UNIT 25 MIOTICS, MYDRIATICS AND CYCLOPLEGICS

Structure

25.0 OBJECTIVES

After completing this unit, you should be able to understand:

- different diagnostic and therapeutic drugs like miotics, mydriatics and cycloplegics;
- the doses and duration of action of these drugs;
- side effects of these drugs along with their contraindications; and
- the newer drugs that are coming to the market regularly.

25.1 INTRODUCTION

Miotics are drugs that cause construction of pupil.

The commonly used miotics belong to two groups, parasympathomimetics that stimulate sphincter pupillae, or sympatholytics that constrict pupil by relaxing dilator pupillae muscle.

Mydriatics are drugs that dilate the pupil while cycloplegics are agents that cause paralysis of ciliary muscle (paralysis of accommodation). Mydriatics usually produce paralysis of ciliary muscle to a, greater or lesser degree.

Currently two classes of drugs, adrenergics and parasympatholytics, are available for mydriatic purpose. For most dilation procedures the adrenergic or anticholinergic agents can be used either alone or in combination for maximum mydriasis. Agents used topically in the eye for the purpose of inhibiting accommodation are termed cycloplegics. Their primary use is for cycloplegic refraction and the treatment of uveitis. Since these agents also inhibit action of the iris sphincter muscle they are effective mydriatics and are coinmonly used for routine pupillary dilation.

All these drugs when instilled into the conjunctival sac are rapidly absorbed through the cornea and become effective in the eye.

25.2 DESCRIPTION OF DRUGS

In this unit you will study the diagnostic and therapeutic drugs in details. They include miotics, mydriatics and cycloplegies.

25.2.1 Miotics

Miotics are drugs that cause constriction of pupil. These are used in the management of glaucomas and the treatment of esotropias and accommodation insufficiency.

Pilocarpine

Pilocarpine is a direct acting parasympathomimetic drug, which duplicates the muscarinic effects of acetylcholine, but has no nicotinic effects. Pilocarpine stimulates secretory glands and smooth muscles, but has no effect on striated muscles. Pilocarpine nitrate, a sterile ophthalmic solution is available as 1 per cent, 2 per cent or 4 per cent drops. Pilocarpine is effective in the treatment of glaucoma by improving the facility of outflow (by contraction of ciliary muscle) and by decreasing aqueous secretion. Onset of miosis occurs within 10-30 minutes and lasts for 4-8 hours following topical application.

Indications and Usage

Pilocarpine is indicated for:

- The control of intra-ocular pressure in angle closure glaucoma.
- Emergency relief of mydriasis in an acutely glaucomalous situation.
- To reverse mydriasis caused by a cycloplegic agent.
- In the treatment of accommodative strabismus.
- Controversial role in the treatment of hyphaema.
- After cataract extraction in cases of intra capsular cataract extraction.

Contraindications

Pilocarpine is contraindicated in persons showing 'hypersensitivity to any of its components. It is also contraindicated in anterior uveitis.

Warnings

Pilocarpine is readily absorbed systemically on topical application. Excessive application may elicit toxicity symptoms in some individuals (manifested as salivation, lacrimation, sweating, nausea, vomiting and diarrhoea, bronchiolar spasm and pulmonary edema can occur).

Precautions

Pilocarpine has been reported to cause retinal' detachment in individuals with pre-existing retinal diseases or predisposed to retinal tears. Safety and effectiveness in children have not been established.

Adverse Reaction

Include visual blurring due to miosis and accommodative spasm, poor dark adaptation caused by the failure of the pupil to dilate in reduced illumination and conjunctival hyperemia. Miotics have been reported to cause lens opacities in susceptible individuals after prolonged use. Allergic blepharo-conjunctivitis, ocular pseudopeinphigoid, corneal epithelial staining and vascularisation, atypical band keratopathy, iris hyperemia and epithelial cyst formation have been reported in some patients.

