UNIT 24 ROUTES OF ADMINISTRATION OF DRUGS

Structure

24.0 OBJECTIVES

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

- different routes *of* drug administration in ophthalmology;
- newer drug delivery systems;
- use of different drugs with appropriate doses and duration; and
- advantages and disadvantages of topical and systemic uses of drugs.

24.1 INTRODUCTION

Ocular pharmacology differs from general pharmacology in the sense, the rate of metabolic exchange is so rapid in the eye that the composition of aqueous differs from posterior to anterior chamber. Also there are active transport systems which change the rate of transport at corneal, ciliary and retinal pigment epithelia.

For ocular diseases, the routes of administration are either local or systemic. Local application of drugs for the treatment of superficial eye diseases is a very satisfactory route. Methods for local application of drugs may be by application to corneal surface, subconjunctival, retrobulbar or direct injection into the aqueous or' vitreous.

Generally due to an effective blood-aqueous and blood-vitreous barrier, intraocular levels of systemically administered drugs are usually lower than serum levels.

24.2 ROUTES OF DRUG ADMINISTRATION IN OPHTHALMOLOGY

The routes of drug administration in ophthalmology are either local or systemic.

24.2.1 Local Application

Local application af drugs for the treatment of superficial eye diseases is a very satisfactory route. When the desired site of action of the drug is inside the eye, then the problems of ocular barrier arises. Local application is better than systemic administration as it is devoid of systemic adverse effects.

The cornea may be compared to fat-water-fa1 sandwich as the lipid content of the epithelium and the endothelium is 100 times more than that of the stroma. All medications that readily enter the eye after topical application have the ability to exist in 'equilibrium in solution either in ionized or non-ionized form depending on the necessity.

Apart from absorption, other factors that affect the bioavailability of the drugs include the enzymatic capacity of the tissue to metabolize the drug, tissue binding of the drug and its protein binding.

Topical drug delivery in ophthalmology is problematic due to difficulty in achieving sufficient quantity of drug at the desired site of action.

Following are the methods for local application of drugs:

1) Topical application
2) Sub-conjunctival injection
3) Anterior and posterior sub-tenon injection
4) Retrobulbar injection
5) Intraocular injections

Topical Application

Topical route of administration of drugs means direct application of medicine to surface of cornea and conjunction. In topical administration, the vehicle in which a drug is applied needs careful attention. As you know, more viscous fluids prolong ocular contact, thereby increasing drug absorption. Other factors which need consideration are mainly pH, toxicity, electrolyte composition and preservatives. While combining two drugs, their compatibility must be studied.

Various medication forms used are:

1) Eye drops (solutions, suspensions and gels)
2) Ointments
3) Inserts (ocuserts)
4) Iontophoresis
5) Drug application with hydrophilic contact lenses

Eye Drops

Eye drops are superior in the sense that they are well absorbed and blurring of vision is often not a problem. But systemic toxicity is more due to drainage through the nasolacrimal duct. Eye drops can be prepared in aqueous or gel vehicles. Common preservatives used in eye drops are benzalkonium chloride, chlorbutanol, thiomersal, chlorhexidine and EDTA. These are used to retard microbial overgrowth. The common side effects due to these preservatives include superficial punctate keratopathy, grey corneal haze, pseudo membrane formation, decreased epithelial villi and delay in wound healing.

Eye Ointment

Ointment form has few advantages like prolonged drug contact time, inhibition of dilution by tears, and resistance to drainage through nasolacrimal system. The disadvantages are blurring of vision and aesthetic considerations.

Ocuserts

Inserts or ocuserts are membrane controlled diffusion.system.

Inserts are prepared as drug impregnated gelatin wafers or cellulose polymer rods. These have the advantages of continuous drug administration at a constant rate. This causes better patient compliance.

However, inserts are predisposed to getting lost accidentally.

Iontophoresis is the method by which drug is introduced into the eye through electromotive forces. This is not used practically.

Hydrophilic Contact Drug Application

Soft contact lenses can be used to absorb the drugs and then release them subsequently into the cul de sac. The drugs should be preservative free, other wise it will damage corneal epithelium.

The following are some suggestions that should be informed to the patients before starting any ophthalmic formulation:

1) Never instill more than one properly placed drop of ophthalmic solution or suspension into the affected eye.
2) Compressing the canaliculus and lacrimal sac for 3-5 minutes after instillation can minimize systemic absorption of ophthalmic solution or suspension.
3) When multi-solution therapy is indicated, instill the drops separately at 5 minutes interval.
4) Ophthalmic ointments should be instilled preferably at bedtime as it may impede deliveiy of other ophthalmic drugs to the affected eye by acting as a barrier to contact.
5) Monitor expiry dates of ophthalmic medications. Do not use outdated drugs.

