Ophthalmic drugs

Part 3 – Mydriatic drugs - which ones to use when and how they work

In the first of a two-part look at mydriatics, Dr Michael Johnson describes the indications for mydriasis, what drugs to use and how they work. Module C19751, one specialist point for therapeutic optometrists, one general CET point for optometrists

The pupil acts to improve optical resolution, allows for rapid control of retinal illumination, and conveys emotion in non-verbal communication. Enlargement of the pupil is termed mydriasis and a reduction in the size of the pupil is termed miosis. Physiological mydriasis occurs when the level of light is dimmed, and in reaction to stress and arousal. Miosis is a reaction to an increase in light. There are times when an optometrist wants to override the physiological control of pupil size, and this article reviews why and how this can be achieved.

When to dilate

The most common reason that an optometrist chooses to dilate the pupil is to improve the view of the internal structures of the eye posterior to the iris. Therapeutic use of mydriatics invariably makes use of chemically related cycloplegic drugs, owing to their longer duration and the sometimes useful attribute of greater action on the ciliary body. These medical indications include lessening painful muscular spasm and breaking posterior synechiae in iritis, disrupting ciliovitreal block in aqueous misdirection (malignant) glaucoma, improving access to the posterior segment in surgery, and penalisation therapy for amblyopia.

Viewing through an undilated pupil can be likened to peering through a keyhole, with the situation compounded by the miosis triggered by the high light level associated with most examination techniques. It is certainly possible to get a view through an undilated pupil in most patients, at least with one eye, but dilation always gives a better view by improving coverage, stereopsis and clarity. In particular, without dilation it is not possible to optimally visualise the peripheral retina, vitreous, or to achieve stereoscopic appreciation of the optic nerve or macula (even when it can easily be seen monocularly). It may be argued that a dilated ocular examination is an ideal that optometrists should offer all of their patients. However, it is not customary to offer dilation routinely in primary eye care sight tests within England and Wales owing to its associated inconvenience and low benefit-cost ratio for the majority of patients. A pragmatic compromise is that patients with larger benefit-cost ratios are identified and offered dilation. There is no definitive list of the patients that ‘must’ be dilated, and this is appropriate given that individual circumstances are by definition individual, and the opinions of clinicians along with the fashions of our profession differ with time and geography. What follows is a guide to help optometrists make better decisions (Table 1).

Risk of retinal detachment

A retinal detachment is a relatively rare event, with an annual incidence of about one in 10,000 – lifetime risk about one in 200. This risk is not shared evenly, and some people are much more likely to develop a detachment. The main risk factors for retinal detachment are trauma (including surgery), and high myopia or a family history of non-trauma related retinal detachment. For comparison with population averages, the lifetime risk of someone with more than six dioptres of myopia developing a retinal detachment is about one in 20. It is my opinion that asymptomatic high myopes should be offered a dilated intraocular examination bi-annually to detect retinal breaks that could be treated before they lead to a rhegmatogenous retinal detachment, and this should be increased to annually for extreme myopes whose refraction exceeds 12 dioptres. Moreover, a dilated view of the anterior vitreous and fundus should be recommended in the strongest terms to anyone who has symptoms suggestive of a retinal detachment or its precursor, a posterior vitreous detachment. Symptoms of a posterior vitreous detachment include a sudden increase in the number of floaters, often with a large central opacity that moves with the eye, representing a Weiss ring, and flashes. A retinal detachment may also be accompanied by a black shadow that extends to the edge of vision.

Risk of macular disease

It is difficult to confidently assess the macula without dilation because its examination is associated with the strongest light-induced miosis. Furthermore, the most important sign in macular disease is elevation or thickening, which represents the accumulation of fluid within or under the retina, and this demands stereoscopic viewing. In my opinion, a diluted examination of the macula is indicated when there are complaints of new distortion, or reduced acuity in persons with AMD or diabetic retinopathy, or at high risk of choroidal neovascularisation due to numerous soft drusen or a history of wet AMD and not being monitored by the hospital eye service.

Specific conditions

There are some specific conditions or clinical scenarios that warrant dilation.
nervous supply that originates from the Edinger Westphal nucleus and arrives at the eye via the oculomotor nerve, ciliary ganglion and short ciliary nerves. The dilator muscle is composed of radial fibres, like spokes of a wheel, that converge from the circumference of the iris towards the centre and blend with fibres of the sphincter muscle near the pupil margin. It is controlled by the sympathetic nervous system with a nerve pathway that originates in the hypothalamus, loops down to the cervical portion of the spine and then travels upward towards the eye via the carotid plexus, cavernous sinus and the long ciliary nerves.

