Anti-Bacterial Agents in Ophthalmology

Dr. Mrs. Indu Pandey DOMS. *This JDOS CME was presented on October 23, 2005 in Hotel Krishna at 4 PM. The meeting was sponsored by Milmet division of Sun Pharma. High tea sponsored by Milmet followed the CME.*

Introduction

A vast array of antibiotics are available to us, right from the discovery of Penicillin by Sir Alexander Fleming in 1929 to the recent introduction of Oxazolindinone - Linezolidin in 2000…

The choice of antibiotics for a given infective condition is governed by the type or genre of the causative agent and it's susceptibility to a given drug. The MIC level at the target tissue is another important factor.

I will be dealing with the infective conditions of the eye and it's adenexa and the drug of choice for the given infective condition.

Where relevant, I shall also point out the important precautions to be used against the specific antibiotic.

Infections of the eyelids: Stye/Hordeolum Externum

A suppurative inflammation of the Zeis Gland.
Commonly caused by Staphylococcus sp.

A stye causing excessive discomfort must be incised.

Hot compresses + Antibiotics

Systemic antibiotic of choice - tetracyclines - Doxycycline 200 mg stat, 100 mg OD for 7 days.

Topical antibiotic of choice - erythromycin eye ointment QID. (Bacitracin (ointment) may also be used topically)

Infections of the eyelids: Hordeolum Internum

Suppurative inflammation of a meibomian gland or possibly an infected chalazion.
The treatment is the same as that of a stye.

If drainage is necessary the incision has to be made as with a chalazion.

Infections of the eyelids: Chalazion

Chronic inflammatory granuloma of the meibomian gland.

The inflammation is usually sterile, postulated due to either chronic irritation to the tissue or due to a build up of secretions within the gland.

Secondary infection may occur, in which case the treatment is the same as that of "stye".

Large chalazia must be incised and curetted.

Very hard chalazia must be sent for biopsy to rule out meibomian cell carcinoma.

Triamcinolone, 40 mg/ml may be used on small chalazia, or chalazia very close to the lacrimal apparatus.
The total dosage depends on the size of the chalazion.

A steroid injection can lead to permanent depigmentation of the skin at the injection site.

Infections of the eyelids: Blepharitis

Allergic (contact dermatitis), Squamous Blepharitis and Ulcerative blepharitis.

Ulcerative blepharitis is an infection caused by staphylococcus sp.

Treatment:

Scrubbing eye lid margins with mild shampoo with a cotton bud BD.

Warm compresses.

Oral doxycycline 200 mg stat, 100 mg OD for 1-2 weeks, locally bacitracin or erythromycin eye ointment.

Infections of the eyelids: Preseptal Cellulitis

May be primarily infectious or inflammatory with secondary infectious potential.

Staph. aureus and streptococci are most common

H. influenzae should be considered in children.

Anaerobes rarely can cause cellulitis (crepitations, foul smelling discharge).

Suspect viral cause if associated with Herpetic infections.

MILD PRESEPTAL CELLULITIS:

Option 1 - Amoxycillin/Clauvanate -

Children: 20-40 mg/kg/day orally divided TID.

Adults: Up to a maximum of 500 mg/day QID.

Option 2 - Cefaclor (Pt. Not sensitive to penicillin)

Children: 20-40 mg/kg/day orally divided TID.

Adults: 250-500 mg orally QID.

Option 3 - Trimethoprim/Sulfamethoxazole

Children: 8-12 mg/kg/day trimethoprim with 40-60 mg/kg/day sulfamethoxazole orally divided BD.

Adults: 160-320 mg trimethoprim with 40-60 mg/kg/day sulfamethoxazole orally divided BD.

Option 4 - Erythromycin

Children: 30-50 mg/kg/day orally divided TDS or QID.

Adults: 250-500 mg orally QID.

MODERATE TO SEVERE CELLULITIS

Admit to hospital for I.V antibiotics:-

Ceftrioxone:

Children: 100 mg/kg/day IV in 2 divided doses.

Adults: 1-2 g IV in 2 divided doses.

And **Vancomycin**:

Children: 40 mg/kg/day IV in 3-4 divided doses.

Adults: 0.5-1 g IV in 2 divided doses.

IV antibiotics can be changed to comparable oral antibiotics after significant improvement is observed.
Systemic antibiotics are maintained for a complete 10-14 days.

