MYDRIATICS AND MIOTICS

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This chapter includes a review of:

- Mydriatics
- Miotics

MYDRIATICS

Mydriatics are used to facilitate the examination of the inside of the eye. They are agents that produce relative dilation of the pupil diameter that would be adopted under moderate to low intensity illumination.

> As a result of the mechanism of action, most mydriatics produce unwanted relaxation of the ciliary body causing cycloplegia. As well as dilating the pupil, they act on the ciliary body. The main aim of mydriatics is to dilate the pupil, not eliminate accommodation.

Pupils can dilate by one of 2 mechanisms:

- Alpha (1) adrenergic drug: there is contraction of the dilator muscle, pupil opens slowly, retains light sensitivity e.g. Phenylephrine.
- Cholinergic blocking drug: the sphincter muscle will relax, the pupil opens faster, no light sensitivity e.g.Tropicamide.

> 1. Sympathetic stimulation: stimulates dilator muscle.
> 2. Anti-muscarinics and anti-cholinergics relax the sphincter muscle causing rapid dilation.

Ideal Mydriatic

• Rapid onset of action	• Adequate duration
• Fast recovery	• Light reflex abolished
• No cycloplegia	• Easy reversal in an emergency
• No rise in IOPs	• No other pharmacological effect
• No local toxic reaction	• No systemic toxic reaction
• No adverse effects or stinging	

Duration: it will last long enough to complete the full examination of fundus.

Table 4.1 Mydriatics

Official name	Strengths % w/v	Single dose?	Mode of action	Mydriatic onset	Mydriatic duration	Reversed by	Adverse reactions	Notes
Atropine sulphate	1.0	Yes	Anti-muscarinic	40 min	7 days	Ecothiopate	Allergic reactions CNS toxic effects	Too strong for routine use
Homatropine hydrochloride	1.0 2.0	1.0 only	Anti-muscarinic	40 min	48 h	Physostigmine	As for atropine	Rarely used
Cyclopentolate	0.5 1.0	Yes	Anti-muscarinic	30 min	24 h	Physostigmine	CNS effects	No longer available
Tropicamide	0.5 1.0	Yes	Anti-muscarinic	15 min	8-9 h	Physostigmine	Some CNS effects	Mydriatic of choice
Phenylephrine	2.5 10.0	Yes	Sympatho-mimetic	30 min	12-24 h	Pilocarpine	Systemic hypertension	Can be used in combination with tropicamide

Source: *Hopkins and Pearson (2007) Ophthalmic Drugs*

Uses of mydratics

- Recent onset floaters in vitreous
    - Looking for retinal detachment
    - Especially in high myope
- Fundus examination (routine) of people with diabetes
- Sudden reduction in VA- macular examination
- Unexplained loss of visual field
- Unexplained ocular pain
- Impaired view of fundus
    - Cloudiness of vitreous or lens- when good mydriasis will enhance fundal view
- Older patients with smaller pupils
- Redness of eye not attributable to superficial infection, allergy, raised IOP'S etc.

- After contusion to eliminate ocular damage

Tropicamide 0.5%/1%

Tropicamide is the mydriatic of first choice and the most commonly used mydriatic. It comes in single use containers (minims) or multidose bottles. It causes a stinging sensation on installation, adn should be stored in a cool dark place.

- Cholinergic blocking – anticholinergic
- 0.5% and 1%
- Quick onset – within 20 minutes
- Short duration
- 8-9 hours recovery (recovery starts after 2-3 hours)
- Perform Van Herricks technique to estimate angle

Cautions

- Angle closure glaucoma:

Contraindications:

- Hypersensitivity
- Narrow angle glaucoma any history of previous episodes of angle closure
- Narrow angles
    - Perform Van Herricks technique: grade 1 or 0 unsuitable to dilate
- IOL: movement of zonules can cause dislocation of an already unstable lens

Cautions

- If the patient is taking any medication which has resulted in a slightly dilated pupil, there may be a prolonged effect.
    - If in any doubt about suitability- contact General Practionner (GP) for advice
- Must be stored in a cool dry place away from light
- It turns into a pink straw colour when degraded
- Pupil is more resistant to dilation in darker irises

Phenylephrine

- Available as 2.5% or 10% drops
- Not generally used by optometrists - it is usually a pre- surgical mydriatic.
- Poor expected efficacy as the pupil retains light sensitivity in normal doses
- Minims contain sodium metabisulphite (antioxidant)- allergies
- Sympathomimetic
- Available as single use units minims or 10ml bottle of 10% soln
- Onset 10 mins
- Duration 12-24 hours
- Alpha agonist which causes vasoconstriction of conjunctival vessels
- Used in low concentrations as an eye brightener
- Little cycloplegic effects
- Reduced effect in highly pigmented eyes

Application

- Principle application is in combination with another mydriatic e.g. Tropicamide 1% resulting in a greater dilation (by 1-2mm). It is good for pupils which are difficult dilate (combination minim available).

Contra-indications

- Cardiac disorders
- Systemic hypertension
- Aneurysms/ stroke
- Usage of systemic medications which would pre-dispose an individual to significant systemic response from unavoidable systemic absorption of phenylephrine.

