UNIT 27 ANTI-INFLAMMATORY AND ANTI-ALLERGIC AGENTS

Structure

27.0 OBJECTIVES

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

- definition and classification of steroids, non-steroids and anti-allergic agents;
- mechanism of action and indications of these agents; and
- formulations, routes of drug administration and their complications.

27.1 INTRODUCTION

Anti-inflammatory agents used in Ophthalmology are broadly classified into two groups—steroidal anti-inflammatory agents and non-steroidal anti-inflammatory agents. Both the groups of these agents are commonly used in various ocular inflammatory conditions. These ocular inflammatory conditions may bc acute or chronic. The principles of management of acute and chronic inflammation are different. So accurate diagnosis is a must so as to initiate proper treatment.

The ocular inflammatory symptoms include redness of conjunctiva, itching, foreign body sensation and in severe cases may cause decrease of vision, If inflammation occurs in deeper' part of the eyeball like sclera, retina, choroid and optic nerve, it may cause irreversible decrease of vision, So it is essential to diagnose these inflammatory conditions. Essentially anti-inflammatory agents are used to control

Steroidal anti-inflammatory agents, though effective in inflammatory conditions, cause adverse effects like opacification of lens (cataract), rise in intra-ocular pressure (glaucoma). They also increase chances of ocular infection as these agents decrease resistance of the tissues. Thus steroids are not prescribed routinely for all ocular inflammatory conditions. For mild inflammatory conditions non-steroidal anti-inflammatory agents we advised. These agents do not cause cataract, glaucoma as adverse effects.

Ocular allergy is a common eye disorder. This condition usually presents as itching, watering, foreign body sensations. In severe cases, it may lead to permanent decrease of vision because of corneal scaring. The complications may occur because of agents used for controlling allergy particularly of steroidal drugs. Most of the anti-allergic drugs give temporary relief.

27.2 STEROIDS

Steroidal anti-inflammatory drugs are very effective, but they cause various adverse effects.

27.2.1 Classification

Commonly used Steroidal Anti-inflammatory Agents include:

1) Dexamethasone Sodium Phosphate
2) Prednisolone acetate
3) Methyl Prednisolone
4) Triamcinolone acetonide
5) Hydrocortisone acetate
6) Flurometholone acetate
7) Medrysone
8) Loteprednol
9) Rimexolone

27.2.2 Mechanism of Action

Steroidal agents cause constriction of blood vessels, reduction of numbers of inflammatory cells, inhibition of activities of inflammatory cells like neutrophils, lymphocytes etc. They also decrease permeability of the blood vessels, so the secretion of fluid from blood vessels is also reduced. The action of steroid as an anti-inflammatory agent is non-specific. It can reduce inflammation caused by any agent whether living or non-living.

The various effects of steroids on inflammatory cells include decreased T cell proliferation, reduced T cell function, lysis of activated T cells, reduced interleukin 2 production by T cells, reduced monocyte chemotactic factor production, reduced secretion of collagenases, decreased release of histamine by basophils and inhibition of stimuli for prostaglandin production by fibroblasts.

Other effects include reduced edema, decreased erythema, reduced neovascularisation and serum IgG and IgA concentration, reduction of complement concentration and stabilisation of vessels.

The use of steroids in ocular disease is largely empirical. But certain general principles are followed:

1) Steroids should be prescribed only when indicated.
2) Therapy with steroid should be reduced gradually, not discontinued abruptly.

3) Minimum effective dose should be used so as to minimize the side effects.

4) Route of administration depends upon the type and location of eye inflammation.

5) Suppression of inflammation is needed until the pathologic process burns out. Hence minimum maintenance therapy is tailored accordingly.

6) Steroids should not be used as the last resort but they should be started immediately when indicated.

Check Your Progress 1

1) Mention various steroidal anti-inflammatory agents.

.....

.....

.....

.....

.....

