



The names of some anaesthetics, along with many other medicines, changed in 2003/04 from British Approved Names (BANs) to recommended International Non-Proprietary Names (rINNs). This was to reduce the risk of error in the prescribing and dispensing of some medicines arising from their availability in the UK under two different names. As a result of these changes, benoxinate was renamed oxybuprocaine, amethocaine was renamed tetracaine, and lignocaine was renamed lidocaine. The drugs themselves and the excipients in their formulations are identical.

Topical medications

Local anaesthetics

There are a number of local anaesthetics available to optometrists (Table 1), and given their similar actions it is not unexpected that they all have a similar chemical structure. These drugs have a lipid-soluble hydrophobic portion and a readily ionisable hydrophilic portion that can readily switch between an uncharged or charged form. It is the ability of local anaesthetics to be both lipophilic and hydrophobic, and uncharged and charged, that enables them to rapidly diffuse across the lipid membrane of epithelial cells and also bind to the intracellular portion of sodium channels.

The lipid-soluble and hydrophilic portions of local anaesthetics are separated by an intermediate alkyl chain, which contains either an ester or an amide linkage and determines the class of the drug. Examples of esters include cocaine, oxybuprocaine, proxymetacaine and tetracaine. Lidocaine is the only amide local anaesthetic available in eyedrop form. The ester linkage is more easily broken than the amide bond, so the ester drugs are less stable in solution and cannot

Ophthalmic drugs

Part 5 – Anaesthetics and analgesics: how to use them

Dr Michael Johnson explains the use of anaesthetics and analgesics in optometric practice. Module C20242, one specialist CET point for therapeutic optometrists, one general CET point for optometrists

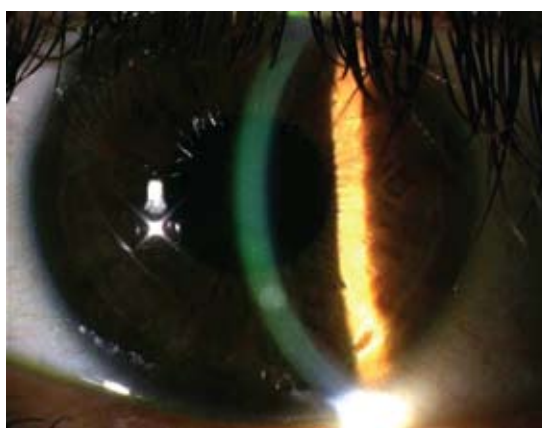


Figure 1 Scar from an old foreign body

be stored for as long as amides. The metabolism of most esters results in the production of metabolites that can act as allergens, although the vast majority of 'allergic' reactions to anaesthetics are toxic, rather than allergic in mechanism.

The more potent the drug, the smaller the amount required to produce a given effect, and the potency of local anaesthetics in the eye largely depends on how easily they pass across the cell membrane. Their lipid solubility depends on their physiochemical features such as the aromatic ring structure and hydrocarbon chain length. It is the lower lipid solubility of lidocaine that accounts for its lower potency than other available ocular anaesthetics, and this is reflected in why it is prepared in a higher concentration (4 per cent versus 0.4-0.5 per cent). Tetracaine is the most potent of the topical anaesthetics available as eyedrops owing to its high lipid solubility. Notwithstanding this fact, my clinical experience, which includes digging foreign bodies out of the cornea (Figure 1), is that any difference in the level of anaesthesia provided by all the available topical anaesthetics is rarely of clinical significance. The duration of action is governed by

how tightly the anaesthetic binds to the sodium channel, and again there is little difference between available anaesthetics.

All topical local anaesthetics sting on instillation as a result of their pH. This is because all of these drugs are weak bases, and so to keep them stable they are formulated with a low pH, necessary because the proportion of a base that is ionised (and thus stable) will increase as the pH of the solution becomes increasingly more acidic than the pKa of the drug. Proxymetacaine is prepared at a slightly less acidic pH than other anaesthetics, presumably a reflection of its higher pKa, and this accounts for why it stings less on instillation.

The commercially available topical anaesthetics all work quickly, with effective action occurring in less than a minute. The duration of anaesthesia has considerable inter-subject variation, which appears to be more important than the specific drug used.¹ Complete resolution of anaesthesia is expected to occur in 20-60min, and so patients should be told of the risk of rubbing the eyes excessively afterwards due to the risk of inadvertently abrading the ocular surface.