These effects are due to systemic absorption of the eyedrops causing an increased systemic sympathomimetic response.

Cautions

- Patients taking any directly or indirectly acting sympathomimetics which would predispose them to adverse effects.
- Individuals with blood pressure problems and who are on medication. The pressure effect may cause blood pressure fluctuations.
- Any agent that causes:
  - A narrowing of an opening of a blood vessel
  - Cold or stress or nicotine or epinephrine or norepinephrine or angiotensin or vasopressin or certain drugs
  - Maintains or increases blood pressure
  - Increasing or tending to increase blood pressure

Other Mydriatics

- 6- Hydroxyamphetamine
- Cyclopentolate, homatropine, atropine and hyoscine (not normally indicated due to lengthy duration of action)

Special Consideration for mydriasis

- Consider combination mydriasis in diabetics, as they are often resistant to mydriasis
- Thyroid disorders: In hyperthyroidism, tropicamide is the agent of choice, often high blood pressure etc- also increased sensitivity to sympathomimetics
- Pregnancy: Tropicamide, sympathomimetic may cause transient foetal hypoxia
- Post surgical patient: avoid dilating especially corneal surgery for 2-3 months unless instructed to carry out- check with surgeon
- Infected eye: Tropicamide may be used
- Use of topical ocular anaesthetics on eye prior to instillation of mydriatic will give increased effect.

MIOTICS

Miotics are drugs that constrict the pupil.

- Reverse of mydriasis- acute angle closure glaucoma
- Treatment of ocular hypertension associated with some types of Open Angle Glaucoma
- Reverse mydriasis after routine eye-exam, which is not usual as there is a risk of pupil block and the mydriatic effect longer lasting than action of pilocarpine. (Physostigmine- pain/ accommodative spasm)
- Reversal of mydriasis: produced by drugs such as phenylephrine and tropicamide. Not first choice glaucoma treatment.

Advantages

- Reduced danger of angle closure
- Avoids photophobia
- Increases return of accommodation
- Reduced IOP

Disadvantages

- Small pupils
- Dimness of vision
- Spasm of accommodation
- Pseudomyopia
- Higher incidence of precipitating adverse drug reactions than other diagnostic ocular drugs
- Chronic use of miotics has higher incidence of precipitating severe adverse reactions
    - Warrants discontinuation of treatment

Mydriatics: Paralysing sphincter (antimuscarinic) or stimulating dilator

Miotics: inhibiting dilator (alpha blocking agents) or stimulating sphincter (parasympathetic or anticholinesterases)

Three modes of action: Direct acting muscarinics or cholinergics close the pupil by contracting the iris sphincter.

Mode of Action

Direct acting

- Parasympathomimetics
  - Contract sphincter pupillae causing miosis
- Alpha adrenergic blockers
  - Relax iris dilator muscle, blocking NA, causing miosis

> - Pupil sphincter stimulated to contract by action of Ach on muscarinic receptors
> - Mimic action of ACh
> - Parasympathomimetics or direct acting muscarinic or cholinergics or preventing breakdown of Ach (therefore more Ach) by cholinesterase at junctions: anticholinesterases
> - Anticholinesterases have a stronger and more prolonged effect
> - Physostigmine rarely used
> - Alpha adrenergic blockers: blocks noradrenaline
> - Thymoxamine not available now
> - Adrenergic blocking drugs are all low potency, efficacy compared to cholinergic miotics

Indirect acting

- Cholinesterase's: increase in ACh levels causes miosis

> Indirect acting agents increase levels of acetyl-choline around the iris sphincter to produce a stronger and more prolonged contraction

- Adrenergic agents: low potency/ efficacy
- Cholinergic: high efficacy
- Pilocarpine most used agent

Ideal miotics:

- Quick in onset
- Length of action appropriate
- Normal pupil light reflex
- No cycloplegia/cyclospasm
- No other pharmacological effects
- No local toxic reaction
- No systemic reaction
- No adverse complaints such as stinging

Table 4.2: Pupillary innervation

	Cholinergic effect	Anticholinergic effect	Adrenergic effect	Adrenergic blocking effect
Iris Radial muscle- dilator (radial muscle)			Contracts- alpha 1- dilates	Relaxes- alpha 1- miosis
Iris sphincter- sphincter pupillae (circular muscle)	Contracts- miosis	Relaxes- dilation		
Ciliary Body	Contraction (myopia)	Relaxation (cycloplegia)	Relaxation (Alpha 1, Beta)	Contraction

Pilocarpine (0.5%, 1%, 2% & 4%)

Pilocarpine is a direct-acting parasympathomimetic that mimics the action of ACh released by the stimulation of postganglionic parasympathetic nerves. It also contracts the ciliary body, causing tension on the trabecular meshwork and increases the aqueous humor outflow leading to drop in intra-ocular pressure.

- 1% most common
- Acts at muscarinic receptors of effector cells
- Action can be blocked by atropine
- Competitive occupation of receptor sites
- Likely to only be used in a hospital clinic
- Minims 2 and 4% concentration
- 1% in multi use bottles.