Dosage and Administration

- To aid in emergency miosis, 1 to 2 drops of one of the higher concentrations should be used.
- The dosage and strength required to reverse mydriasis depends on the cycloplegic used..
- The drops are used bd - qid in the treatment of angle closure glaucoma,

Carbachol

Carbachol is a cholinergic prepared as a sterile topical ophthalmic solution. Carbachol is a direct acting parasympathomimetic that is sometimes used when

allergy or resistance to pilocarpine develops. Unlike pilocarpine, carbachol has both nicotinic and muscarinic actions. It is available as 0.75 per cent to 3 per cent drops.

Clinical Pharmacology

It is a cholinergic (parasympathomimetic) agent. Carbachol has a double action, it not only stimulates the motor end plate of the muscle cell, as do all cholinesters, but it also partially inhibits cholinesterase.

Indications and Usage

For lowering intra-ocular pressure in the treatment of glaucoma.

Contraindications

Miotics are contraindicated where constriction is undesirable such as acute iritis. It is also contraindicated in those patients showing hypersensitivity to any component of this preparation.

Warnings

The preparation is for topical use'only and not for injection. Carbachol should be used with caution in the presence of corneal abrasion to avoid excessive penetration that can produce systemic toxicity and in patients with acute cardiac failure, bronchial asthma, active peptic ulcer, hyperthyroidism, gastrointestinal spasm, urinary tract obstruction and Parkinson's disease. As with all miotics, retina! detachment has been reported when used in certain susceptible individuals.

Precautions

Avoid over dosage. The rniosis usually causes difficulty in dark adaptation. Patient should be advised to exercise caution in night driving and other hazardous occupations in ,poor light.

Adverse Reaction .

This preparation is capable of producing systemic symptoms of a cholinesterase inhibitor even when the epithelium is intact. Transient ciliary and conjunctival injection, headache and ciliary spasm with resultant temporary decrease of visual acuity may occur. Salivation, syncope, cardiac arrhythmia, gastrointestinal cramping, vomiting, asthma and diarrhoea may occur.

Dosage and Administration

It is administered three to four times per day.

Phospholine Iodide

Phospholine iodide is available in the following concentrations: 0.03 per cent, 0.06 per cent, 0.125 per cent, **0.25** per cent.

Phospholine iodide is a long acting cholinesterase inhibitor for topical use that enhances the effect of endogenously liberated acetylcholine of iris, ciliary muscle and other parasympathetically innervated structures of the eye. It thereby causes miosis, increase in facility of aqueous humor, fall in intra-ocular pressure and potentiation of accommodation.

Indications and Uses

In Glaucoma — chronic open angle glaucoma, sub-acute or chronic angle closure glaucoma after iridectomy or where surgery is refused or contraindicated.

Contraindications

- Active uveal inflammation.
- Most cases of angle closure glaucoma due to the possibility of increasing angle block.
- Hypersensitivity to the active or inactive ingredients.

Adverse Reaction

- Stinging, burning, lacrimation, lid muscle twitching, conjunctival and ciliary redness, browache, induced myopia with visual blurring may occur.
- Activation of latent iritis or uveitis may occur.
- Iris cysts may form and, if treatment is continued, may enlarge and obscure vision. This occurrence is more frequent in children.

  Prolonged use may cause conjunctival thickening, obstruction of nasolacrimal canals.
- Lens opacities, paradoxical increase in inha-ocular pressure.

Dosage and Administration

Early chronic glaucoma, 0.03 per cent instilled twice a day. Refrigerated aqueocs solution shows a drop in potency within four weeks.

Physostigmine Sulphate

Physostigmine is an alkaloid obtained from the seeds of physostigmine venenosum. Tt is an indirectly acting parasympathomimetic agent. It is available as a solution of 0.25 per cent, 0.5 per cent and .0 per cent and an ointment containing 2 per cent of the drug. It is a reversible anticholine-esterase. The mechanism of action involves inhibition of choline-esterase with consequent accumulation of acetylcholine at the neuromuscular junctions.

Indications

It can be used in conjunction with pilocarpine in the treatment of acute glaucoma, in angle closure glaucoma and in diagnosis and treatment of myasthenia gravis.

Contraindications

Hypersensitivity to the drug and conditions predisposing to retinal detachment.