Relatively mild superficial epithelial damage is not uncommon following the use of topical local anaesthetics in the eye, especially with tetracaine, and this represents local toxicity. A profound toxicity reaction that results in a necrotising keratitis is reported to occur in about one in 1,000 patients with ester drugs, and in these patients it is appropriate to use an amide for subsequent topical anaesthesia. These cases are often distressing to the patient (when the anaesthetic wears off), but the condition is normally self-limiting and does not require treatment other than ocular lubricants for comfort. A true allergy to topical ocular anaesthetics leads to a blepharoconjunctivitis, which is again self-limiting. Systemic

TABLE 1

Topical local anaesthetic eyedrops

Esters
Cocaine (not commercially available)
Oxybuprocaine 0.4% (formerly benoxinate)
Proxymetacaine 0.5%
Tetracain 0.5% (formerly amethocaine)
Amides
Lidocaine 4% (formerly lignocaine)



reactions to anaesthetics result from systemic absorption of excessive quantities of drug, and such reactions are virtually non-existent after topical ocular anaesthesia because of the small quantities of drug involved.

Epithelial toxicity is cumulative, and so prolonged or repeated use of topical anaesthetics can result in serious keratopathy, which includes epithelial loss and consequent stromal oedema, and corneal infiltrates and anterior chamber reaction that can mimic a microbial keratitis. It is for this reason, in addition to dulled awareness of disease worsening that may delay seeking early review, that the use of anaesthetics is limited to within practice and they should not be supplied to patients. Indeed, most cases of anaesthetic abuse occur in doctors who choose to self-medicate and should know better.

Cocaine

Cocaine is found naturally in the leaves of erythroxylon cola. In addition to its local anaesthetic actions on nerve membranes it also blocks the re-uptake of norepinephrine at sympathetic neurones and so is a vasoconstrictor, and this property is particularly useful in reducing bleeding during nasal surgery. Cocaine is only rarely used nowadays owing to its risks and the availability of safer alternatives. The unwanted actions of cocaine include corneal toxicity and the systemic effects of hypertension, tachyarrhythmias (disturbance of heart rhythm with increased pulse rate), tachypnoea (rapid breathing), nausea and a myriad of central nervous system effects. Its addictive properties also present the temptation of theft by patients and the public, and personal abuse by clinicians.

Although optometrists do not use cocaine, they may still encounter patients presenting with ophthalmic side-effects of the drug from recreational use (Figure 2). A colleague who worked in the financial district in London told me of a characteristic inferior epitheliopathy in bankers in the 1980s that was caused by the drug spluttering into the eye when it was snorted, and I have examined a young man with a pre-retinal macular haemorrhage that was suspected to be a consequence of drug emboli who admitted to use of cocaine when asked about non-prescription substances.

Oxybuprocaine

This topical anaesthetic is commonly used by optometrists, and is suitable for all procedures requiring anaesthesia.



Figure 2 Optometrists may encounter patients presenting with side-effects from recreational use of cocaine



Figure 3 Episcleritis: Topical NSAIDs may be helpful in reducing discomfort

Tetracaine

This topical anaesthetic is the most potent of those available to optometrists. This higher potency is rarely needed, and the drug has the drawback of greater toxicity to the cornea and so it is used less commonly than alternatives.

Proxymetacaine

This topical anaesthetic is popular with optometrists because it stings the least on instillation and is available combined with fluorescein that is convenient for contact tonometry. It is also the preferred anaesthetic to use when scraping a corneal ulcer for culture owing to being the least toxic to bacteria and so lessening the chance of a false negative result. The downside of proxymetacaine relative to its alternatives is the inconvenience that it should be stored in a refrigerator.

Lidocaine

The main difference between this topical anaesthetic and others available to optometrists is that it is an amide, rather than an ester. When injected, amides are preferred to esters because the latter are degraded quicker and they are more likely to cause allergies. However, these advantages are less marked when applied topically, where no consistent pattern of variations in duration of effect have been reported and true allergic reactions are rare.

The main utility of lidocaine is that it is available combined with fluorescein that is convenient for contact tonometry, but relative to the proxymetacaine-fluorescein combination it does not fluoresce so well, but it has the advantage that it does not have to be refrigerated. There is also a utility for lidocaine when a previous significant toxic reaction or allergy to an ester anaesthetic is suspected because no cross-reactivity is expected between esters and amides.

Topical NSAIDs

The two topical NSAIDs available in the UK are diclofenac (Voltarol) and ketarolac (Acular). They may be helpful in reducing discomfort in mild inflammatory ocular surface diseases, such as episcleritis (Figure 3). However, some clinicians feel that when medication is deemed necessary for these conditions a drug should be prescribed that effectively treats the root of the problem, namely inflammation, and thus prefer a short course of topical steroids. The main utility of topical NSAIDs may be when there are specific reasons to avoid the use of steroids, such as when the patient is known to be a steroid responder where use of these medications results in a dangerous elevation of intraocular pressure.

Unfortunately, the NSAID formulations sting or burn on instillation, although this can be lessened by storing in a refrigerator, and require frequent four times daily dosing. Also, the topical NSAIDs are specifically indicated for the treatment of pain and inflammation in and around cataract surgery, and so alternative uses are off-label. Stinging and frequent dosing reduces the acceptance of topical NSAIDs by patients, and the restricted labelling deters clinicians from prescribing.