Considerations

- Onset of miosis takes 15 to 30mins to constrict pupil by 2mm
- (Apraclonidine/ dapiprazole/ thymoxamine are weaker miotics).
  - Pupillary light response is slowed down or absent with miosis- pupil fixed at certain diameter
  - Efficacy dependent on ocular pigmentation
  - Increased tone of ciliary body- pseudomyopia in younger individuals
- Onset 10 mins, max 30 mins
- Depends on concentrations, usually 1%
- Lasts 6 hours
- Causes effective miosis (reversal of mydriasis) after use of phenylepherine and hydroxyamphetamine
- Darker eyes: lesser effect
- Ocular pigment binds the drug and reduces the quantity available for binding to receptors on the iris and ciliary body
- Miotics (cholinergic) cause contraction of ciliary body
- Pseudomyopia can occur, which will reverse when the drug wears off
- Sustained contraction can cause headches and eye strain
- Will wear off in 1-4 hours
- If repeated, dosing adaptation occurs over a few days

Side Effects

- Vasodilation of conjunctival vessels, which is unappealing cosmetically
- Conjestion of vessels on repeated dosing and discomfort

Features:

- Opposition of vasoconstriction with mydriatics
- Conjunctival hyperaemia lasts for several hours
- Aqueous production less with direct acting cholinergic agents
- Additive to effect of opening trabecular meshwork
- Reduction in IOP

Systemic Effects

- HEADACHE (Most commonly reported side effect)
- Slows heart/ pulse
- Increases peristalysis
- Broncho-constriction
- Increased tearing, salivation, sweating (pancreas/ GIT also)
- Generalised flushed appearance
- Stimulates then depresses CNS

Features:

- Chronic use in glaucoma
- Side effects: with large doses
- Headache resulting from the contraction of the cilicary body and eye strain
- Broncho constriction: stimulation of muscarinic receptors (asthma patients)
- Reduced IOP – trabecular meshwork opens and increases outflow
- Parasympathetic NS supplies many structures and effects could be noted involving respiratory, cardiovascular and Gastro-intestinal (GI) system

Other Miotic Agents - not available for use by Optometrists

- Apraclonidine- alpha2 adrenergic drug.
    - preservative free unit dose preparations (Iopidine)
    - Used by Ophthalmologists pre and post operatively
- Carbachol- direct acting cholinergic
    - not commercially available
- Physostigmine- indirect acting cholinergic
    - No products currently listed
- Echothiopate- indirect acting cholinergic(inhibits Ach)

    - High incidence of ADR following conjunctival absorption
    - No longer available in UK but can be obtained on a named patient basis from a hospital
- Demacarium- Indirect acting cholinergic
    - Only available in hospital
- DFP (disopropylfluorophosphate)- indirect acting ACh inhibitor
    - No longer used in UK
    - Drug was available for many years but recently discontinued
- Thymoxamine- direct acting alpha adrenergic blocking drug (use after phenylephrine)
    - Used to be available to Optometrists
- Dapiprazole- direct acting adrenergic blocker
    - used in UK and Europe
    - Store in a cool dark and dry place

Contraindications to Miosis

- Known allergy
- Iridectomy/ iridotomy
- Iris supported IOL
- Intra ocular inflammation- risk of iris bombe
- Posterior synechiae
- Exfoliative disorders of lens
- Lens subluxation/ dislocation
- History of or presenting symptoms of retinal detachment

Pupil Block (Caused by Pilocarpine)

- Pupil closure towards crystalline lens, and there is a forward movement of the crystalline lens, causing a potential position for pupil block- mid dilated position
- Hypermetropes more at risk
- Shallow drainage angle more at risk

Pupil block occurs during surgery/mydriasis reversal. The sequence of events are as follows:

1. Lens moves forward and forms posterior synechiae. i.e. back surface of lens touches iris
2. Resticted flow of aqueous from posterior to anterior chamber
3. Aqueous accumulates in posterior chamber and iris is pushed forward
4. Iris bombe
5. Drainage angle blocked
6. Depth of anterior chamber decreases

Acute Angle Closure (Treatment by Pilocarpine)

- If mydriatic induces rise in IOP- miotic use considered.
- Dose commensurate with severity of condition- dose of mydriatic used (instill 1 drop of miotic every 15 mins until angle has opened).
- More required to reverse cyclopentolate than tropicamide

Angle Closure – Employment of Other Agents

- Oral acetazolamide (2x250mg diamox)- works in 30 mins- remember sulphonamide though
- IV acetazolamide (500mg over few mins)- works in 15 mins
- Mannitol infusion- osmotic diuretic
- Oral glycerin- osmotic diuretic- not if diabetic (100-200ml over 5 mins)
- Apraclonidine- prior to iridotomy/ iridectomy
- B-Blocker
- Latanoprost
- Alcohol- osmotic diuretic- not usual

Contraindications

Pupil block, patients with intraocular inflammation with marked iris involvement (iritis)

Miosis may precipitate pupil block. Even though miosis is used to treat Angle closure glaucoma (ACG), it can also precipitate an attack, especially in shallow Anterior Chamber (AC) and pupil block, due to anterior displacement of lens.

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