
UNIT 28 ANTIBIOTICS, ANTIFUNGALS AND ANTIVIRAL AGENTS USED IN OPHTHALMOLOGY

Structure

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- 28.1 Introduction
- 28.2 Antibacterial Agents
- 28.3 Antifungal Agents
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- 28.5 Let Us Sum Up
- 28.6 Answers to Check Your Progress

28.0 OBJECTIVES

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

- the commonly used antibacterial, antifungal and antiviral agents;
- the mechanism of action of the antiviral drugs;
- the indications and contraindications of these agents; and
- the side effects and doses of these drugs.

28.1 INTRODUCTION

The rational selection of antimicrobial drugs depends upon the diagnosis and microbial sensitivity. Diagnosis can be made on the basis of clinical impression but it is important to obtain proper specimen for bacteriological or fungal agent. The antimicrobial can be started after taking the specimen for the culture. The eye is particularly suitable for local application of antibiotics. The use of systemic antibiotics is limited by relatively poor penetration of antibiotics into the eye though the blood-eye barrier is reduced when the eye is inflamed.

The goal of achieving high antibiotic concentration in anterior segment can be achieved by frequent instillation of antibiotic drops into the conjunctival sac.

28.2 ANTIBACTERIAL AGENTS

Bacterial infection is the commonest cause of ocular infection. The mainstay of therapy for any ocular infection is an antibiotic. However, proper selection of antibiotics is one of important step in the management of ocular infections. The ideal way to select an antibiotic is to isolate the bacteria in the laboratory and to find its antibiotic sensitivity. But in most of the routine ocular infections, antibiotics are given which are effective against common organisms causing these types of infections.

Antibiotics in Ophthalmology

A more general discussion of antibiotics including their classification, mechanisms of action and side effects are given in the general pharmacology booklet. In this unit, we will discuss the relevant antibiotics that are mostly used for various ocular infections.

Commonly Used Antibiotics for Ocular Infection

Chloramphenicol

A broad-spectrum antibiotic. It is a bacteriostatic antibiotic and acts by interfering with protein synthesis.

Dosage

Ophthalmic solution 0.4 to 1 per cent

Ophthalmic ointment 0.5 per cent

Sub conjunctival injection dose 5 to 10 mg/ml

Parenteral dose 30-100 mg/kg/day

Indications

Conjunctivitis, blepharitis, mild form of keratitis.

Adverse Reaction

Local application: Usually a safe antibiotic, mild allergic reaction may sometimes occur.

Systemic administration:

Dose dependent inhibition of bone marrow

Aplastic anemia

Gray baby Syndrome

Tetracyclines

A broad spectrum antibiotic having bacteriostatic activity. It inhibits the protein synthesis of the bacteria.

Indication

- 1) Ocular Chlamydial disease:
 - Trachoma
 - Adult inclusion conjunctivitis
- 2) Ocular Toxoplasmosis
- 3) Ocular Rosacea

Dosage

Ophthalmic drops 1 per cent

Ophthalmic ointment 1 per cent

Oral dose 250-500 mg 6 hourly

Side Effects

Systemic administration may cause:

Gastrointestinal disturbances

Yellowish discoloration of teeth in children

Kidney toxicity, Rise in Intracranial pressure

Sulphonamides

A bacteriostatic antibiotic, acts by inhibiting bacterial folate synthetase activity.

Sulphacetamide is commonly used sulphonamide in ocular infections.

Indications

Trachoma

Ocular toxoplasmosis

Dosage

Ophthalmic eye drops 10 per cent, 20 per cent, and 30 per cent

Ophthalmic ointment 10 per cent

Oral dose 2-4 gm/day

Adverse Reaction

Local–Hypersensitivity Reaction

systemic-[Skin Rash

Gastrointestinal disturbances: Nausea, vomiting, diarrhoea

Hypersensitivity Reaction

Polymyxin B

Bacteriostatic antibiotic, acts by altering the bacterial cell membrane permeability

Indication

It is mainly effective against Gram-ve organisms like E. coli, pseudomonas, H. influenza etc.

Dosage

Ophthalmic drops 0.5 – 1 per cent

Ophthalmic ointment 1 to 1.5 mg/gm

Adverse Reaction

Local – Itching, Hypersensitivity

Systemic – Kidney toxicity

Ciprofloxacin

A bactericidal agent, acts by inhibiting bacterial **DNA** gyrase enzyme which is necessary for **DNA** synthesis.

Indication

Effective against infections caused by Gram positive and Gram negative organism.