Systemic medications

Before initiating any oral pain management, a more thorough medical history of the patient is warranted. The



clinician should ask about alcohol intake, antidepressant use, smoking, history of stomach ulcers, kidney or liver disease, and pregnancy in appropriate patients, because these may be contra-indications for certain treatments. Enquiry should also be made about any current medications as well as over-the-counter preparations that the patient may be taking, especially warfarin, digoxin and antidepressants. Lastly, the patients should be asked about previous allergy to any pain killers.

Oral NSAIDs

Oral NSAIDs include aspirin, paracetamol and ibuprofen. These drugs are often useful in managing pain in ocular disease in combination with topical medication that addresses the disease process. These tablets are generally prescribed at a similar dosage as recommended for headaches in conditions that include marginal keratitis, microbial keratitis, and uveitis. When pain is severe and disrupting ability to function or sleep it may be more appropriate to use a stronger opioid for analgesia to avoid gastrointestinal problems. Any clinician prescribing NSAIDs must be aware that these medications are associated with gastrointestinal upset and nephrotoxicity, and so should ordinarily be avoided in patients with peptic ulcers or kidney disease. Additionally, owing to its blood-thinning properties, aspirin should not be advised for patients with bleeding disorders or aneurysms. These drugs are not suitable for the management of chronic conditions owing to the cumulative risk of side-effects and medication overuse headaches.

Opioids

This class of drugs are all derivatives of opium, found in the seed pod of the opium poppy. The most commonly used opioid in ophthalmology is codeine, which has the same indications as oral NSAIDs, but when a higher level of analgesia is required. Codeine is not as potent as morphine, but has far less potential for toxicity and undesired effects. The drug is often used in combination with paracetamol (Co-codamol) because they work on separate areas of the central nervous system to produce a synergistic effect. Indeed, combinations of analgesic agents with different mechanisms of action can achieve improved efficacy, tolerability and safety compared with equi-analgesic doses of the individual drugs. It should be noted that codeine can be fairly sedating, so patients should

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1 Which of the following is not a possible complication of anaesthesia?

- A Allergy
- B Toxicity
- C Accidental trauma
- D Angle-closure

2 Which of the following anaesthetics must be stored refrigerated?

- A Lidocaine
- B Oxybuprocaine
- C Proxymetacaine
- D Tetracaine

3 Which of the following anaesthetics is an amide?

- A Lidocaine
- B Oxybuprocaine
- C Proxymetacaine
- D Tetracaine

4 Which of the following anaesthetics is the most potent?

- A Lidocaine
- B Oxybuprocaine
- C Proxymetacaine
- D Tetracaine

5 Which of the following is not an analgesic?

- A Cocaine
- B Codeine
- C Ketarolac
- D Tramadol

6 Which of the following would be most appropriate for episcleritis requiring analgesia?

- A Proxymetacaine eye drops
- B Paracetamol tablets
- C Corticosteroid tablets
- D Morphine suppository

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The deadline for responses is November 22 2012



be cautioned about this, especially if they have not used the drug previously. Also, constipation is a common side-effect.

Tramadol is a synthetic analogue of codeine that has a dual central-acting mechanism, in that it weakly binds opioid receptors and weakly inhibits serotonin and norepinephrine re-uptake. The analgesic effects of tramadol are similar to codeine, but it has the advantages of reduced somnolence and constipation. However, in some patients it causes dizziness, headaches and nausea, and it has many interactions with other drugs including digoxin and warfarin. The use of tramadol is not recommended in epilepsy or persons with a history of seizures.

Opioid drugs are not suitable for the management of chronic conditions owing to a gradual loss in effectiveness, ie tolerance, and their risk of dependence. Opioids should also be avoided in patients with significant respiratory disease owing to their tendency for respiratory depression, and advanced kidney disease because this interferes with drug metabolism.

Anticonvulsants and antidepressants

In cases of prolonged or chronic eye pain, especially neuropathic eye pain, for example following herpes zoster ophthalmicus, it is not recommended to use topical anaesthetics, NSAIDs or opioids owing to their potential

for toxicity, side-effects and addiction. Instead, it is preferable to use centrally acting substances that are more commonly prescribed as anticonvulsives (pregabalin, gabapentin and in more serious cases carbamazepine) or antidepressants (for example the tricyclic antidepressant amitriptyline). Even very small amounts of an anticonvulsant or an antidepressant can almost completely stop eye pain and does not damage the eye at all. Owing to the multiple actions of these medications and their frequent prolonged use it is usually most appropriate for these drugs to be prescribed by a patient's general practitioner.

Summary

Anaesthesia and analgesia are essential for proper diagnosis and management of eye disease. Patient group directives, supplementary prescribing and independent prescribing now permit optometrists with further qualifications and relevant clinical experience to provide more completely care for patients with painful ocular conditions. ●

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