COST EFFECTIVE ANALYSIS OF COMMONLY USED TOPICAL DRUGS IN OPHTHALMOLOGY

Corresponding Author:

Anil Kumar. P
H.No: 2548, E-Block, 13th Main, 9thCross, Sahakar Nagar,
Bangalore-560092, India.
E-mail: anilkumarpothuru@gmail.com

ABSTRACT

Objective: *The objective of this study was to compare the cost-effectiveness of commonly used topical drugs in ophthalmic conditions like conjunctivitis, keratitis, blepharitis, uveitis, etc.*

Materials and Methods:*Data was collected from the Ophthalmology department at Dr. B.R Ambedkar Medical College for conditions like conjunctivitis, keratitis, blepharitis, uveitis, etc. Cost effective analysis was done for anti infectives, anti-inflammatory and corticosteroids used in the treatment of above mentioned conditions.*

Results and Conclusions*: Toram was cost effective among antimicrobials. Ketolas - NSAID as analgesic and Predmet for ocular postoperative conditions as a steroidal anti-inflammatory agent was most economical. Toram (tobramycin –Rs26/- per bottle), Ketolas (ketorlac-Rs 29/- per bottle), Predmet (prednisolone-Rs 13/- per bottle).*

Key Words: *Pharmacoeconomics, NSAIDs, antimicrobials, Prednisolone, Fluoromethaolone.*

INTRODUCTION

Pharmacoeconomics is a subdivision of health economics. It is analysis of the cost of drug therapy to health care system and society. This has now expanded in incorporating pharmacoeconomic research in to the process of drug development.[1] Pharmacoeconomic analysis increases the efficiency of allocation of health care resources. Globally, purulent bacterial conjunctivitis is mainly caused by Gram-positive organisms. The most common causative agents are *Staphylococcus epidermidis* (39% of cases), *Staphylococcus aureus* (22% of cases), and *Streptococcus pneumonia* (6% of cases). The most common Gram-negative microorganism found in acute conjunctivitis is *Haemophilus influenza* (9% of cases).[2] In addition to development of new antibacterial agents, the strategies to control further development of resistant ocular pathogens should always include judicious use of antibiotics in the treatment of human, animal or plant disease.[3] Recent changes in practice suggest that empirical monotherapy treatment with a fluoroquinolone antibiotic may be appropriate for certain cases of bacterial keratitis.[4]

Prior to use of ophthalmic non-steroidal anti-inflammatory drugs, topical ophthalmic steroids were the mainstay treatment of post-operative, surgically induced ocular inflammation. Although considered very effective, the use of topical corticosteroids is limited by well-known side effects which in some serious cases can precipitate vision loss, hence short and intermittent use is advisable.

Topical non-steroidal anti-inflammatory drugs (NSAIDs) are notable for a definitive lack of corticosteroid-defined toxicity and have secured an important role. InNSAIDS, Nepafenac is the first prodrug ophthalmic NSAID formulation approved for use in the US for the treatment of post-operative pain and inflammation after cataract surgery.[5] Prophylactic postoperative ketorlac 0.4% may have a role in reducing the frequency and severity of CME (cystoid macular edema) in diabetic eyes post-cataract surgery. NSAIDs are also indicated for treating post-operative pain and inflammation after cataract surgery.

The main objective of Pharmacoeconomics is to assist in making informed clinical decision by providing information about costs and consequence of alternative methods of treatment. Hence this study was undertaken.

MATERIALS AND METHODS

Data was collected from the Department of Ophthalmology at Dr. B.R Ambedkar Medical College. Both outpatients and inpatients prescription data were collected for conditions like conjunctivitis, keratitis, blepharitis, uveitis, cataract etc. Cost effective analysis was done for anti infectives, anti-inflammatory and corticosteroids used in the treatment of above mentioned conditions.For this analysis, the frequency and duration of the topical drugs were considered after review of the prescriptions. Only the direct costs of drug therapy were considered in the economic analysis. The drug costs were obtained from a standard reference (CIMS) source.

RESULTS

Antimicrobial agents were prescribed in bacterial conjunctivitis, infectious keratitis, and pre and post-operative period. NSAIDs in allergic conjunctivitis, pre and post-operative period and corticosteroids in allergic keratoconjunctivitis, uveitis, scleritis, episcleritis and pre and post-operative period. (Table -1)

Table 1: Common Indications for Topical Antibiotics&Anti-inflammatory Drugs in Ophthalmology.