Adverse Reaction

These include twitching, irritation and allergic reaction. Depigrnentation of the lid skin has been noted in some patients with the use as an ointment.

'Dosage and Administration

It is administered every 4 to 6 hours,

25.2.2 Mydriatics

Mydriatics are drugs that cause dilatation of pupit.

Phenylephrine Hydrochloride

Phenylephrine hydrochloride 5 per cent and 10 per cent ophthalmic solution is primarily a direct acting drug that stimulates the alpha-receptors of those structures innervated by the post ganglionic sympathetic nerve fibres. It also causes blanching of the conjunctival vessels. It is a mydriatic with no cycloplegic effect.

Indications and Uses

Although the mydriasis produced by 2.5 per cent phenylephrine alone is generally not adequate for detailed examination of the retinal periphery, it is often sufficient

for viewing the poste ior pole. Mydriasis produced is not accompanied by cycloplegia. It is a fast acting mydriatic.

One drop of 2.5 per cent phenylephrine causing >5 mmHg rise in IOP has been used as a provocative test for diagnosis of angle closure glaucoma.

It is used in diagnosis of ptosis of Homer's syndrome as it responds to the instillation of 0.125 per cent phenylephrine drops. The diagnosis of Horner's syndrome can also be established as 1.0 per cent phenylephrine causes dilation of a horner's pupil but not of a normal pupil.

Contraindications

Angle closure glaucoma.

- Hypertensive patients: Phenylephrine is a powerful vasoconstrictor and is absorbed systemically when applied topically to the eye.
- 10 per cent Phenylephrine is contraindicated in infants.
- In patients receiving reserpine, guanethidine and tricyclic antidepressants, phenylephrine is contraindicated because of their increased susceptibility to vasopressor action.
- In eyes where corneal epithelium is denuded it may cause corneal clouding.
- Persons with a known hypersensitivity to any component.

Adverse Effects

Ophthalmic: Mild stinging on initial instillation, rebound conjunctival congestion on prolonged use, and rebound miosis may occur in some elderly patients and subsequent instillation may produce less mydriasis.

Systemic: The major difficulty in using this drug is the possibility of inducing systemic hypertension, tachycardia. Headache or browache may occur. Episodes of myocardial infarction and arrhythmias in elderly patients are reported.

Stability: One other disadvantage is relatively short shelf life as once the bottle is opened Phenylephrine rapidly oxidizes, which makes it less effective.

Dosage and Administration

Topically 1 or 2 drops into the conjunctiva of each eye for refraction, in conjunction with some cycloplegic of choice. Maximum dilation with phenylephrine alone occurs within 15-60 minutes. The pupil size returns to normal within 4-6 hours. Initial instillation of a topical anaesthetic before phenyephrine prevents the stinging caused by phenylephrine and enhances pupillary dilation.

In premature infants for dilation, 2.5 per cent phenylephrine is used in conjunction with 0.2 per cent cyclopentolate or 0.5 per cent tropicamide.

25.2.3 Mydriatics and Cycloplegics

Cycloplegics are drugs that cause paralysis of ciliary muscles, i.e., cause relaxation of accommodation.

Atropine Sulphate

Atropine sulphate is an anti-cholinergic prepared as a sterile topical ophthalmic solution and ointment supplied in three strengths: 0.5 per cent, 1 per cent and 3.0 per cent. Intramuscular injections are available as 0.3, 0.4 and 0.6 mg/ml preparations.

Mechanism of Action

Atropine sulphate is a naturally occurring alkaloid that acts directly on the muscarinic receptors of structure innervated by the post-ganglionic parasympathetic fibres. It does not reduce liberation of acetylcholine, but tissues are rendered insensitive to it. It is the competitive inhibitor of the muscarinic action of acetylcholine and is the strongest of the drug available for cycloplegic purposes. It causes mydriasis and cycloplegia by paralysing sphincter pupillae and ciliary muscle respectively.

