Original Article

An analysis of the use of antimicrobial agents in outdoor patients of ophthalmology

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Abstract

Objectives: The study was aimed to analyze commonly used antimicrobials in outdoor patients of ophthalmology department. **Materials and Methods:** The study was an observational, cross-sectional study carried out in the Department of Pharmacology and Ophthalmology after approval from the head of departments and Institutional Ethics Committee. All the patients age 18 years and above who were prescribed antimicrobials and gave consent were included in study. Data were recorded in a case study form containing relevant patient information and results of general, ocular, and special examinations along with the details of antimicrobials prescribed. Data were analyzed according to the World Health Organization/International Network for Rational Use of Drugs indicators and appropriate statistical tests. **Results:** A total of 900 patients who were prescribed antimicrobial agents (AMAs) were included in the study. The most common chief complaint was diminution of vision (25.78%). The most common indication of use of AMAs was for treating ocular infections (50.22%). The most commonly prescribed antimicrobial group was fluoroquinolone (FQ) (63.8%) and the most common drug was moxifloxacin (35.95%). The most common dosage form of AMAs was eye drops (68.55%). The average number of drugs per encounter was 4.41. The percentage of encounters with injectables prescribed was 0.67%. The percentage of use of antibiotics was 100%. The percentage of total drugs and AMAs prescribed by generic name was 41.5 and 11.92, respectively. The percentage of antimicrobial drugs prescribed from essential drugs list was 34.24%. The mean duration of antimicrobial therapy was 7.2 ± 4.54 days. **Conclusion:** More than half of the patients are prescribed multiple AMAs. Moxifloxacin, a newer generation FQ , was the most commonly prescribed AMA in our study. Educational interventions and strict adherence to hospital antimicrobial use policy are needed to restrict the use of AMAs and increase rational prescribing.

Keywords: Antimicrobial agents (AMAs), WHO/INRUD, Fluoroquinolone (FQ)

Introduction

Ocular infections need urgent attention as secondary infections in eye are high due to its peculiar anatomy and physiology, and there is a risk for permanent damage to eye and hence loss of vision. Antimicrobials form a chunk load of the drugs used in ophthalmology for treatment of blepharitis, hordeolum, acute conjunctivitis, infective corneal ulcers, ophthalmia neonatorum, iridocyclitis, and so on as well as for postoperative prophylaxis. The choice of the appropriate antibiotic depends on clinical diagnosis, the suspected infective agent, and its predicted antibiotic sensitivity.[1]

With new drugs rapidly coming up in the market, there is a lot of misinformation and lack of information about the rational use of antimicrobials. This is leading to an increase in antimicrobial resistance.

Very few drug utilization studies have been performed in ophthalmology. Moreover, the antimicrobials are used in a

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specialized dosage form like eye drops and eye ointments. Hence, this study on the use of antimicrobials in ophthalmology will help us study the choice, dosage, route, and frequency of use of antimicrobials for different infections in ophthalmology.

Materials and Methods

This study was an observational, single-center, cross-sectional study carried out in the Department of Pharmacology and Ophthalmology of a tertiary care teaching hospital from June 2017 to July 2017 after approval from the head of departments and Institutional Ethics Committee. This study was performed as a part of ICMR-STS 2017 (Indian Council of Medical Research – Short Term Studentship) program. All the patients aged 18 years and above who attended the outdoor patient department (OPD) of Ophthalmology between 9 a.m. and 1 p.m. and who were prescribed antimicrobials and gave consent were included in the study. Data were recorded in a predesigned and validated case record form containing relevant patient information and the results of general, ocular, and special examinations along with the details of antimicrobials prescribed. All collected data were entered in Microsoft Excel 2007 and analyzed according to the World Health Organization (WHO)/International Network for Rational Use of Drugs (INRUD) indicators[2] and specific statistical tests. The socio-economic status of the study population was assessed using Prasad classification. The appropriateness of antimicrobial treatment was evaluated using modified Kunin's criteria.[3] The evaluation and categorization of antimicrobial treatment was carried out based on the literature obtained from standard textbooks, National Treatment Guidelines for Antimicrobial Use in Infectious Diseases (2016) and All India Ophthalmological Society guidelines.

Results

This observational study was conducted in OPD patients in ophthalmology to study the use of antimicrobial agents (AMAs). Out of 2850 patients attending OPD, 900 patients were prescribed AMAs during the selected study period and hence were included in the study. The mean age of the study population was 45.04 ± 17.09 years. It was observed that the most common age group of the study population was 51–60 years. The male: female ratio was 1.17:1. More than half (54.78%) of the patients had primary level of education. About two-thirds (62.22%) of the patients belonged to lower socioeconomic class as per Prasad's classification.

The most common chief complaint was diminution of vision (25.78%) followed by pain in eye (22.67%) and redness of eye (21.67%). The most common indication of use of AMAs was for treating ocular infections which was seen in 50.22% of patients followed by postoperative prophylaxis in 25.89% of patients and prophylaxis for post foreign body removal or ocular trauma in 11% of patients [Figure 1].