DRUG	INDICATIONS
ANTIBIOTICS Moxifloxacin Gatifloxacin Tobramycin	Bacterial conjunctivitis and infectious keratitis. Pre-operative and Post-operative period.
NSAIDS Napefenac Ketorlac	Allergic conjunctivitis. Following ophthalmic surgeries (after cataract &corneal refractive surgeries), pre and post-operative period.
CORTICOSTEROIDS Prednisolone Fluoromethaolone	Allergic keratoconjunctivitis,adenoviral keratoconjunctivitis,uveitis,episcleritis,scleritis, corneal graft rejection, immunogenic keratitis, Pre and post-operative period.

The most cost effective brands were Moxiblu (moxifloxacin), Toram (tobramycin) (Table-2). Neypace (napefenac), Ketolas(ketorlac) (Table -3). Predmet (prednisolone) and Flone in fluoromethaolone (Table -4 and Table -5).

Table 2: Cost of Various Antibiotics

DRUG	VOLUME (ml)	COST/BOTTLE	DOSE DROPS/DAY (BOTH EYES)	COST/ML (INDIAN RUPEES)
MOXIFLOXACIN 5% (MOXIBLU, LUPIN)	5 ml	RS 54	2 (TID)	RS 10
MOXIFLOXACIN 0.5%(MOXICIP, CIPLA)	5 ml	RS 99	2 (TID)	RS 19
GATIFLOXACIN 3% (GATIBLU, LUPIN)	5 ml	RS 28	2 (TID)	RS 5
GATIFLOXACIN 0.3%(GATIQUIN, CIPLA)	5 ml	RS 39	2 (TID)	RS 7
TOBRAMYCIN 0.3% (TORAM, OYSTER LAB)	5 ml	RS 26	2 (TID)	RS 5

Table 3: Cost of NSAIDs (Non-SteroidalAntiinflammatory Drugs) (After Cataract and Corrective Laser Surgery).

DRUG	VOLUME (ml)	COST /BOTLE	DOSE (DROP/DAY) FOR ONE EYE	COST/ML
NAPEFENAC 0.1%(NEPALACT, SUNPHARMA)	5 ml	Rs 107	1 (TID)	Rs 21
NAPEFENAC 0.1%(NEYPACE,INTAS LAB)	5 ml	RS 95	I (TID)	RS 19
KETORLAC (0.50%,KETLUR ,SUNPHARMA)	5 ml	RS 44	1 (QID)	RS 8
KETORLAC (0.50%KETOLAS EYE DROPS)	5 ml	RS 29	1 (QID)	RS 3

Table 4: Cost of AntiinflammatoryDrugs for 6-wks Course in Post–Operative Cases(After cataract and corrective laser surgeries).

DRUG	VOLUME (ml)	COST/ BOTTLE	DOSE(DROPS/DAY) FOR ONE EYE	COST/ML	COST/6 WEEKS(REQUIRE 4 BOTTLES FOR ONE EYE)
PREDNISOLONE 10mg, (PREDMET,SUNPHARMA)	5 ml	RS 13	2DROPS FOR SIX TIMES(with gradual tapering in frequency in the following weeks)	Rs 2	Rs 52
PREDNISOLONE 10mg,(PREDNI,BIOMEDICAL LAB)	5 ml	RS 28	-DO-	RS 5	RS 112
FLUOROMETHALONE 5 ml(FLURISONE, MICROLAB)	5 ml	RS 70	-DO-	RS 14	RS 280
FLUOROMETHALONE 5ml(FLONE,SYNTHOPHARM A)	5 ml	RS 46	-DO-	RS 9	RS 184

Table 5: Cost of Antiinflammatory Drug for 4 weeks Course in Inflammatory Conditions (Uveitis, Iritis, Cyclitis and Allergic Keratitis)

DRUG	VOLUME (ml)	COST/ BOTTLE	DOSE (DROPS/DAY), BOTH EYES	COST/ML	COST/4 WEEKS(require 4 bottles for both eyes)
PREDNISOLONE 10mg,(PREDMET, SUNPHARMA)	5 ml	RS 13	2 DROPS FOR 4 TIMES(with gradual tapering in frequency in following weeks)	Rs 2	RS 52
PREDNISOLONE 10mg,(PREDNI, BIOMEDICAL LAB)	5 ml	RS 28	-DO-	RS 5	RS 112
FLUOROMETHALONE 5 ml (FLURISONE, MICROLAB)	5 ml	RS 70	-DO-	RS 14	RS 280
FLUOROMETHALONE 5 ml (FLONE,SYNTHO PHARMA)	5 ml	RS 46	-DO-	RS 9	RS 184