Indications and Usage

- It is used for mydriasis and cycloplegia (in young patients in which accomodation is very active).
- Pupillary dilation in inflammatory conditions of the iris (to prevent pain, release synechiae and give rest to inflamed tissue).
- In ciliary block glaucoma.
- It is used to prevent undue vagal response in tensilon test.
- Amblyopia therapy (penalisation)

  In cases of accomodative spasm.
- Pre and post operatively in many intra-ocular surgeries,

Contraindications

Contraindicated in persons with primary glaucoma or a tendency towards glaucoma e.g., narrow anterior chamber angle and in those persons showing hypersensitivity to any component of this preparation.

Subluxated lens (lens may dislocate into anterior chamber and cause pupillary block glaucoma.

Precautions

Atropine solution should not be used in children as it causes systemic absorption through nasolacrimal mucosa.

To avoid excessive systemic absorption the lacrimal sac should be compressed for one minute after instillation.

Adverse Reaction

Local: Atropine can cause allergic responses, usually wound the eyelids and conjunctiva. The allergic responses include redness and crusty flaking of the eyelid margins, dryness and wrinkling of the skin around the eyelids and injected bulbar conjunctiva with some watery discharge. Blurred vision and photophobia are consequent to the cycloplegic and mydriatic effect of atropine.

Systemic: Dryness of skin and mouth, tachycardia, irritability or delirium, flushing of face, skin rash, abdominal distension in infants and hyperpyrexia may occur in children. Severe reactions are manifested by hypotension with progressive respiratory depression. The elderly are more susceptible to anticholinergic toxicity like cognitive impairment and delirium.

Plasma concentrations peak after 10 min of topical application. Two drops of 1 per cent solution contain 1 mg of the drug which is twice the preoperative injectable dose.

Dosage and Administration

Because of a long duration of its effect and delay in the onset of action it is not routinely used for office procedures.

Children: For refraction, administer 1 per cent ointment to each eye, thrice daily for three days prior to examination,

Hornatropine Hydrobromide

Homatropine 2 per cent sterile ophthalmic solution was the first anti-cholinergic to be developed specifically as an alternative to atropine.

It is a synthetic anti-cholinergic agent that directly blocks the muscarinic action of acetylcholine, causing mydriasis and cycloplegia. Its effect generally lasts longer than those of either cyclopentolate or tropicamide but it is not necessarily more effective. Homatropine is therefore not commonly used as a diagnostic agent, however its relatively long lasting effect makes it valuable in the treatment of anterior ocular inflammations such as iritis.

Indications and Usage

As a moderately long acting mydriatic and cycloplegic agent for cycloplegic refraction and in the treatment of inflammatory condition of the uveal tract. It is inferior to atropine for penalization therapy of amblyopia.

Contraindications

In persons with a tendency of occludable angles.

It should not be used in patients who have shown allergy to atropine.

Patient Warning

Patient should be advised not to drive or engage in other hazardous activities while pupils are dilated. Caution also in pregnant and lactating mothers.

Adverse Reaction

Adverse reactions are similar to atropine but much less in frequency. Prolonged use may produce local irritation characterized by follicular conjunctivitis, vascular congestion, edema, exudate and an eczematous dermatitis.

Dosage and Administration

For refraction instill one or two drops topically in the eye(s). May be repealed in 5 to 10 minutes if necessary.

Cyclopentolate Hydrochloride

Cyclopentolate 1 per cent is an anticholinergic prepared as a sterile ophthalmic solution. Also available as 0.5 per cent and 2 per cent solution.

Indications

Cyclopentolate is an effective antimuscarinic agent and the cycloplegic of choice for children under age 12 and for youths between 12 and 20 when latent hyperopia or accommodative esotropia is suspected. Its cycloplegic efficacy is greater than hornatropine.. Also used for pre and post-operative states when mydriasis is required and when a short acting mydriatic cycloplegic is needed in the therapy of iridocyclitis. Unlike atropine and homatropine onset of maximum cycloplegia approximates the onset of maximum mydriasis.

It can also be used in patients with central lenticular changes, if they feel better with mydriasis, till the patient is ready for surgery.

