OCULAR THERAPEUTICS

T. A. Raji
and
T. Sarada Amma
Department of Veterinary Surgery and Radiology
College of Veterinary and Animal Sciences,
Mannuthy, Thrissur

A range of agents with diverse actions is used in ocular therapeutics, including antimicrobials, anti-inflammatory agents, tear replacement preparations, immuno-suppressants, ocular hypotensive agents and modulators of pupil size. A wide selection of veterinary and human ophthalmic preparations are available today. A working knowledge of the pharmacology and species variation in response to specific drugs allows the veterinarian to make effective and safe use of human therapeutic agents.

CHARACTERISTICS OF OPHTHALMIC DRUGS

Drug characteristics that influence biologic activity include solubility characteristics, toxicity, pH, stability, sterility, concentration of the active agent, viscosity and additives. Therapeutic response also depends on the bioavailability of a drug and the desired pharmacologic effect at the site for sufficiently long duration.

Unless specifically indicated to achieve a specific therapeutic effect, preparations that are isotonic with respect to the tear film (0.9% sodium chloride equivalent) are desirable because of their tolerability by the eye. Normal saline or balanced salt solutions are ideal.

Sterility of the ophthalmic solutions is important. Benzalkonium chloride, chlorbutanol, polymixin B sulphate, organic mercurials, phenols and substituted alcohols are added to these products to minimize contamination. These additives may be responsible for some degree of irritation upon instillation.

The amount of drug that penetrates through the cornea increases as the concentration of the active ingredient increases, upto a point. Similarly increasing frequency of topical application of a drug is just as effective as increasing the concentration of the preparation. Ointment vehicles provide the largest contact time, but decrease drug availability to the tissues. They are easier to administer in large animals. Solutions and suspensions are more easily administered and better tolerated and are preferred to ointments in small animals.

Application of more than one drop is not recommended, the limited capacity of the external eye to retain medication will result in loss of majority of additional medication. In the same way, application of a 5 mm long 'squeeze' of ointment medication in small animals and twice that in large animals provides adequate medication.

ROUTES OF ADMINISTRATION

Generally, eyelid, superficial corneal, conjunctival and nasolacrimal disease may be managed with topical and occasionally subconjunctival medications. Diseases of the episclera, sclera, lacrimal glands, urea, anterior and posterior segments and orbit require parenteral therapy, which can be supplemented by administration of drugs through other routes also.

TOPICAL: For this, the drugs are placed and retained upon the cornea and in the conjunctival sac. Contact time is increased if the medication is applied under the lower eyelid. Rapid systemic absorption occurs via the conjunctival vessels. This process is accentuated if the conjunctiva is inflamed. Drug penetration in the normal cornea is limited and is markedly increased in the presence of keratitis and corneal ulceration. Maximum penetrability is achieved by a drug with both lipid and water soluble characteristics.

SUB-CONJUNCTIVAL OR SUB-TENON'S INJECTION:

Bulbar subconjunctival injections may be placed subconjuctivally or beneath Tenon's capsule. The technique usually requires topical anaesthesia, restraint and in the horse, an auriculo palpebral nerve block. A

25 to 26 gauge needle on a tuberculin syringe or 3 ml syringe is used. A noticeable bleb should appear when the medication has been deposited. This route in indicated for acute anterior uveitis, panophthalmitis, episcleritis, initial control of chronic superficial keratitis (pannus) and infections keratitis. Injection following intra ocular surgery near the surgical site is contra indicated.

PARENTERAL: Oral, intravenous or intramuscular administration may be utilized to treat diseases of the posterior and anterior segments of the eye, orbit, sclera, eyelids and optic nerve. Systemically administered drugs that are lipid soluble unbound to plasma protein and of smaller molecular weight penetrate the blood-aqueous barrier best.

ANTIMICROBIALS

Antimicrobials are the most commonly used drugs in veterinary ophthalmology. Before employing such a drug, it should be ascertained that condition is an infection or not an inflammation associated with various factors.

General Principles

In external infections of the eye, a smear or scraping should be prepared prior to antimicrobial therapy and stained with the Gram's, Wright's or Giemsa stain. In acute severe and chronic infectious problems culture and sensitivity determination should be performed routinely. Broad spectrum antibiotics may be administered until the antibiotic sensitivity of the organism is determined.

Applications of antiviral therapy in veterinary ophthalmology are limited because of the infrequent incidence of external viral diseases and the difficulty in establishing a definitive diagnosis.

CHEMOTHERAPEUTIC AGENTS

The sulphonomides are the chemotherapeutic agents utilized in veterinary ophthalmology. They are effective against gram positive and some gram-negative organisms and, in high concentrations, against some viruses, fungi and toxoplasma. Of the topical sulphas, sulphacetamide penetrates the cornea best.