DISCUSSION

In this study, commonly prescribed antibiotics were Moxifloxacin, Gatifloxacin and Tobramycin. Most cost effective drug was Tobramycin (Toram-Rs 26/- per bottle).-TABLE 2. Ocular infections can be vision threatening, and hence generally broad spectrum antibiotics are prescribed for bacterial conjunctivitis on empirical basis. Fluoroquinolones act against broad spectrum of bacteria and attain high concentrations in conjunctiva. Hence they are commonly being prescribed, but should be better prescribed for resistant cases. FQs penetrate into the anterior chamber at more effective levels than many of the common non-FQ antibacterial agents.[6]

Gatifloxacin has not only antibacterial activity but also an anti-inflammatory action caused by inhibiting TNF-alpha production at the doses used in topical ophthalmic therapy.[7]Most commonly prescribed NSAIDS were napefenac and ketorlac. Most cost effective drug was ketorlac (ketolas eye drops –Rs 29/- per vial).TABLE-3. Nonsteroidal anti-inflammatory drugs (NSAIDs) act by inhibiting cyclooxygenase enzymes (COX-1 andCOX-2) thereby limiting prostaglandin production and providing both analgesic and anti-inflammatory activity. Ophthalmic NSAIDs are used to limit pain, discomfort, inflammation and edema associated with ocular conditions (e.g. non-infectious ocular inflammation or allergic conjunctivitis) or following ophthalmic surgeries (e.g. cataract and corneal refractive surgeries) or trauma. Napefenac is a prodrug. After instillation, nepafenac penetrates the cornea and is converted by ocular tissue hydrolases to its active form, amfenac. Ketorlac is administered four times daily and nepafenac three times daily.[8] Hence napefenac is more patient compliant. It has an ability to inhibit PG synthesis in the retina/choroid following topical administration indicates the drug also targets suppression of PG synthesis in the posterior segment. Nepafenac may therefore have a clinical role in conditions that are caused by PG-mediated vascular leakage, such as anterior chamber inflammation and cystoid macular edema (CME) following cataract surgery.[9]

Nepafenac was more effective than fluoromethaolone in preventing angiographic CME and BAB (blood aqueous barrier) disruption, and results indicate nepafenac leads to more rapid visual recovery.[10] Though ketorolac is cost effective, these additional beneficial properties ofnepafenac can be considered and hence preferred to be prescribed.

Most commonly prescribed topical steroids were prednisolone and fluoromethaolone.Most cost effective drug was prednisolone (predmet R 13/- per bottle).TABLE-4 & 5.The most important anti-inflammatory effect of topical ocular corticosteroids may be due to inhibition of arachidonic acid release, preventing the liberation of prostaglandins and other potent inflammatory mediators. Prednisolone acetate 1% (i.e. Pred Forte) exhibits the greatest anti-inflammatory activity of all the corticosteroids on the anterior segment of the eye. It therefore has a high risk of steroid-related complications. Gemifloxacin, pazufloxacin may be as effective as moxifloxacin for topical prophylaxis and for the treatment of staphylococcus aureus- induced endophthalmitis. Gemifloxacin similar to gatifloxacin can significantly lower the clinical severity in staphylococcus aureus keratitis.[11, 12]Advantages of using other routes of moxifloxacin apart from topical routes are - iv moxifloxacin may be a useful prophylactic medication against post-operativeendophthalmitis.[13]A significant advantage in using moxifloxacin relative to gatifloxacin was observed in prophylaxis of keratitis.[14]Intravitrealmoxifloxacin injection is effective in experimental Bacillus cereus endophthalmitis.[15] preoperative intracameralmoxifloxacininjection for endophthalmitis prophylaxis is a safe and effective method in uncomplicated phacoemulsification surgery.[16]

CONCLUSION

Toram (tobramycin) as antimicrobial, ketolas as NSAID, predmet as steroidal anti-inflammatory for pre and post-operative and allergic conditions were most economical. Understanding the natural progression of the disease co

morbidities and treatment enables us to estimate the variables that may have pharmacoeconomic implications with regard to cost of illness and quality of life. Pharmacoeconomic studies may be planned and conducted at the clinical development and during post marketing surveillance. Cost-effective analysis is the tool for weighing different costs and health outcomes when policy makers have to make resource allocation decisions. Clinicians should include a clinical pharmacologist for bedside discussions as this will help in improving adherence to drug treatment and hence contribute for a positive health outcome. More studies are required to provide good policy guidelines .These studies can be used as an educational and communicational tool which may have high impact on the society.

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