2) Briefly mention the mechanisms of action of steroidal anti-inflammatory agents.

.....

.....

.....

.....

.....

27.2.3 Routes of Drug Administration

1) Topical as eye drops or ointments
2) Sub conjunctival route
3) Sub-tenon route
4) Retrobulbar injections
5) Intravitreal route
6) Systemic route (oral, intramuscular, intravenous)

27.2.4 Indications

Indications of Topical Steroidal Agents

Topical steroids are used in steroid responsive inflammatory conditions of conjunctiva, lid, cornea and anterior chamber, Common indications of topical steroid use are:

1) Contact dermatitis
2) Allergic bleparitis and conjunctivitis
3) Vernal conjunctivitis
4) Phlyctenular conjunctivitis and keratitis
5) Ocular pemphigus
6) Mucocutaneous conjunctival lesions
7) Acne rosacea keratitis
8) Mooren's ulcer

9) Interstitial keratitis
10) Sympathetic ophthalmia
11) Disciform keratitis
12) Temporal arteritis
13) Sclerosing keratitis
14) Sclerokeratitis
15) Certain chemical burns of the cornea
16) Juvenile xanthogranuloma
17) Optic neurits, retrobulbar neuritis
18) Thyroid malignant exophthalmos
19) Pseudotumor orbit
20) Anterior segment ischaemia
21) Keratoplasty to prevent rejection
22) Post-operative state
23) Anterior and posterior uveitis
24) Episcleritis/Scleritis

Check Your Progress 2

1) Mention different routes of steroidal drug administration.

.....

.....

.....

.....

.....

2) Mention the indications of topical steroids.

.....

.....

.....

.....

.....

27.2.5 Formulations

Commonly used topical formulations include:

Dexamethasone

1) Dexamethasone sodium phosphate solution – 0.1 per cent, 0.05 per cent and 0.01 per cent
2) Dexarnethasone phosphate solution – 0.1 per cent.
3) Dexamethasone phosphate ointment – 0.5 per cent

Betamethasone

1) Betamethasone sodium phosphate solution – 0.1 per cent
2) Betamethasone sodium phosphate ointment – 0.1 per cent

Prednisolone

1) Prednisolone acetate suspension– 0.25 per cent, 1 per cent
2) Prednisolone sodium phosphate solution – 0.5 per cent, 1 per cent
3) Prednisolone phosphate solution – 0.5 per cent
4) Prednisolone phosphate ointment– 0.2 per cent

Hydrocortisone

1) Hydrocortisone acetate suspension – 0.5 per cent to 2.5 per cent
2) Hydrocortisone acetate solution – 0.2 per cent
3) Hydrocortisone acetate ointment – 1.5 per cent

Loteprednol

1) Loteprednol etabonate solution – 1 per cent

Flurometholone

1) Flurometholone suspension-0.1 per cent

Systemic Steroidal Anti-inflammatory Agents

These agents are mainly used for inflammation of choroid, retina and optic nerve.

Specific indications include:

1) Choroiditis
2) Retinitis
3) Optic neuritis
4) Sympathetic Ophthalmia

27.2.6 Complications

Ocular Complications of Topical Steroids

1) Rise in intra-ocular pressure
2) Cataract
3) Activation and progression of infections
4) Delayed wound healing
5) Dry eye
6) Ptosis

Ocular Complications of Systemic Steroids

1) Cataract
2) Glaucoma
3) Activation of infection
4) Ptosis, mydriasis
5) Delayed wound healing after surgery
6) Papilledema
7) Central retinal vein occlusion

Systemic Complications of Systemic Steroids

1) Gastrointestinal– Gastritis, visceral perforation, perforation
2) Central nervous system– Headache, convulsions, pseudotumor cerebri, psychiatric disturbances
3) Cardiovascular system– Hypertension
4) Renal– Sodium retention, potassium loss, fluid retention
5) Musculoskeletal– Distal weakness, myopathy, osteoporosis, fractures
6) Metabolic– Glucose intolerance, hyperlipidemia, obesity

7) Endocrine– Retardation of growth in children, secondary amenorrhoea, hypothalmic-pituitary axis suppression, cushingoid state

8) General–Weight gain, hirsuitism, decreased wound healing, easy bruisibility, increased susceptibility to infections.