Dosage

Ophthalmic solution 0.3 per cent

Ophthalmic ointment 0.3 per cent

Oral –500-1500 mg bd

Parenteral – 5-10 mg/kg/day 12 hourly

Side Effect

Systemic – Gastrointestinal disturbance

– Allergic Reaction

Local – Prolonged use can cause precipitation of ciprofloxacin.

Ofloxacin

A bactericidal antibiotic like ciprofloxacin, it inhibits **DNA** gyrase enzyme.

Indication

Infections caused by Gram +ve and Gram –ve organisms, It may be effective against organisms resistant to ciprofloxacin eye drops.

Dosage

Ophthalmic solution 0.3 per cent

Ophthalmic ointment 0.3 per cent

Oral dose 200-400 mg tablet 6 hourly

Local - Burning sensation

Systemic - Nausea, vomiting, headache

Norfloxacin

A bactericidal antibiotic, acts by inhibiting the enzyme DNA gyrase.

Indication

Effective against Gram +ve and Gram -ve organisms.

Dosage

Ophthalmic solution 0.3 per cent

Ophthalmic ointment 0.3 per cent

Orally 400 mg twice a day

Adverse Reaction

Topical - Corneal Epithelial Toxicity

Systemic - Nausea, vomiting, depression

Newer Fluroquinolones

These include Gatifloxacin, Lomefloxacin and Sparofloxacin. These are the latest drugs and effective against various multi drug resistant strains like Neisseria, Pseudomonas, Chlamydiae etc. These drugs have good ocular penetration after topical as well as systemic use. These are all available as 0.3 per cent drops.

Gentamycin

A bactericidal antibiotic, which acts by inhibiting protein synthesis of bacteria.

Indication

It is effective mainly against Gram-ve bacilli like E. coli, Enterobacteria, Klebsiella pneumoniae, Proteus and Pseudomonas aeruginosa etc.

Dosage

Ophthalmic drops 0.3 per cent

Ophthalmic ointment 0.3 per cent

Intravitreal dose 0.2 mg/0.1 ml

Intravenous dose 3-3.5 mg/kg/day/8 hourly

Adverse Reaction

Local - Occasional irritation

Systemic - Nephrotoxicity and ototoxicity

Tobramycin

A bactericidal antibiotic, inhibits protein synthesis of bacteria.

Indications

More effective against P. aeruginosa than gentamicin. It is effective against most of the Gram-ve bacilli.

Dosage

Ophthalmic drops 0.3 per cent

Ophthalmic ointment 0.3 per cent

Intravitreal dose 0.2 mg/0.1 ml

Intravenous 3-3.5 mg/kg/day/8 hourly

Amikacin

A bactericidal antibiotic, inhibits protein synthesis of bacteria.

Indications

It is effective against most gram negative bacilli.

Dosage

Fortified drops– 6.7 mg/ml

Intravitreal dose– 0.4 mg/0.08 ml

Intravenous dose– 240 mg/8 hr

Vancomycin

This is a bactericidal antibiotic and acts by inhibiting the bacterial cell wall synthesis.

Indications

It is effective against methicillin resistant staphylococcal strains. It is used as fortified drops in corneal ulcers and as intravitreal injection in cases of endophthalmitis.

Dosage

Fortified drops– 31 mg/ml

Intravitreal dose– 1 mg/0.1 ml

Intravenous dose– 1 mg iv. 12 hourly

Cephalosporins

These are bactericidal drugs acting by inhibition of bacterial cell wall synthesis.

Indications

Various generations of cephalosporins are active against different spectrum of bacterial species. The third generation cephalosporins are effective against E.coli, Klebsiella and Pseudomonas as well.

These are used as fortified eye drops in cases of severe corneal ulcers and as intravitreal injections in selected cases of bacterial endophthalmitis based on the sensitivity reports.

Dosage

Fortified drops– 50 mg/ml

Intravitreal dose (cefazolin)– 2.25 mg/0.1 ml

Parenteral dose (cefazolin)– 1-6 mg/day

Check Your Progress 1

1) Mention the commonly used antibiotics.

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2) What are the various mechanisms of action of antibiotics?

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28.3 ANTIFUNGAL AGENTS

Invasion of cornea by fungus cause fungal keratitis. The incidence of fungal infection is gradually increasing. The chances of fungal infection are more in individuals who have a history of prolonged steroid use and are contact lens users. Common fungi causing ocular infections include:

Filamentous Fungi — Aspergillus
 Fusarium
 Cephalosporium

Yeast Fungi — Candida

Various antifungal agents are as below:

Polyenes

Polyene compounds bind preferentially to ergosterol in the fungal plasma membrane, thereby alter membrane permeability and disrupt fungal cell membrane. Polyene compounds include:

Amphotericin B

Indication

Acts against **Candida**, **Aspergillus**, **Cryptococcus**, **Histoplasma** and **Mucormycosis**.