Infections of the lacrimal apparatus: Canaliculitis.

Bacterial : Actinomyces israelii - most common, other bacteria : Fusobacterium and Nocardia.

Removal of obstructing concretions: by gentle pressure over the lacrimal sac rolled towards the punctum. Smears may be taken to identify the causative agent.

After removing the concretions, the canaliculus is irrigated with 1% iodine solution (earlier Penicilin G 100,000 U/ml was used). The patient is made to sit in an upright position so that the solution drains out of the nose and not the naso-pharynx.

Infections of the lacrimal apparatus: Dacryocystitis

ALWAYS DRAIN A POINTING ABSCESS.

Antibiotics:

Afebrile children - Amoxycillin/Clauvanate (20-40 mg/kg/day in 3 divided doses) or Cefaclor (20-40 mg/kg/day in 3 divided doses).

Febrile/acutely ill children - hospitalize and treat with cefuroxime, 50-100 mg/kg/day IV in 3 divided doses.

Afebrile adults - Cephalexin 500 mg orally QID or Amoxycillin/Clauvanate 500 mg orally TDS.
Infections of the lacrimal apparatus: Dacryocystitis

Febrile, acutely ill adults: Hospitalize and treat with cefazolin 1 g IV TDS.

Infections of the lacrimal apparatus: Acute Infectious Dacryoadenitis

Bacterial (Staphylococcus aureus, Neisseria gonorrhoeae, streptococci) or Viral (mumps, infectious mononucleosis, influenza, herpes zoster).

For bacterial, drug of choice -

Amoxicillin/Clauvanate
Cephalexin
Cefazolin (used IV in severe cases)

Amoxicillin/Clauvanate:
Children: 20-40 mg/kg/day orally divided TDS
Adults: 250-500 mg orally TDS.

Cephalexin:
Children: 20-50 mg/kg/day orally divided QID
Adults: 250-500 mg orally QID.

Cefazolin:
Children: 50-100 mg/kg/day IV divided TDS or QID.
Adults: 1 g IV TDS

If there are any signs of orbital involvement (decreased motility or proptosis) hospitalize and start IV Cefazolin as above.

Infections of the Orbit: Orbital Cellulitis

Usually a direct extension from the ethmoidal sinuses (ethmoiditis), therefore the common organisms are Staphylococcus sp., Streptococcus sp., H. influenzae, bacteriodes, gram negative rods.

The patient has to be hospitalized and antibiotics given need to cover gram positive, gram negative and anaerobic organisms due to the above reasons.

CHILDREN

Ceftriaxone, 100 mg/kg/day IV divided BD. PLUS
Vancomycin 40 mg/kg/day IV divided BD.

ADULTS
Ceftriaxone, 1-2 g IV BD PLUS
Vancomycin 1 g IV BD

OR ampicilin/sublactam 3 g IV QID.

Metronidazole loading dose 15 mg/kg and then 7.5 mg/kg 6 hourly for adults. Metronidazole is usually not added for children unless there is a strong suspicion of anaerobic infection.

When the orbital cellulitis is clearly and consistently improving, then the regimen can be changed to oral antibiotics -

Amoxycillin/Clauvanate OR
Cefaclor
for a total duration of 14 days.

Infectious Corneal Infiltrates/Ulcer

Causative agents : Staph. aureaus; Strept pneumoniae
Pseudomonas
Enterobacteriaceae
Gram - ve: Tobramycin & Genta.
Gram +ve: Cefuroxime & Gatiflox

Topical cycloplegics

Postoperative Endophthalmitis: Acute

Microbes responsible:
Commonest organism - Staphylococcus epidermidis.
Common - Staphylococcus aureus, Strepotococcus sp.
Rarely - Gram negative organisms and anaerobes.

Treatment:

Hospitalize and atropinize.
Intravitreal antibiotics are the treatment of choice. Immediate pars plana vitrectomy is beneficial if visual acuity on presentation is light perception or worse. Otherwise, vitreous aspiration combined with placement of intravitreal antibiotics (and possibly steroids) is usually performed.
Amikacin 0.4 mg in 0.1 ml
Ceftriaxone/Ceftazimidine 2 mg in 0.1 ml
Vancomycin 1 mg in 0.1 ml
Clindamycin 1 mg in 0.1 ml

Topical fortified antibiotics

Fortified Cefazolin or fortified Vancomycin one hourly alternating with:
Fortified Gentamycin or Tobramycin one hourly, so that one of the combinations is instilled every 30 minutes.