Check Your Progress 3

1) Mention different indications of systemic steroidal drugs in ophthalmology.

.....

.....

.....

.....

.....

2) Mention different complications of steroidal drugs.

.....

.....

.....

.....

.....

27.3 NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

Non-steroidal anti-inflammatory drugs are labelled as NSAIDS.

27.3.1 Classification

Commonly used:

a) **Topical Non-steroidal Anti-idammatory Agents**

Drug name	*How supplied commercially*	
– Flurbiprofen	0.03% solution	1 drop 3 to 4 times/day
– Diclofenac	0.1% solution	1 drop 3 to 4 times/day
– Ketorolac	0.5% solution	1 drop 3 to 4 times/day
– Indomethacin	0.1% solution	1 drop 4 times/day

b) **Systemic Non-steroidal Anti-inflammatory Agents**

- Ibuprofen
- Ketoprofen
- Flurbiprofen
- Naproxen
- Indomethacin
- Diclofenac sodium

4.3.2 Mechanism of Action

NSAIDs act by inhibiting the formation of prostaglandins and other inflammatory agents like thromboxane and prostacyclin. NSAIDs have three types of, effects which are:

1) Anti-inflammatory effect
2) Analgesic effect
3) Antipyretic effect

27.3.3 Routes of Drug Administration

Topical as eye drops.

Oral in tablet/capsule form.

27.3.4 indications of NSAIDs in Ophthalmology

1) Allergic conjunctivitis
2) Mild form of uveitis
3) Maintenance of intra-operative mydriasis
4) Post-operatively to reduce inflammation
5) Mild form of scleritis and Episcleritis.

Check Your Progress 4

1) Mention the advantages of non-steroidal drugs over steroidal agents,

.....

.....

.....

.....

.....

.....

2) Mention the indications of non-steroidal anti-inflammatory agents in various ocular diseases.

.....

.....

.....

.....

.....

.....

27.3.5 Formulations

Flurbiprofen	**0.03** per cent solution
Suprofen	1.0 per cent solution
Diclofenac	0.1 per cent solution
Ketorolac	0.5 per cent solution
Indomethacin	0.5-1.0 per cent suspension, 0.1 per cent solution

27.3.6 Complications

- GI disturbances like nausea, vomiting, constipation, anorexia, pain, ulceration and bleeding (GI = Gestrointestinal).
- CNS effects like headache, dizziness, depression, confusion and insomnia (CNS = Central Nervous System).
- Haematological toxicity like blood dyscrasias and prolonged bleeding time
- Renal and liver toxicity
- Dermatological reactions
- Hypersensitivity reactions

Check Your Progress 5

1) Name at least three formulation of NSAIDs used in ophthalmology.

.....

.....

.....

.....

.....

2) Name at least five complications of NSAIDs.

.....

.....

.....

.....

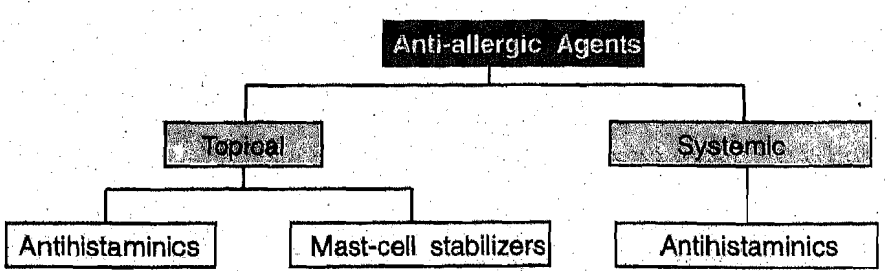
.....