Contraindications

Angle closure glaucoma and in patients with hypersensitivity to the drug. Cyclopentolate is also not recommended for children with emotional problems since it can have marked central nervous system effects that may be increased in susceptible youngsters,

Dosage and Administration

One drop followed by second drop in 5 minutes or as desired by the physician. Complete recovery usually occurs in 24 hours.

Adverse Reaction

Local: Increased intra-ocular pressure, blurred vision, and photophobia.

Systemic: psychotic reactions, behavioural disturbances, seizures, disorientation and cardio-respiratory collapse in children have been reported. Dryness of the mouth, tachycardia, headache or allergic reaction may occur. Because toxic reactions occur with multiple installations of 1 per cent solution, the smallest dose should be used.

Management of over dosage in life threatening toxicity includes slow injection of physostigrnine intravenously.

Tropicamide

Tropicamide is one of the most commonly used anti-cholinergic mydriatic because of its powerful mydriatic effects, rapid onset of action and low incidence of side effects. It is available as 0.5 per cent or 1 per cent eye drops.

Tropicamide acts by blocking muscaranic acetylcholine receptors. The stronger preparation (1 per cent) also paralyses accommodation. The 0.5 per cent strength may be useful in producing mydriasis with only slight cycloplegia.

Indications and Usage

For mydriasis and cycloplegia, for diagnostic procedures and when a short acting mydriatic is needed for some pre and post-operative stages. Unlike atropine, homatropine and cyclopentolate, pupillary dilation with tropicamide is less dependent on iris pigmentation. For premature infants a combination of 2.5 per cent phenylephrine and 0.5 per cent tropicamide is recommended because the latter alone fails to dilate adequately.

Contraindications

Contraindicated in angle closure glaucoma and in persons showing hypersensitivity to any component of this preparation.

Precautions

In the elderly and others where increased intra-ocular pressure may be encountered, mydriatics and cycloplegics should be used with caution. This preparation may cause CNS disturbances that may be dangerous in infants and children.

Patient should be advised not to drive or engage in other hazardous activities while pupils are dilated,

Dosage and Administration

One or two drops of 1 per cent solution in each eye 2 to 3 times at 5 minutes intervals or as directed by the physician.

Adverse Reaction

Local: Stinging sensation.

Systemic: Rarely in children, confusion or hyperactivity may occur.

Onset and Recovery of Cycloplegics					
Drug	Strength of solution %	Mydriasis		Paralysis of accommodation	
		Maximal	Recovery	Maximal	Recovery
Atropine	1%	30-40 min	7-10 days	1-3 hr	6-12 days
Homatropine	2%	30-40 min	1-3 days	30-60 min	1-3 days
Cyclopentolate	0.5-1%	30-60 min	24 hr	30-60 min	24 hr
Tropicamide	0.5-1.0%	20-40 min	6 hr	30 min	6 hr

Check Your Progress

1) What are miotics and mydriatics?

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2) Name at least three mydriatics and cycloplegics.

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3) Which is only mydriatic?

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4) Which cycloplegic is used in children with squint?

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25.3 LET US SUM UP

In this unit you have learnt that mydriatics are the drugs, which produce dilatation of the pupil, and cyclopegics are the agents that cause paralysis of the ciliary muscle (paralysis of accommodation). You have also learned that mydriatics usually produce paralysis of the ciliary muscle in greater or lesser degree. All these drugs when instilled into the conjunctival sac are rapidly absorbed through the cornea and become effective in the inner eye.

The mydriatics may be divided into two groups: (a) Para-sympatholytics, and (b) Sympathornirnetics. The parasympatholytic agents block the action of the parasympathetic nervous system. You know that acetylcholine is the neurohumoral transmitter at the receptor site, and all the drugs in this group act by competing with Acetylcholine. As a result, due to unopposed action of dilator pupillae mydriasis and cycloplegia are produced.

In next unit you will study the antiglaucoma drugs.

25.4 ANSWERS TO CHECK YOUR PROGRESS

1) The drugs that constrict the pupil *are* called miotics **and** which dilate the pupil are called mydiiatics.
2) Atropine, Homatropine and Tropicamide
3) Phenylephiine
4) Atropine