Dosage

Ophthalmic eye drops—0.1-0.2 per cent/hourly

Sub conjunctival—2-5 mg in 0.5 ml

Intravitreal—5 microgram in 0.1 ml

Adverse Reaction

Local — Burning sensation, chemosis and SPKs, necrosis of conjunctiva on sub conjunctival injection

Systemic — Anaphylaxis, nephrotoxicity, thrombophlebitis and anemia

Natamycin

Indication

Effective against filamentous fungi infections, particularly of **Fusarium** and **Aspergillus**. Most commonly used topical antifungal agent in ocular use.

Dosage

Ophthalmic suspension 5 per cent. Given 1 hourly at day time and 2 hourly at night time for first 48-72 hours, then 6/day for 2-3 weeks.

Adverse Reaction

A well tolerated drops

Can cause burning sensation, allergic reaction, SPKs, should not be given sub conjunctivally as conjunctival necrosis occurs.

Imidazole Compounds

Mechanism

Inhibit ergosterol synthesis and cause direct damage to fungal cell membrane.

The Imidazole compounds used in Ophthalmology:

- Clotrimazole
- Miconazole
- Econazole
- Ketoconazole
- Fluconazole
- Itraconazole

Indication

Imidazole compounds are effective against Candida, Aspergillus, Fusarium species.

Miconazole

Dosage

Ophthalmic solution 1 per cent: Given 1 drop 1 hourly

Ketoconazole

Effective against Candida, Aspergillus, Fusarium and Curvularia.

Dosage

Oral route - 200 mg/day as a single dose for 1 week.

Local route - 1 per cent/hourly as topical preparation.

Clotrimazole

Effective against Candida, Fusarium, Penicillium, Cladosporium.

Dosage

Local 1% topical drops: 1 hourly basis

Adverse Reaction

Irritation, corneal epithelial toxicity.

Fluconazole

Effective against yeasts specially candida albicans, cryptococcus species, Histoplasma capsulatum etc. Fluconazole is used in candida endophthalmitis.

Dosage

Topical Route-0.3 per cent ophthalmic solution. Given 6 times/day up to 2 to 3 weeks.

Oral Route-200 mg/day for 3 weeks.

Adverse Reaction

Irritation and transient burning.

Fluorinated Pyrimidines

Mechanism of Action

Act as an antifungal agent by blocking the synthesis of fungal thymidine.

Indication

Effective against Candida, Cryptococcus, Aspergillus, Cladosporium and penicillium species.

Dosage

Oral - 50-150 mg/kg/day in 4 divided doses for 1 week.

Topical - 1 per cent ophthalmic drop 1 drop/hourly

Adverse Reaction

Irritation, itching, burning sensation with topical use.

GI disturbances and bone marrow suppression on oral dosing.

Check Your Progress 2

Mention the common antifungal agents.

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28.4 ANTIVIRAL AGENTS

Viral infections of eye are of common occurrence and their incidence is gradually increasing. Common viruses causing viral eye infection include Herpes Simplex, Herpes Zoster, Adenovirus etc. The viral infections of conjunctiva are usually mild and self limiting. However, viral infections of cornea, particularly of Herpes Simplex and Herpes Zoster may cause a permanent decrease of vision because of corneal scarring caused by them.

The chemotherapy of intracellular DNA viral infections is based primarily on the disruption of viral DNA synthesis.

Commonly used Antiviral agents include:

Acyclovir

Idoxuridine (IDU)

Vidarabine (Ava-A)

Trifluridine (TFT)

Bromovinyl Deoxyuridine (BVDU)

Acyclovir

Mechanism of Action

Acyclovir is activated by virus induced thymidine kinase and converted to an acyclovir monophosphate form and then triphosphate form. The triphosphate form selectively inhibits virus induced DNA polymerase.

Indications

- Herpes Simplex Keratitis
- Herpes Zoster Keratitis
- Herpes Simplex Iritis
- Herpes Blepharitis
- Acute Retinal Necrosis

Formulations

Acyclovir is available as intravenous, oral and topical forms:

- *Topical Acyclovir* eye ointment 3 per cent
- *Oral Acyclovir* tablet in the strength of 200 mg, 400 mg and 800 mg
- *Intravenous preparation* 250 mg powder is available commercially

In Herpes Simplex and Herpes Zoster Keratitis 3 per cent ophthalmic ointment is applied 5 times/day for 2 to 3 weeks. If the disease is severe and local skin is affected oral acyclovir is advised. 200-800 mg tablet given 5 times/day for about 10 days. Intravenous acyclovir (5-10 mg/kg body weight) is given in immunocompromised patients.

