technique of anaesthetising large areas of adipose tissue. It is commonly used for liposuction,[38] but more recently has also been used for

procedures such as hair transplantation, ambulatory phlebectomy, wide cutaneous excision, and facial resurfacing.[39] This technique involves infiltrating adipose tissue with large volumes of a dilute lignocaine solution (0.05 to 0.2%) with adrenaline (1:1 000 000).[38] Sodium bicarbonate (1 mEq/100 mL LA solution) may also be added to buffer the LA solution.[38] Large total doses of lignocaine up to 55 mg/kg are frequently used[40]; although this exceeds the maximum recommended dose for infiltration anaesthesia, toxic complications are rare. This may be due to the slow systemic absorption of lignocaine from adipose tissues, resulting in plasma concentrations of lignocaine below the toxic range.[39] However, several deaths have been reported following liposuction, and LA toxicity masked by the concomitant use of sedatives has been suggested as a possible cause.[41]

Intravenous regional anaesthesia

This is the technique of producing anaesthesia by administering an LA intravenously in an exsanguinated and tourniquet-occluded limb. Proper monitoring and immediate availability of resuscitation facilities are essential for management of toxic reactions that may occur in the event of a tourniquet failure. The tourniquet should not be released for at least 30 minutes after the LA injection. Prilocaine, because of its high therapeutic ratio, is recommended for IVRA.[42] However, since it is unavailable in Hong Kong, 0.5% lignocaine is used. Bupivacaine, because of its cardiotoxicity, should not be used for IVRA.[18] Contraindications include sickle cell disease or trait, untreated heart block, and local infection.

Haematoma block

This is the technique of injecting LA directly into the haematoma, which has been used in management of fractures such as Colles' fracture. However, IVRA has been shown to be superior to haematoma block in terms of efficacy, radiological result, and remanipulation rate.[43]

Peripheral nerve block

Simple peripheral nerve blocks, such as digital and penile nerve block, can be used for minor surgery. More complex nerve blocks, such as brachial plexus block, require a thorough understanding of the anatomy and adequate training. The use of adrenaline-containing LA must be avoided in areas supplied by end-arteries (eg in digital nerve block, penile block), because of the potential risk of producing ischaemia. Ropivacaine has intrinsic vasoconstrictor properties, and in a recent case report was implicated as a cause of ischaemia of the glans penis after penile nerve block.[44] Thus, until further evidence is available, it may be wise to exercise caution when using ropivacaine for local anaesthesia in areas where there is potential for end-artery ischaemia.

Safety aspects with clinical use of local anaesthetics

In order to avoid inadvertent intravascular injection and toxicity, the syringe should be intermittently aspirated for blood, the smallest volume of the lowest concentration of LA producing anaesthesia should be used, and the LA should be administered slowly in small aliquots. Patients should lie supine during the block, in case unexpected syncope occurs. In the event that the patient becomes unconscious, LA administration should be discontinued immediately, and basic cardiopulmonary resuscitation (CPR) initiated, with oxygen supplementation as indicated. At the same time, the physician must distinguish between vasovagal reaction, systemic toxicity, and anaphylactic reaction (Table 2). Subsequent management depends on the cause of the syncope.

Dosage of local anaesthetics

Local anaesthetic agents currently available in Hong Kong, together with their clinical profile and the maximum recommended doses,[45] are summarised in Table 1. As these doses are based on animal studies, and as the plasma concentration of an LA varies considerably with the site of injection, this 'maximum recommended dose' has been challenged.[46,47] Lignocaine has been used in doses of 900 mg (approximately 18 mg/kg) for brachial plexus block,[46] and in dosages up to 55 mg/kg for tumescent anaesthesia,[40] without producing toxic plasma levels, or clinical signs or symptoms of toxicity. Clinicians should exercise clinical judgement, depending on experience and available facilities, when deciding on the dose of an LA agent.

Monitoring and resuscitation equipment

Recommendations on office-based surgical facilities for surgical procedures outside the hospital setting were published recently.[48] For surgical procedures performed under local anaesthesia, and in cases where oral or

Table 2. Differential diagnosis of local anaesthetic reactions and treatment[9]

Aetiology	Main clinical features	Treatment
Local anaesthetic toxicity		
Intravascular injection	Immediate convulsions ± cardiac arrhythmias	Cardiopulmonary resuscitation, benzodiazepines; consider bretylium for refractory ventricular fibrillation
Relative overdose	Onset of irritability within 5-15 minutes progressing on to convulsion	
Reaction to vasoconstrictor	Tachycardia, hypertension, headache, apprehension	General supportive measures; consider short-acting β-blocker if persistent tachycardia and hypertension
Vasovagal reaction	Rapid onset of bradycardia, hypotension, pallor, faintness	Leg elevation, atropine
Anaphylaxis	Hypotension, bronchospasm, urticaria, oedema	Subcutaneous adrenaline injection

intramuscular sedation may be administered, the following should be available:

(1) a blood pressure measuring device, such as a sphygmomanometer and stethoscope;
(2) a source of airway maintenance, such as a mouth-to-mouth resuscitation device, or a self-inflating bag and mask; and
(3) a source of oxygen delivery up to 5 L/min.

In addition, adrenaline 1:1000 for subcutaneous administration and injectable antihistamines should be readily available for possible allergic reactions. The physician and appropriate staff should be trained in basic CPR, and there should be a well-established plan of action to deal with unexpected emergencies.