The role of intra-vitreal steroids is controversial.

Making Fortified Antibiotics

Making Fortified Topical Antibiotics

FORTIFIED TOBRAMYCIN OR GENTAMYCIN

Inject 2 ml of 40 mg/ml directly into a 5 ml bottle of Tobramycin/Gentamycin ophthalmic solution. This gives 7 ml of 15 mg/ml. Refrigerate, expires after 14 days.

FORTIFIED CEFAZOLIN

Add water for injection to 500 mg Cefazolin dry powder to form 10 ml solution. This provides 50 mg/ml. Refrigerate, expires after 7 days.

FORTIFIED VANCOMYCIN

Add water for injection to 500 mg of vancomycin dry powder to form 10 ml solution. This provides 50 mg/ml. To achieve 25 mg/ml take 5 ml of the above solution and add 5 ml water. Refrigerate, expires after 4 days.

Specific Antibiotics, Drug Interactions And Important Adverse

Effects

Sulphonamides

MIC for Chlamydia trachomatis is just 0.1µg/ml
Adequate hydration and alkalization is required to prevent development of crystalluria.
Acute hemolytic anaemia (in G6PD deficiency), Agranulocytosis, Aplastic Anaemia
Hypersensitivity reactions: Steven-Johnson Syndrome, Bechet's syndrome.
Drug interactions: Oral anti-coagulants, sulphonylurea hypoglycemic agents, hydantoin anti-convulsants - the dose of these needs reduction.

Quinolones

Generally well tolerated. Common side effects are nausea, abdominal discomfort, headache, dizziness.
Patients on theophylline or NSAIDS - hallucinations, delirium, seizures may occur.
Produce arthropathy in several species of immature animals.
Arthralgias and joint swellings have developed in children - therefore not to be used pre-puberty and pregnancy.
PHOTOTOXICITY (Lomefloxacin)
Achilles Tendinitis and Tendon rupture - avoid strenuous exercise.
In case of impaired renal and hepatic function the dose of quinolones and fluoroquinolones needs to be reduced since none of these agents is removed by peritoneal or hemodialysis.
ALL QUINOLONES ARE CONTRAINDICATED IN PATIENTS WITH HISTORY OF CONVULSIONS.
Can increase the serum levels of theophylline and warfarin due to interference in hepatic biotransformation.
Gatifloxacin and Moxifloxacin (systemic)
Antacids reduce absorption
Concurrent insulin/oral hypoglycemics: symptomatic hypo- or hyper-glycemia
Antipsychotics, cisapride, erythromycin, tricyclic depressants, anti-arrhythmics - prolongation of QT interval
Digoxin half-life is prolonged - toxicity can occur
Probenecid increases half-life
Concurrent use of NSAID's increases the risk of seizures
Enhanced effect of warfarin
Photosensitivity - avoid excessive sunlight/UV exposure
Ocular - blurring, photophobia, keratitis/corneal opacity (on prolonged topical use).

Penicillins And Aminopenicillins

Hypersensitivity reactions are the most common adverse effect. 0.7 to 10% of the patients develop some kind of such reactions according to different studies.
The most dreaded adverse reaction is angioedema and anaphylaxis. The incidence is 0.004 to 0.04% according to different studies.
About 0.001% of patients treated with these drugs die from anaphylaxis.
A negative PRE-PEN (benzylpenicilloyl polylysine) test can eliminate the patient's chances of developing an anaphylactic response.

Reactions unrelated to hypersensitivity -
Pseudomembranous collitis (due to elimination of the commensals and overgrowth of C. difficile)
Toxicity (very very rare) - bone marrow depression, granulocytopenia, hepatitis.
No drug interactions have been reported.

Cephalosporins

20% of patients sensitive to Penicillin exhibit cross-sensitivity to Cephalosporins.

Adverse reactions are the same as that of penicillins.

Potentially nephrotoxic especially with very high doses (Acute Renal Tubular Necrosis). Therefore care needs to be exercised in Renal Function impaired patients.

Aminoglycosides

All aminoglycosides have the potential to produce reversible and irreversible vestibular, cochlear and renal toxicity.

