A Primer on Local Anesthetics for Plastic Surgery

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KEYWORDS

• Local anesthetics • Mechanism • Sodium channel • Tumescent anesthesia • Duration of action • Complications

KEY POINTS

- Local anesthetics are efficacious for several plastic surgery procedures.
- Amino amides are the most commonly used local anesthetics.
- Potency, onset, and duration are related to lipid solubility and protein binding.
- Different agents have differing duration and onset.
- Local anesthetics block the voltage-gated sodium channel nonselectively.
- The voltage-gated sodium channel offers the potential for selectivity.
- Metabolism of amide local anesthetics depends on liver function.
- The addition of adjuvants can alter efficacy and safety.
- Local anesthetic systemic toxicity is life threatening.
- Bupivacaine in large doses is potentially fatal.
- Levobupivacaine and ropivacaine are safer agents and are suitable substitutes for bupivacaine.
- Where large doses of local anesthetic are used, lipid rescue kits, which can reduce morbidity and mortality, should be available.

INTRODUCTION

Local anesthetics are a major contributor to medical and dental practice throughout the world. No doubt most, if not all readers are aware of the effectiveness of this class of medication through personal experience. Provision and delivery of anesthesia and/or analgesia using local anesthetic can be accomplished in several ways. Local anesthetics have been administered as a field block, injection near minor or major nerves and plexuses, and injection into the epidural or intrathecal space. Other methods include transcutaneous application, tumescent anesthesia, and intravenous delivery.

HISTORY

Since the introduction of cocaine to medical practice in 1884, local anesthetics have been and continue to be a valuable tool in surgical practice. Since its isolation in 1855, cocaine was first synthesized in 1898. All synthetic local anesthetics are derivatives of cocaine. Many readers will recognize a handful of the 20 or so synthetic agents used historically. Like any pharmaceutical agent, there have been continued attempts to improve the efficacy and safety of this class of medication. Between 1891 and the 1970s several amino-ester (ester) and amino-amide (amide) local anesthetics have been synthesized.[1] Two newer agents have since been developed and introduced, primarily to address improved safety.

BASIC AND CLINICAL SCIENCE OF LOCAL ANESTHETICS

Amides

The most versatile of the group continues to be lidocaine. Lidocaine and the majority of local

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anesthetics currently used in surgical practice are amides. First developed in 1943, it is functional, relatively rapid in onset and removed, safe, and its use is extensive. The vast majority of plastic surgeons have a working clinical knowledge of lidocaine use. Perhaps the second most commonly used agent is bupivacaine, first developed in 1957 and released for clinical use in 1963. It is more potent and longer acting than lidocaine, and provides suitable anesthesia and/or postprocedure pain control on the order of 2 to 4 times that of lidocaine. The major drawback to its use is safety. Several fatalities caused by local anesthetic systemic toxicity (LAST) have involved the use of bupivacaine.[1]

Prilocaine was first synthesized in 1953. Its most common usage today is as a component of EMLA (a mixture of lidocaine and prilocaine). Some see this as a useful agent for intravenous regional anesthesia (IVRA). Prilocaine is also known for one of its toxic reactions, methemoglobinemia.

Mepivacaine, first synthesized in 1956, is similar to lidocaine with regard to onset and duration of action. It is thought to have some vasoconstrictive properties, which is a characteristic of few local anesthetics. Mepivacaine is a chiral molecule, and is sold as a racemic mixture of *R* and *S* optical isomers.

Articaine (synthesized in 1969) has extensive use in dental anesthesia. A PubMed search results in more than 300 references since the year 2000, most of which are related to dental practice, with some anesthesia studies. Its use in tumescent anesthesia for liposuction has been evaluated.[2] Possible advantages are rapid onset and short duration, attributable to an additional ester group on the lipophilic side chain that is rapidly metabolized.

Esters

Cocaine is still used in medical practice, primarily in nasal surgery. Other agents with fewer side effects are available, but cocaine's vasoconstrictive effects remain the primary reason for its use. Systemic absorption of cocaine can result in hemodynamic alteration in the patient.

Benzocaine, first synthesized in 1890, is not used in the clinical situation but is present in some over-the-counter cough drops.

Tetracaine was synthesized in the 1930s; its primary use is in topical anesthesia (ophthalmology) and in wound anesthesia.

Chlorprocaine, first introduced in 1955, is a rapid-onset, short-acting agent. Like most esters, it is rapidly metabolized by plasma esterases, so it is viewed as being very safe. In those with pseudocholinesterase deficiency, duration may be longer and the safety reduced. Since 2013, its availability in North America has been limited because of a manufacturing issue.

Newer Agents

For several years the agents listed thus far were the basis of local anesthesia. In response to fatalities involving bupivacaine, a search for a safer alternative was undertaken. Two commercially available amides were the result of this search: ropivacaine and levobupivacaine.

Synthesized in 1993 and introduced in 1996, ropivacaine is a single enantiomer. It has an improved risk profile in comparison with bupivacaine, and a similar duration of action. Ropivacaine does not cause the same degree of vasodilation as many local anesthetics. Use of ropivacaine in plastic surgery is limited,[3] although its use has been evaluated in digital nerve blocks[4] and infiltrative anesthesia.[5]

Similarly, levobupivacaine is the *S*-enantiomer of bupivacaine. Released in the late 1990s, its safety profile is better than that of racemic bupivacaine. The clinical effect is similar to that of ropivacaine and bupivacaine,[6] but studies do exist demonstrating superiority of one over the other.[7–9] Much of the research regarding comparison with ropivacaine has been in peripheral nerve block and neuraxial anesthesia/analgesia.

The difference between agents is frequently identified as potency. Lack of familiarity, cost, and limited improvement on currently available local anesthetics have hindered the adoption of these 2 agents. However, in situations where large doses of local anesthetic are used, either of these newer agents should be considered.

Mixing of Local Anesthetics

Depending on the intended use of a local anesthetic, a clinician may look at the various properties of a particular anesthetic (speed of onset, duration, dosage, toxicity, and so forth) and "wish" for an improved picture. The mixing of local anesthetics has been evaluated, with varying results.[10,11] Caution should be exercised when mixing agents because the risk of error is possible. The practice of mixing agents is most commonly used in peripheral nerve block.

Structure

Synthetic local anesthetics are all derivatives of cocaine, are small molecules with molecular weights of less than 500, and fall primarily into 2 categories (**Fig. 1**). A lipophilic portion and a hydrophilic portion are linked by either an amino ester or an amide. Modification to either of the side chains can change the physical properties of the agent.