Medication devices used in ophthalmology are:

1) Contact Lenses
2) Corneal Shields
3) Cotton Pledgets
4) Filter Paper Strips
5) Artificial Tear Inserts
6) Membrane Bound Inserts

Sub-conjuctival Injections

It is injection of the drug under the conjunctiva. Injections should be with bevel down of the needle to avoid injury to episclcral vessels and inadvertent perforation of the globe. The drug penetrates into the eye primary by diffusion across sclera, partly by absorption through sub conjunctival space and partly by leaking out of the sub conjunctival space and getting absorbed through cornea after mixing with tears.

This route is specially *indicated in:*

i) Emergency,
ii) Post-operative cases where surgeon does not want to open the eye of the patient frequently for drops,
iii) Low penetration drugs like antibiotics, arid
iv) Cases where combination of drugs is required, e.g., mydricaine.

Sub conjunctival route has following advantages:

i) Single injection will achieve higher level of intra-ocular drugs as compared to frequent instillation of drops, and
ii) Repeated sub conjuctival injections. will achieve intra-ocular levels comparable to intra-ocular injections.

Some of the ***disadvantages*** include:

i) Patient's apprehensions
ii) Subsequent inflammation and pain
iii) Inconvenience and cost, and
iv) Possible intra-ocular perforation.

Sub-tenon Injection

It is injection of the drug below the tenon in sub-tenon space. It is always better to give injection under the Tenon's capsule 'by holding both the conjunctiva and Tenon's. It can be anterior sub-tenon or posterior sub-tenon, the later one is more useful in posterior segment conditions.

Retrobulbar Injections

It is a blind injection into the retrobulbar space. It "is suitable for regional anesthesia, but its efficacy in other medications is debatable. The most common uses of this route, apart from anesthesia are injections of vasodilators and corticosteroids in inflamed eyes. Advantages of this route are doubtful, especially because of impending complications Like retrobulbar hemorrhage, globe perforation, optic nerve injury, etc.

Intra-ocular Injections

Intra-ocular injections means injection of drugs directly into aqueous (anterior chamber) or vitreous. The dangers inherent in intra-ocular injections outweigh possible benefits. In cases of endophthalmitis where vitrectomy is warranted, injection of gentamicin, vancomicin or dexamethasone, etc., may be justified. It is more useful in cases of drugs which can not penetrate into the eye.

24.2.2 Systemic Administration

General rules for systemic drug administration apply, but there is an effective blood aqueous and blood vitreous barrier, so the intra-ocular levels of systemically administered drugs are usually lower than the serum.

Most drugs will cross the aqueous and vitreous barrier in cases of ocular inflammatory diseases, which increases permeability. In systemic administration, drugs can be given orally, or by intra-muscular or intravenous injections.

This route is required in cases of severe infections like panophthalmitis and orbital cellulitis.

24.3 ROUTES OF DRUG ADMINISTRATION IN COMMAN OCULAR INFLAMMATORY CONDITIONS

Condition	Route
Orbital Cellulitis	Systemic
Blepharitis	Topical
Conjunctivitis	Topical
Keratitis	Topical
Scleritis	Topical + Systemic
Anterior uveitis	Topical + Sub conjunctival + Anterior sub-tenon
Endophthalmitis	Inrtavitreal + Systemic
Posterior uveitis	Systemic + Posterior sub-tenon
Optic neuritis	Systemic + Posterior sub-tenon
Sympathetic ophthalmia	Systemic + Topical

Check Your Progress

1) Name the methods for local application of drugs.

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2) What are the medication devices used in Ophthalmology?

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3) In how many ways medications can be used in Ophthalmology?

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4) Role of systemic administration in ophthalmic drug delivery.

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24.4 LET US SUM UP

In this unit you have learned that proper administration of ophthalmic drugs is absolutely essential to achieve optimal therapeutic results.

You have also studied various routes of administration of drugs with their advantages and disadvantages. In next unit you will study about the drugs which constrict or dilate the pupils.

24.5 ANSWERS TO CHECK YOUR PROGRESS

1) Methods of local application of ophthalmic drugs are:
   a) Application to corneal surface
   b) Sub-conjunctival route
   c) Anterior and posterior sub-tenon injection
   d) Retrobulbar route
   e) Direct injection into the aqueous or vitreous

2) Medication devices used in ophthalmology are:
   a) Contact Lenses
   b) Corneal Shields
   c) Cotton Pledgets
   d) Filter Paper Strips
   e) Artificial Tear Inserts
   f) Membrane Bound Inserts

3) Different forms of medications used in Ophthalmology are:
   a) Eye drops (solutions, suspensions and gels)
   b) Ointments
   c) Inserts
   d) Iontophoresis
   e) Drug application with hydrophilic contact lenses

4) In systemic administration drugs can be given orally, as intramuscular or intravenous injections, but due to blood aqueous and blood vitreous barrier, the concentration at the site of action is lower than the serum concentration.