27.4 OCULAR ANTI-ALLERGIC AGENTS

Allergy is caused by release of histamine by mast cells. Anti-allergic drugs act at this level.

27.4.1 Classification

Agents used for allergic disorders are:



27.4.2 Description of Anti-allergic Agents

a) Antihistamines

Histamine, a chemical agent causes allergic reactions. Anti-histamine agents are used so as to counteract the actions of histamine.

Topical Anti-histaminic Agents

1) Pheneramine Maleate
2) Levocobastine hydrochloride
3) Emedastine difumarate ophthalmic solution
4) Antazoline ophthalmic solution
5) Azelastine hydro-chioride

1) Pheneramine Maleate

A histaminic agent used extensively in mild to moderate ocular allergic disorders. Most of the time it is used along with Phenylephrine and or Naphazoline Eye drops.

2) *Levocabastine Hydrochloride*

A potent antihistaminic agent. It provides relief within few minutes.

Dosage

Ophthalmic suspension 0.05 per cent 1 drop 4 times/daily dose.

3) *Emedastine Difumarate*

Selective H1 receptor antagonist.

Indication

Allergic conjunctivitis

Dosage

Ophthalmic solution 0.05 per cent 1 drop 4 times/day.

Adverse Reaction

Burning sensation, headache, blurred vision

4) *Azelastine Hydrochloride*

Mechanism of Action

It is an antihistaminic agent. It also has leukotriene and platelet aggregating factor antagonistic activity.

Indications

i) Seasonal allergic conjunctivitis
ii) Vernal kerato conjunctivitis

Dosage

Ophthalmic solution 0.05 per cent, 3 drop 3 to 4 times/day.

Adverse Reaction

Burning sensation, local irritation

b) Topical Mast Cell Inhibitors

Mechanism of Action

Stabilization of mast cell, so that the release of inflammatory agents is inhibited.

Topical mast cell inhibitors include:

1) *Sodium Cromoglycate*

Indications

i) Vernal kerato conjunctivitis
ii) Giant papillary conjunctivitis
iii) Allergic Keratoconjunctivitis

Dosage

Ophthalmic solution 2 per cent and 4 per cent

1 drop 4 timeslday

Adverse Reactions

Burning sensation

Feeling of Dryness

2) *Lodoxamide*

A more potent mast cell stabilizer as compared to sodium cromoglycate.

Indications

i) Vernal Keratoconjunctivitis

ii) Giant papillary conjunctivitis

iii) Atopic Keratoconjunctivitis

iv) Allergic conjunctivitis

Dosage

Ophthalmic suspension 0.1 per cent

1 drop 4 times/day

Adverse Reactions

Burning sensation, Allergic reaction, crystalline deposits in cornea

3) *Nedocromil*

Mechanism and Indications

Same as Sodium Crornoglycate.

Dosage

Ophthalmic drop 1 per cent, 4 times/day

4) *Ketotifen Fumarate*

It acts both as an antihistaminic as well as a mast cell stabilizer.

Indications

Can be used in all moderate to severe allergic disorders of eye,

Dosage

Ophthalmic solution 0.025 per cent, 1 drop *2* to 3 times/day

Adverse Reaction

Usually a safe agent.

In less than 5 per cent cases burning, dry eye, allergic reactions may occur.

5) Olaptadine Hydrochloride

Mechanism

Acts both an antihistaminic and mast cell stabilizer agent.

Indication

Allergic disorders of diverse etiology.

Dosage

Ophthalmic solution 0.1 per cent, 1 drop **2** to **3** times/day

c) **Systemic Antihistaminics**

In severe ocular allergic conditions, topical anti-allergic agents may not be of great help. In such conditions, systemic anti-allergic agents like oral antihistaminics may be tried. Systemic antihistamines are particularly helpful when ocular allergic

diseases are associated with eyelid oedema and chemosis.