Management of systemic toxicity

When signs and symptoms of CNS toxicity occur, the injection should be stopped immediately. Minor symptoms seldom require treatment, other than constant verbal contact, CVS monitoring, and oxygen supplementation as indicated. Airway maintenance and assisted ventilation with oxygen supplementation is essential if respiration stops (Box 3). Should convulsions develop, diazepam 5 to 10 mg or thiopentone 50 to 100 mg (if available) should be administered intravenously. Prevention of hypoxia and acidosis are of utmost importance during treatment.[9]

Hypotension should be treated with intravenous fluid, leg elevation, correction of hypoxia, and vasopressors (eg ephedrine 15 to 30 mg). Cardiopulmonary resuscitation should be initiated when profound CVS depression is present. Ventricular tachycardia or fibrillation should be treated with cardioversion (higher energy may be required). As bupivacaine dissociates from sodium channels slowly, CPR should be continued for at least 60 minutes or more in patients with bupivacaine-induced VF. The medical treatment for bupivacaine-induced ventricular arrhythmias remains controversial. Lignocaine, paradoxically, has been used.[49] Bretylium may facilitate cardioversion in refractory VF.[50] Ventricular arrhythmias resistant to bretylium have been reverted successfully by phenytoin in neonates.[51] In anaesthetised animals, dobutamine and clonidine have been found to be beneficial in correcting the haemodynamic and electrophysiological abnormalities.[52]

Box 3. Treatment of systemic local anaesthetic toxicity[9]

Airway
Establish clear airway; suction, if required

Breathing
Oxygen with face mask
Encourage adequate ventilation
Artificial ventilation, if required

Circulation
Elevate legs
Increase IV* fluids if ↓ blood pressure
CVS† support drug if ↓ blood pressure persists or ↓ heart rate
Cardioversion for ventricular arrhythmias

Drugs
Central nervous system depressant
- Diazepam 5-10 mg IV, midazolam 2-5 mg
- Thiopental 50 mg IV, incremental doses until seizures cease
  CVS support
- Atropine 0.3-0.6 mg IV, if ↓ heart rate
- Ephedrine 15-30 mg IV, to restore adequate blood pressure
- Adrenaline for profound cardiovascular collapse

* IV intravenous
† CVS cardiovascular system

Special patient groups

Following the report of 31 maternal deaths after the use of 0.75% bupivacaine for epidural anaesthesia, this concentration has been withdrawn from obstetric anaesthetic use in the United States.[18] It is suggested that the increased susceptibility of pregnant patients to the cardiotoxic effects of bupivacaine is due to the direct effects of progesterone.[53] On the other hand, lignocaine, because of its low pK_a and propensity for ion trapping, is not indicated in large doses for obstetric patients, especially where foetal distress is present, in order to avoid foetal toxicity.[17] Moreover, concerns have also been raised recently regarding transient neurological symptoms occurring after spinal anaesthesia with lignocaine.[54] Being less cardiotoxic than bupivacaine, ropivacaine is gaining popularity among obstetric anaesthetists. Nevertheless, LAs should be used with caution in obstetric patients, and foetal monitoring may be required. Elective surgical procedures should be delayed until after the period of organogenesis.[55]

In children, the recommended maximum LA dosages adjusted to body weight are similar to those in adults (Table 1).[56] However, LA doses in neonates must be reduced, especially during infusion, because of diminished protein binding and immature hepatic clearance.[56] In older infants and children, because of their inability to describe warning symptoms, and the difficulty of reliably detecting intravascular injection, it is essential that LA injection occurs slowly, in small increments, with constant assessment of the child for signs of toxicity.[56]

Drug interactions

Caution should be exercised in patients on concurrent medications. Monoamine oxidase inhibitors may precipitate a hypertensive crisis when exogenous adrenaline contained in the LA solution is administered. Phenothiazines, because of their irreversible α-blocking properties, may cause hypotension and cardiac arrest, due to additional vasodilatation caused by the LA.[1] Serious hypertension-bradycardia has been reported in a patient on a β-blocker because of interaction with adrenaline.[57] Cimetidine, β-blockers, and procainamide, by reducing hepatic blood flow, may decrease lignocaine metabolism and lead to accumulation of the LA.[58] Hence, a detailed drug history should be taken before administration.

Multidose vials

Four patients were infected with human immunodeficiency virus (HIV) in a doctor's surgery in Australia.[59] These patients underwent minor skin surgery after another patient who was HIV-infected, and no identifiable breach of

infection control guidelines was found. A separate report later described the observation that needles and syringes retained small volumes (25 mL) of fluid after use, which could be transferred to multidose vials, and that active HIV could be isolated from the contaminated multidose vial after up to 4 hours.[60] Hence, use of multidose vials of LA for more than one patient is no longer recommended.

Conclusion

Currently available LA agents are safe if used with due care and caution. One must exercise extra caution when using these drugs outside the operating room, as monitoring and resuscitation equipment may not be readily available. Clinicians should have a clear understanding of LA pharmacology, toxicity, and factors predisposing to LA toxicity before administering these drugs. The amount of LA injected should be carefully calculated to avoid unintentional overdose. Inadvertent intravascular injection must be avoided. There should be a well-established plan of action to deal with unexpected complications in settings where LAs are administered.

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