LOCAL ANESTHETIC DRUGS

Local anesthetics are drugs that, when applied locally to nerve tissue (endings or fibers), cause reversible blockade of nerve impulse conduction. At effective concentrations, local anesthetics block transmission of autonomic, somatic sensory and somatic motor impulses. Thus, depending on the nerve and the area innervated, autonomic nervous system blockade, anesthesia, and/or skeletal muscle paralysis may result.

General properties

The typical local anesthetic molecule consists of an unsaturated aromatic group (imparting lipid solubility) linked by an intermediate chain to a tertiary amine end (imparting water solubility). The clinically important local anesthetics are divided into two distinct chemical groups based on their intermediate chain. The aminoesters contain an ester link, while the aminoamides contain an amide link, between the aromatic and amine ends. The agents most commonly administered in veterinary anesthesia are chloroprocaine, lidocaine, mepivacaine, and bupivacaine. All, except chloroprocaine, are aminoamides. Generally speaking, lidocaine and bupivacaine

will suffice for most veterinary practice situations. The clinically important properties of the local anesthetics include potency, speed of onset, duration of anesthetic action, and differential sensory/motor blockade. The clinically observed rates of onset and recovery from blockade are governed by the relatively slow diffusion of local anesthetic molecules into and out of the whole nerve. While, in vitro, these depend on the physicochemical properties of the different agents, in vivo, dose and concentration also affect onset of action. For example, 0.25% bupivacaine has a slow onset of action, but increasing the concentration to 0.75% results in a significant acceleration of anesthetic effect. Generally, lidocaine is considered to have a rapid onset of action (10–15 minutes), while bupivacaine has an intermediate onset of action (20–30 minutes). Lidocaine has a moderate duration of action (60–120 minutes) while bupivacaine has the longest duration (three to eight hours). Lidocaine is one of the most widely used local anesthetics and is available in concentrations from 0.5 to 5.0% with or without epinephrine, as well as in gel and ointment preparations. It can be used for all forms of regional anesthesia. Bupivacaine is available as 0.25, 0.5 and 0.75% solutions and is used most commonly for all forms of regional anesthesia except topical.

Bupivacaine demonstrates significant separation of sensory and motor blockade, meaning that it is able to produce adequate antinociception without profound inhibition of motor activity, particularly when dilute solutions are employed. For this reason, dilute bupivacaine is the choice in people for obstetrical anesthesia.

Mechanism of action

Local anesthetics inhibit the generation and propagation of nerve impulses by blockade of voltage-gated sodium channels in the nerve membrane. Local anesthetics are capable of blocking all nerves, thus their action is not limited to the usually more desirable sensory block but also motor loss. However, nerve fibers differ substantially in their susceptibility to local anesthetic blockade due to size and, presence and absence of myelin.

Factors influencing anesthetic activity

As the dosage of local anesthetic is increased, the probability and duration of satisfactory anesthesia increase, and the time to onset is shortened. The dosage of local anesthetic can be increased by administering either a larger volume or a more concentrated solution.

Vasoconstrictors, usually epinephrine (5 µg/mL or 1:200,000), are frequently included in local anesthetic solutions to decrease the rate of vascular absorption, thereby allowing more anesthetic molecules to reach the nerve membrane and so improve the depth and duration of anesthesia. The extent of this effect depends on the specific local anesthetic and the site of injection. Generally, epinephrine significantly extends the duration of both infiltration anesthesia and peripheral nerve blocks with many agents, such as lidocaine.

Site of injection also influences local anesthetic activity, with the most rapid onset but the shortest duration occurring following spinal or subcutaneous administration of local anesthetics. The longest latencies and durations are observed following brachial plexus block.

LOCAL ANESTHETIC TECHNIQUES

Local anesthetics are most often used to produce regional anesthesia (implying that a region rather than the entire body is affected). Regional anesthesia is usually divided into topical anesthesia, local infiltration, peripheral nerve block, intra-articular administration, intravenous block, epidural block and spinal (subarachnoid) block. Since epidural and spinal blocks form the basis of another lecture, this talk will exclude these two

categories of regional anesthesia. All local anesthetic agents can induce systemic toxicity manifested as convulsions followed by cardiac arrest. To prevent this, total doses administered by the various techniques need to be calculated and maximal safe doses known. As a general rule, the total infiltrative dose of lidocaine should be < 8 mg/kg in dogs and < 4 mg/kg in cats, while the dose of bupivacaine should be < 2 mg/kg in both dogs and cats.

Topical anesthesia

Lidocaine is effective when placed topically on mucous membranes and maybe used in the mouth, tracheobronchial tree, esophagus and genitourinary tract. Compared to infiltration, the time for onset of action is generally longer and the analgesia less; for example, topical application on mucous membranes penetrates to a depth of 2 mm and anesthesia lasts 15–20 minutes. The cream most commonly used on skin contains a 5% eutectic mixture of lidocaine and prilocaine (EMLA), which penetrates the cornified skin barrier within 1 hour of topical application. In people, topical application of lidocaine to wound edges was effective in reducing postoperative pain and the effect outlasted the expected duration of action of the drugs.(1,2) In dogs, bupivacaine solution left in contact with the surgical site for 20 minutes (splash block) was not found to be beneficial in

dogs undergoing ear ablation.(3) In cats, wound irrigation with bupivacaine prior to wound closure following onychectomy did not reduce postoperative pain compared with saline treated controls.(4) Interpleural administration of local anesthetic is advocated as a technique for providing postoperative analgesia following thoracotomy. Its popularity in people has waxed and waned and its efficacy is variable probably because of technical problems related to blood in the pleural space, chest tube drainage and pleural disease. Evaluation of this technique in dogs after intercostal thoracotomy demonstrated better pulmonary function and a more comfortable and quieter recovery compared to dogs treated with intramuscular morphine.(5)