Commonly used systemic antihistaminic agents are:

1) Cetrizine
2) Levocetrizine
3) Fexofenadine
4) Pheniramine
5) Chlorpheniramine
6) Promethazine

Check Your Progress 6

1) List the commonly used topical antihistaminic agents.

.....

.....

2) Mention the various mast cell stabilizers.

.....

.....

3) Which are the commonly used oral antihistaminic drugs?

.....

.....

27.5 LET US SUM UP

In this unit you have learned that anti-inflammatory agents are used for various inflammatory conditions of the eye. Steroidal anti-inflaminatoiy agents are used for severe inflammatory conditions. Non-steroidal anti-inflammatory agents are used in mild to moderate inflammatory conditions. Steroidal agents can cause rise in intra-ocular pressure and also predispose the eye to various ocular infections. Steroidal therapy should not be stopped abruptly as abrupt stoppage may cause recurrence of inflammation. You have also learned that NSAIDs lack the side effects of steroidal agents like glaucoma and cataract. NSAID agents can be used in milder forms of ocular inflammations. NSAIDs act by inhibiting the synthesis of prostaglandins. Further you have learned that topical antihistaminic drugs act by counte ing the effects of histamine on vaiious receptors. Mast cell stabilisers prevent the degranulation of mast cells and thus the release of various inflammatory mediators. Oral antihistamines are indicated in severe cases of ocular allergy.

In next unit, you will learn about anti-infective agents like antibacterials, antifungals, antivirals.

27.6 KEY WORDS

Cataract : Opacification of the lens
Choroditis : Inflammation of the middle vascular coat of eyeball
Episcleritis : Inflammation of tissues between sclera and conjunctiva
Inflammation : Response **of** vascular tissue to any injury
Intra-vitreal : Within the vitreous
Retinitis : Inflammation of the retina
Scleritis : Inflammation of sclera
Steroids : Organic compounds derived from cholesterol

Sub-tenon : Below the tenon

Sympathetic Ophthalmia: Effect of injured eye to the other eye

Uveitis : Inflammation of middle coat of the eye ball

27.7 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) Commonly used Steroidal Anti-inflammatory Agents include:
   i) Dexamethasone Sodium Phosphate
   ii) Prednisolone acetate
   iii) Methyl Prednisolone
   iv) Triamcinolone acetonide
   v) Hydrocortisone acetate
   vi) Flurometholone acetate
   vii) Medrysone
   viii) Loteprednol
   ix) Rimexolone

2) Steroidal agents cause constriction of blood vessels, seduction of numbers of inflammatory cells, inhibition of activities of inflammatory cells like neutrophils, lymphocytes etc. They also decrease permeability of the blood vessels, so the secretion of fluid from blood vessels is also reduced. The action of steroid as an anti-inflammatory agent is non-specific. It can reduce inflammation caused by any agent whether living or non-living.

   The various effects of steroids on inflammatory cells include decreased T cell proliferation, reduced T cell function, lysis of activated T cells, reduced interleukin 2 production by T cells, reduced monocyte chemotactic factor production, reduced secretion of collagenases, decreased release of histamine by basophils and inhibition of stimuli for prostaglandin production by fibroblasts.

   Other effects include reduced edema, decreased erythema, reduced neovascularisation and serum IgG and IgA concentration, reduction of complement concentration 'and stabilisation of vessels.