ANTIBIOTICS

Effective use of this group of drugs on bacterial infections depends on: 1) use of a drug that is effective against specific infectious agent. 2) attainment of adequate therapeutic levels of the drug at the site of infection and 3) knowledge of possible side effects.

Antibiotics are commonly used prophylactically in veterinary ophthalmology. They are especially useful in preventing infections before and after extra and intraocular surgery, in traumatic corneal disease, and kerato-conjunctivitis sicca. Some of the common drugs used are : Penicillins, Cephalosporins, Bacitracin, Vancomycin, Polymixin B and Colistin, Chloramphenical, Erythromycin, Gentamicin, Neomycin, Streptomycin, Tetracyclines, Isoniazid, Nitrofurans, Nalidixic acid, Ciprofloxacin

ANTIMYCOTIC AGENTS

Ocular and adenexal fungal infections are manifested by three distinct disease processes: Mycotic keratitis, mycotic endophthalmitis and blepharodermatomycosis.

Topical Antimycotics

There are characterized by poor corneal and intraocular penetration and local toxicity - Nystatin, Amphotericin B, Notamycin (pimaricin), Flucytosine and Imidazole compounds (not recommended).

Amphotericin B is effective topically against a broad spectrum of fungi including common agents of keratomycosis. Treatment involves intravenous preparation in concentrations upto 5 mg/ml applied 8 to 12 times daily. 5-fluorocytosine and clotrimazole are other drugs with proven antimycotic activity.

ANTIPARASITIC AGENTS

Ocular toxoplasmosis with or without systemic involvement is classically treated with high concentration of parenteral sulphonamides and/or pyrimethamine. Sulphadiazine, sulphamerazine and sulphamethazine are the most effective.

ANTI-INFLAMMATORY AGENTS

The nature of the ocular tissues predisposes the eye to inflammatory insults and such changes frequently results in permanent structural change and thus results in loss or impairement of function.

Corticosteroids

Corticosteroids are the most frequently used agent in non specific therapy and are indicated when the inflammatory reaction is potentially severe enough to produce significant, permanent structural change

These drugs decrease capillary dilation, capillary permeability, exudation and the migration of phagocytes to the site of inflammation. They suppress scar formation due to decreased proliferation of fibroblasts, extent of fibrous tissue response, capillary proliferation and collagen deposition. Route of administration depends upon the location of the inflammatory process. Severe disease should be treated initially with maximal dosage which is decreased as the disease responds to the treatment.

Immunosuppressants

These drugs act primarily by eliminating or reducing specific antibodies. This group include radiation, folic acid antagonists, purine analogs, alkylating agents and antilymphocyte serum.

Antihistamines

The rationale for the use of histamine antagonists involves preventing histamine formation within and release from mast cells, competing with released histamine at its site of action, and blocking its effect on the receptor cells. Corticosteroids interfere with degranulation of mast cells.

Nonsteroid Anti-inflammatory agents

These drugs do not have the side effects of corticosteroids and can potentiate the anti-inflammatory effect if used in combination with corticosteroids. Release of prostaglandins in vivo plays a role in ocular inflammatory processes. These drugs act by suppressing the synthesis or action of prostaglandins.

OCULAR HYPOTENSIVE AGENTS

Three groups of ocular hypotensive agents are currently available for medical treatment of faricoma. These drugs are often used in a combination.

1. Carbonic anhydrase inhibiting diuretics

These drugs reduces intraocular pressure by inhibiting the production of aqueous humor by the ciliary body epithelium. Eg. Acctazolamide, Ethoxzolamide, Dichlorphenomide and Methazolamide.

These can be administered orally and intravenously

a) Acetazolamide

Only carbonic anhydrase inhibitor available that is administered parenterally. For emergency use as in congestive glaucoma, intravenous acetazolamide rapidly decreases aqueous production. Single oral dose results in significant decrease in intraocular pressure within one hour. The average-size dog (12 to 14 kg) may be administered 125 mg initially the dosage may be altered according to patient tolerance and response to the drug. Treatment twice daily is adequate in dogs. Treatment three times daily may maximize total daily drug dosage while minimizing side effects. Long term use is to be avoided.

Clinical use: Carbonic anhydrase inhibitors are useful in the treatment of glaucoma in the dog and cat usually in conjunction with autonomic stimulators and hyperosmotic agents. Acts additively with miotics. Acetazolamide may produce omitting and diarrhoea.

2. Parasympathomimetic agents

They have a primary action of stimulating cholinergic nerves. The muscle fibers of the ciliary body and iris sphincter are predominantly under parasympathetic control. Contraction of ciliary muscle fibers alter the intraocular pressure by increasing the facility of aqueous humor outflow.