Adverse Reactions

Generally acyclovir is a well-tolerated drug and relatively free from toxicity. However topical burning sensation and corneal epithelial toxicity may occur in some patients.

Gastro-intestinal disturbances and renal dysfunction may occur with systemic acyclovir.

Idoxuridine (IDU)

Mechanism of Action

IDU competes with thymidine for phosphorylation by thymidine kinase, then the viral DNA synthesis becomes defective due to incorporation of IDU into DNA.

Indication

Herpes simplex keratitis

Dosage and Penetration

Topical 0.1 per cent eye drops

0.5 per cent eye ointment

Topical IDU is given 1 hourly at daytime and 2 hourly at night time for about 2 weeks. The ointment can be applied 4 times a day. The dose can be reduced according to the response to therapy.

Side Effects

- Irritation and edema of lids.
- Conjunctival congestion, edema and infiltrates
- Reduced tear secretion
- Punctal occlusion
- Corneal epithelial toxicity

Vidarabine (Ava-A)

Mechanism of Action

Vidarabine act as an antiviral agent by blocking viral DNA synthesis.

Indication

Herpes simplex viral infection.

Dosage

- Ointment (3 per cent), Given 5 times/day for 2-3 weeks
- Intravenous Infusion (200 mg/ml) – 10-15 mg/kg/day by intravenous infusion
Intravenous vidarabine is administered in life threatening Herpes simplex viral infection particularly Herpes simplex encephalitis (infection of brain tissue by Herpes Simplex virus).

Adverse Reaction

Allergic Reactions

Superficial punctate keratitis

Trifluridine (TFT)

Mechanism of Action

The mechanism of action is the same as IDU.

Indication

Primary and recurrent dendritic Herpes simplex virus keratitis.

Dosage

Solution 1 per cent.

For Herpes simplex keratitis, 1 hourly dosing in daytime and 2 hourly in night is advisable. Once the epithelium heals, the dose is reduced to 4 times/day for 7 days.

Adverse Reaction

- Irritation/burning sensation
- SPKs
- Hypersensitivity
- Hyperemia
- Bone marrow depression in systemic administration.

Bromovinyl Deoxyuridine (BVDU)

Mechanism of Action

Inhibition of DNA synthesis.

Indication

Herpes simplex keratitis

Herpes zoster keratitis

Dosage

Ophthalmic solution 0.1 per cent 1 drop 8-9 times/day.

Adverse Reaction

Local hypersensitivity reaction.

Check Your Progress 3

Mention the commonly used antiviral agents.

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28.5 LET US SUM UP

In this unit you have studied that the commonly used antibiotics act by inhibition of cell wall synthesis, alteration of cell membrane permeability or active transport, inhibition of protein synthesis, inhibition of nucleic acid synthesis and interfering with the bacterial metabolism. The common indications for antibiotics are corneal ulcers, blepharitis, conjunctivitis, chlamydiae infections, toxoplasmosis and bacterial endophthalmitis.

You have also studied that the commonly used antifungal agents act by interfering with the fungal ergosterol metabolism and by the direct damage to fungal cell membrane. The antifungal agents have the disadvantages of poor corneal penetration and toxicity to the epithelium.

Further, you have studied that the commonly used antiviral drugs act by inhibiting the DNA synthesis or getting incorporated in the DNA chain, leading to termination of DNA synthesis. The commonest indication for antiviral drugs is herpes keratitis.

In next unit you will study ophthalmic dyes, irrigating solutions and ocular lubricants.

28.6 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

- 1) Commonly used antibiotics include:
 - Chloramphenicol
 - Tetracycline
 - Sulfonamides
 - Polymyxin B
 - Ciprofloxacin
 - Ofloxacin

- Norfloxacin
- Newer fluoroquinolones
- Gentamycin
- Tobramycin
- Amikacin
- Vancomycin
- Cephalosporins

- 2) The various mechanisms of action of antibiotics are:
- i) Inhibition of cell wall synthesis
 - ii) Alteration of cell membrane permeability or active transport
 - iii) Inhibition of protein synthesis
 - iv) Inhibition of nucleic acid synthesis
 - v) Interfering with the bacterial metabolism.

Check Your Progress 2

The commonly used antifungal agents are:

- Amphotericin B
- Natamycin
- Clotrimazole
- Miconazole
- Fluconazole
- Itraconazole
- Ketoconazole

Check Your Progress 3

Commonly used antiviral agents include:

- Acyclovir
- Idoxuridine (IDU)
- Vidarabine (Ava-A)
- Trifluridine (TFT)
- Bromovinyl Deoxyuridine (BVDU)
- Flucytosine