Tobramycin, Amikacin and gentamycin: incidence of ototoxicity up to 25%, initially reversible.

Deafness may occur several weeks after therapy is discontinued.

The first symptom is a high-pitched tinnitus, if the drug is not discontinued auditory impairment occurs within a few days.

Nephrotoxicity - 8 to 26% patients on aminoglycosides for several days will develop mild renal impairment that is almost always reversible.

Neuromuscular blockade leading to apnea - neomycin. Rarely seen with other aminoglycosides, least with tobramycin.

Streptomycin - enlargement of the blind spot.

Hypersensitivity - skin rash seen with neomycin.

Chloramphenicol and Gentamycin may not be used together as this combination promotes the growth of pseudomonas sp.

The combination of Streptomycetin and Penicillin is controversial due to the bacterostatic nature of the former drug against the bacterocidal effect of the latter drug.

Tetracyclines

Mainly produce gastrointestinal side effects - burning, distress, nausea and vomiting. Diarrhea mimicking pseudomembranous colitis can occur.

Can be given after meals to reduce GI effects, should not be taken with dairy products.

Photosensitivity - demeclocycline.

Hepatic toxicity with oxytetracycline and tetracyline more so if large quantities given.

Renal toxicity - aggravate uremia. Doxycycline is least renal toxic.

Fanconi Syndrome - Nausea, vomiting, polyuria, polydipsia, proteinuria, acidosis, glycosuria and gross aminoaciduria with outdated and degraded tetracycline.

Effects on teeth: Children - brown discoloration of teeth. Permanent.

Hypersensitivity reactions are rare.

Important precautions: Pregnant patients, children under 8 years should not be given tetracyclines. Old, unused supplies should be discarded.

Chloramphenicol

Hypersensitivity uncommon (skin rashes, fever, Jarisch-Herxheimer reaction in therapy for syphilis, brucellosis, typhoid)

Hematologic toxicity is the most important adverse reaction.

Dose related presents as anemia, leukopenia or thrombocytopenia and bone marrow depression.
Idiosyncratic presenting as aplastic anaemia or fatal pancytopenia (a genetic predisposition is suggested).

GI irritation is common.

Optic neuritis occurs in 3-5% children with mucoviscidosis.

"Gray baby syndrome" in premature children on chloramphenicol therapy (2-9 days after starting therapy) - fatal.

Drug interactions: Prolongation of half-lives of dicumarol, phenytoin, chlorpropamide, tolbutamide. Severe toxicity and death may occur.

Drug interactions: Chronic administration of phenobarbital or acute administration of rifampicin shortens the half-life of chloramphenicol and may result in sub-therapeutic concentrations of the drug.

The risk of aplastic anemia does not contraindicate the use of chloramphenicol in situations in which it is necessary; however, it emphasizes that the drug should never be used when other safer anti-microbials can be used.

Macrolides

Erythromycin, Clarithromycin, Azithromycin.

Azithromycin is more commonly used with a loading dose of 500 mg followed by 250 mg once daily.

Serious untoward effects are very rare - Cholestatic jaundice (reversible), and GI irritation.

Significant drug interactions: Potentiation of effects of ; astemizole, carbamazepine, corticosteroids, cyclosporine, digoxin, ergot alkaloids, terfenadine, theophylline, tiazolam, valproate, warfarin.

Vancomycin

Rapid intravenous infusion can cause "red neck" or "red man" syndrome - erythema or urticaria, flushing, tachycardia and hypotension. To avoid this, the infusion must be given over a period of 60 minutes.

Reversible ottotoxicity and nephrotoxicity, however it must be considered if aminoglycosides are administered concurrently.

Bacitracin

Serious nephrotoxicity results from the parentral use of this anitbiotic. Hypersensitivity reactions result from topical application, but very rarely.

Summary

In all serious (sight/life threatening) infective conditions the aim is to use a

broad spectrum antimicrobial agent that may cover gram positive, negative and anaerobic organisms.

Till a single such drug is available the current recommended combination:

Vancomycin for gm +ve organisms.

III generation cephalosporins for gm -ve org.

Metronidazole for anaerobes.

Fluorinated 4-quinolones are slowly evolving in this direction.

Azithromycin can be used instead of tetracyclines in children under 8 years of age and pregnant/nursing women.