3. Sympathomimetic Agents

Sympathomimetic agents such as epinephrine, norepinephrine, phenylephrine hydrochloride and naphazoline decrease intraocular pressure in many species of animals. Alpha adrenergic agonists like norepinephrine, increase the facility of aqueous outflow and beta adrenergic agonists, like salbutamol reduce intraocular pressure without affecting the facility of outflow, possibly decreasing the aqueous humor production.

4. Osmotic Diuretics

Osmotic diuretics are used in veterinary ophthalmology to reduce intra ocular pressure in the management of acute glaucoma and prior to intraocular surgery when vitreous loss is anticipated. Eg.: Mannitol, glycerol and occasionally urea.

MYDRIATICS

The topically applied autonomic drugs which produce mydriasis (puppillary dilatation) and cyeloplegia (paralysis of accommodation) are among the most useful pharmacologic agents in veterinary ophthalmology. The common mydriatics comprise two groups of drugs. Sympatho mimetics and parasympatholytics.Sympathomimetic agents imitate (direct) or potentiate (indirect) the action of adrenalin

resulting in the stimulation of the dilator muscle of the iris. Parasympatholytic drugs render the iridal sphincter and ciliary muscles insensitive to acetylcholine, producing pupil dilatation and paralysis of the ciliary musculature. Tear replacement therapy – Used in keratitis sicca and where lacrimation is poor or absent.

The drugs used are:a) Hypromellose,b) Polyvinyl alcohol Both of these have short contact times and has to be applied hourly.c) Ointment lubricant like liquid paraffin is a useful adjunct to therapy, d) Polyacrylic acid gels- provide longer contact time. Applied 4 to 6 times daily,e) Sodium hyaluronate, a glycosaminoglycan with viscoelastic and lubricating properties is developed recently,5. Soft contact bandage lenses - Provide useful alternative to the third eyelid flap in the management of superficial ulcers.

It acts as a protective layer over cornea, stabilizes the tear film, reduces stimulation of exposed corneal nerves and enhances the contact between regenerating corneal epithelium and the underlying basement membrane. They are contra indicated in the treatment of keratoconjunctivitis sicca and infected ulcers.

Its use is beneficial in controlling or preventing glaucoma associated with trauma, hypharma and uvlitis. They may also be utilized preoperatively for cataract surgery to reduce intraovular pressure. Response to the drug diminishes after few weeks of therapy. Gradual narrowing of iridocorneal angle or other factors in progression of glaucoma may result in resi in intraocular pressure which may incorrectly be attributed to drug olerance.Eg. Pilocarpine, physostigmine, neostigmine, Demecacium bromide, Diisopropyl phosphorofluoridate (DEP) and eothiophanate

There are administered orally or intravenously to act by increasing the osmotic pressure of blood plasma relative to that of the vitreous body and aqueous humor.Eg. Phenylepharine 10%, epinepherine 1%, hydroxyamphetamine 1.0% cocaine 1% and ephedrine 10.0%.Eg. Atropine 1% and 4%, Homatropine 5%, Hyoscine (Scapolamine) 0.25%, cyclopentolate 1%, Trepicamide 1% and Eucatropine 5%.

Clinical use

Most commonly used in the treatment of iridocyditis to relieve pain associated with ciliary spasm. Pain associated with concomitant diseases like corneal ulceration and keratitis is not much diminished by this drug. In the normal eye 1% atropine sulphate every 2 to 3 days is sufficient for mydriasis in dog and cat. In an inflamed eye, instill it 3 to 4 times daily supplemented with 10% phenylephrine.Contraindications: Glaucoma especially with narrow indocorneal angles and shallow anterior chambers. It is also contraindicated in keratoconjunctivitis sicca.Side effects: Salivation, especially in cats. Occasional vomiting, local irritation.

b) Homotropine: It is having about one tenth the potency of atropine and is available in solutions from 1 to 5%. Rapid onset and short duration of cation. Can be combined with 10% phenylephrine.

c) Cydopentalate: Synthetic compound available from 0.5 to 2.0% solutions. Rapid onset (faster than Hematropine). Shorter duration and greater intensity. Salivation and local irritation may occur.

d) Tropicamide: Most rapidly acting parasympatholytic drug available. Preferred mydriatic for ocular fundus examination. Available in concentrations from 0.5 to 2.0%, the 0.5% and 1% solutions are most commonly used in animals. Maximal mydriasis occurs in 30 minutes. ❑

INFOMANIA

ANSWERS

1. Nakula and Sahadeva
2. Onychectomy
3. Medetomidine
4. Genetic Pollution
5. Wildlife trade
6. Red jungle fowl
7. Amritmahal
8. 0.2%
9. Intra osseous administration
10. Colposuspension.

Complied by : **Dr. Jayesh V.,** Veterinary Surgeon, District Veterinary Centre, Kalpetta, Wayanad