Check Your Progress 2

1) The various routes of steroid administration include:
   i) Topical as eye drops and ointments
   ii) Sub-conjunctival route
   iii) Sub-tenon route
   iv) Retrobulbar injections
   v) Intravitreal route
   vi) Systemic route (oral, intramuscular, intravenous)

2) Topical steroids are used in steroid responsive inflammatory conditions of conjunctiva, lid, cornea and anterior chamber. Common indications of topical steroid use are:
   i) Contact dermatitis
   ii) Allergic blepharitis and conjunctivitis
   iii) Vernal conjunctivitis
   iv) Phlyctenular conjuctivitis and keratitis
   v) Ocular pemphigus
   vi) Mucocutaneous conjunctival lesions

vii) Acne rosacea keratitis
viii) Mooren's ulcer
ix) Interstitial keratitis
x) Sympathetic ophthalmia
xi) Disciform keratitis
xii) Temporal arteritis
xiii) Sclerosing keratitis
xiv) Sclerokeratitis
xv) Certain chemical burns of the cornea
xvi) Juvenile xanthogranuloma
xvii) Optic neuritis, retrobulbar neuritis
xviii) Thyroid malignant exophthalmos
xix) Pseudotumor orbit
xx) Anterior segment ischaemia
xxi) Keratoplasty to prevent rejection
xxii) Post-operative state
xxiii) Anterior arid posterior uveitis
xxiv) Episcleritis/Scleritis

Check Your Progress 3

1) These agents are mainly used for inflammation of choroid, retina and optic nerve. Specific indications include:
   i) Choroiclitis
   ii) Retinitis
   iii) Optic neuritis
   iv) Sympathetic Ophthalmia

2) The various complications of steroids can be divided into ocular and systemic complications.
   a) Ocular Complications of Topical Steroids
      i) Rise in intra-ocular pressure
      ii) Cataract
      iii) Activation and progression of infections
      iv) Delayed wound healing
      v) Dry eye
      vi) Ptosis
   b) Ocular Complications of Systemic Steroids
      i) Cataract
      ii) Glaucoma
      iii) Activation of infection
      iv) Ptosis, mydriasis
      v) Delayed wound healing after surgery
      vi) Papilledema
      vii) Central retinal vein occlusion
   c) Systemic Complications of Systemic Steroids
      i) Gastrointestinal: Gastritis, visceral perforation, perforation
      ii) Central nervous system: Headache, convulsions, pseudotumor cerebri, psychiatric disturbances

iii) Cardiovascular system: Hypertension

iv) Renal: Sodium retention, potassium loss, fluid retention

v) Musculoskeletal: Distal weakness, myopathy, osteoporosis, fractures

vi) Metabolic: Glucose intolerance, hyperlipidemia, obesity

vii) Endocrine: Retardation of growth in children, secondary amenorrhoea, hypothalmic-pituitary axis supression, cushingoid state

viii) General: Weight gain, hirsutism, dec eased wound healing, easy bruisibility, increased susceptibility to infections.

Cheek Your Progress 4

1) The advantages of NSAIDs over steroids include lack of side effects like cataract, glaucoma, inhibition of wound healing and decreased resistance to infections.

2) Indications of NSAIDS in Ophthalmology:

i) Allergic conjunctivitis

ii) Mild form of uveitis

iii) Maintenance of intra-operative mydriasis

iv) Post-operatively to reduce inflammation

v) Mild form of scleritis and episcleritis

Check Your Progress 5

1) Flurbiprofen , 0.03% solution
Suprofen 1.0% solution
Diclofenac 0.1% solution

2) i) GI disturbances like nausea, vomiting, constipation, anorexia, pain, ulceration and bleeding

ii) CNS effects like headache, dizziness, depression, confusion and insomnia

iii) Haematological toxicity like blood dyscrasias and prolonged bleeding time

iv) Renal and liver toxicity

v) Dermatological reactions

Check Your Progress 6

1) The commonly used topical antihistaminic drugs are pheniramine, levocobastine, emedastine and antazoline.

2) Sodium cromoglycate, Nedocromil sodium and Lodoxamide are the most common mast cell stabilisers.

3) Oral antihistamines commonly used for ocular allergy are cetrizine, levocetrizine, phenirarnine, chlorpheniramine, fexofenadine and promethazine.