Mydriatics can work on either end of the push-pull system controlling pupil size, namely by preventing contracture of the iris sphincter muscle, or augmenting the contraction of the iris dilator muscle. It should also be appreciated that the tone of the ciliary body is also controlled by cholinergic nerves, and so anticholinergic mydriatics have a spill-over of effect on accommodation. Indeed, mydriatic and cycloplegic drugs that act on cholinergic nerves differ in their strength, rather than in their pharmacological mechanism of action. Cycloplegic drugs always cause pupil dilation in addition to their effect on the ciliary body, whereas drugs marketed as mydriatics are less potent and so have reduced effect on accommodative function.

Natural alkaloids
The first mydriatics were plants such as mandrake, which was used (and abused) by many ancient civilisations, including the Hebrews, Greeks and Romans. This perennial herb is a narcotic and so serves to dull the perception of pain through central mechanisms. In ocular inflammation it also lessens pain caused by iris spasm as a result of the anticholinergic effect from its high alkaloid content. In addition to pain relief, the Greeks and Romans made use of the dilating properties of mandrake to improve access to the cataractous lens in enucleation operations, and to simulate the pupil signalling of sexual arousal in courtship and religious ceremonies.

The vogue of mydriatics in Greece and Rome was lost during the succeeding centuries. It was only towards the end of the 18th century that the mydriatic effect of the herb belladonna, more commonly known as deadly nightshade due to its lethal effect as a poison, was recognised by the medical establishment, which subsequently led to the isolation of atropine. As an aside, the name belladonna, meaning ‘beautiful lady’, comes from the first use of the plant leaves to dilate women’s pupils to make them appear more amorous. Also, it has been argued that the alkaloids produced by this genus of plants have evolved to poison unwanted insects tempted to feast on their foliage in a manner analogous to chemical warfare.

Atropine is an anticholinergic drug, which means that it acts to frustrate cholinergic nerves (those using acetylcholine, a neurotransmitter) that form part of the parasympathetic nervous system. The drug binds to cholinergic receptors on the sphincter (and the ciliary body) where it shields them from acetylcholine and prevents it from triggering muscular contraction. In essence, anticholinergic drugs cover the ears of the iris sphincter so it cannot hear the nerves shouting. The effect is pupil dilation, and importantly, an abolition of the normal light reflex. Atropine also causes pronounced cycloplegia.

**Tropicamide**
The natural alkaloid atropine was used for many years in ophthalmology, but clinicians, and especially patients, were inconvenienced by its long half-life that meant its dilation and cycloplegic effects persisted for many days, perhaps for as long as a week. This prompted the development of a short-acting alternative, and the fruit of this labour was a synthetic compound that answered many of the practical failings of atropine. The synthetic derivative was named tropicamide, which produces dilation quicker and has a much shorter duration. As an added benefit, it does not cross the blood-brain barrier, and so in contrast to atropine there is no risk of central nervous system dysfunction that can lead to amnesia, confusion and excitement. Tropicamide gives good dilation in about 20min, and this rapid action is the result of a relatively low PKt of 5.4 (versus 9.8 for atropine), which means that its penetration across the lipid membrane of the corneal epithelium is enhanced by the low proportion of the drug in ionised form at physiological pH (about 2.3 per cent). Dilation begins to diminish after 2hrs and pupil size has typically returned to its habitual level after 4-6hrs. The cycloplegic effect of tropicamide is generally only noticed by early incipient presbyopes, especially those with uncorrected hypermetropia, and early presbyopes who have little accommodative reserve and incomplete near correction.

Tropicamide is available in 0.5 per cent and 1 per cent concentrations in both preserved multiuse bottles and more popularly as non-preserved single-use
MULTIPLE-CHOICE QUESTIONS - take part at opticianonline.net

1. Which of the following drugs is not an anticholinergic?
   A. Atropine
   B. Cyclopentolate
   C. Tropicamide
   D. Phenylephrine

2. How is phenylephrine eliminated in the eye?
   A. Metabolised by the liver
   B. Absorbed by cornea
   C. Oxidised by enzymes
   D. Diffuses into the blood

3. Which of the following drugs acts the fastest?
   A. Atropine
   B. Cyclopentolate
   C. Tropicamide
   D. Phenylephrine

4. Which of the following drugs has the least effect on accommodation?
   A. Tropicamide
   B. Cyclopentolate
   C. Tropicamide
   D. Phenylephrine

5. Which of the following drugs could raise blood pressure?
   A. Atropine
   B. Cyclopentolate
   C. Tropicamide
   D. Phenylephrine

6. Which of the following is expected to give the best dilation?
   A. Tropicamide 1%
   B. Phenylephrine 10%
   C. Tropicamide 1% and Cyclopentolate 1%
   D. Tropicamide 0.5% and Phenylephrine 2.5%

Successful participation in this module counts as one credit towards the GOC CET scheme administered by Vantage and one towards the Association of Optometrists Ireland’s scheme. The deadline for responses is September 20 2012.

References

Dr Michael Johnson is an independent prescribing optometrist who owns Johnson & Furze Optometrists, works in the Glaucoma and Accident & Emergency departments at Bristol Eye Hospital, and maintains the patient website www.eyepedia.co.uk