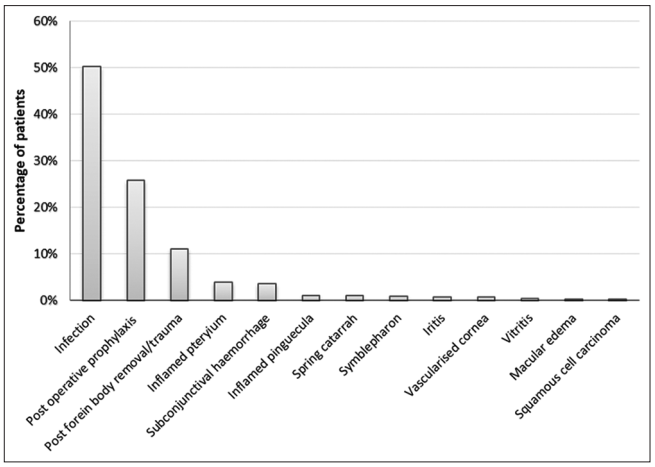

Figure 1: Indications of use of AMAs in ophthalmology OPD

The most commonly prescribed antimicrobial group was antibacterial (84.65%) followed by antiviral (7.92%), antifungal (7.17%), and antiprotozoal (0.25%). Fluoroquinolones (FQs) (63.8%) were the most commonly prescribed group with moxifloxacin (35.95%) as the most commonly prescribed drug followed by ciprofloxacin (13.44%) and gatifloxacin (12.87%) [Table 1]. Chloramphenicol (8.18%) was the second most commonly used antibacterial agent followed by B-lactams, aminoglycosides, tetracyclines, macrolides, and glycopeptides. Among antivirals which were prescribed to 7.92% of patients, acyclovir (4.18%) and gancyclovir (3.74%) were used. Among antifungals in 7.17% of patients, natamycin was prescribed in 5.20% of patients. Among antiprotozoals, metronidazole was prescribed to 0.25% of patients.

The most common dosage form of AMAs was eye drops (68.55%) followed by oral tablets (19.76%), ointments (8.2%), gels (2.73%), and injections (0.76%).

Analysis of the use of AMAs was done as per WHO/INRUD criteria as shown in Table 2. The average number of drugs per encounter was 4.41. The percentage of encounters with injectables prescribed was 0.67%. The percentage of use of antibiotics was 100%. The percentage of total drugs and AMAs prescribed by generic name was 41.5 and 11.92, respectively. The percentage of antimicrobial drugs prescribed from essential drugs list was 34.24%. The mean duration of antimicrobial therapy was 7.2 ± 4.54 days.

In all, 537 patients were prescribed multiple AMAs, either as fixed dose combinations (FDCs) or concomitant drug therapy. Of these, 163 patients were prescribed FDCs and the rest were prescribed concomitant AMAs in combinations as shown in Table 3. In the total 900 prescriptions, 212 FDCs were prescribed. The most common FDC in our study was chloramphenicol + hydrocortisone (95 patients) followed by gatifloxacin + dexamethasone (53 patients) and polymyxin B + chloramphenicol + dexamethasone (34 patients) and gatifloxacin + prednisolone (22 patients) and amoxicillin + clavulanic acid (4 patients) and ofloxacin + dexamethasone (4 patients).

Table 1: Commonly prescribed antimicrobials in ophthalmology OPD

Antimicrobials	No. of AMAs (%) (*n*=1577)
Antibacterials	1335 (84.65%)
Fluoroquinolones	1006 (63.8%)
Moxifloxacin	567 (35.95%)
Others[1]	439 (27.83%)
Chloramphenicol	129 (8.18%)
B-lactams	86 (5.45%)
Cefpodoxime	49 (3.11%)
Others[3]	37 (2.34%)
Aminoglycosides	86 (5.45%)
Tobramycin	70 (4.44%)
Amikacin	16 (1.01%)
Tetracyclines	10 (0.63%)
Doxycycline	10 (0.63%)
Macrolides	9 (0.57%)
Azithromycin	9 (0.57%)
Glycopeptides	9 (0.57%)
Vancomycin	9 (0.57%)
Antivirals	125 (7.92%)
Acyclovir	66 (4.18%)
Gancyclovir	59 (3.74%)
Antifungals	113 (7.17%)
Natamycin	82 (5.20%)
Others[2]	31 (1.97%)
Antiprotozoals	4 (0.25%)
Metronidazole	4 (0.25%)

OPD: outdoor patient department; AMA: antimicrobial agent. Others[1]: ciprofloxacin, gatifloxacin, ofloxacin, besifloxacin. Others[2]: fluconazole, voriconazole, amphotericin B. Others[3]: cefazolin, amoxicillin, amoxiclav

Table 2: Analysis the use of AMAs as per WHO/INRUD criteria

WHO/INRUD prescribing indicators (prescribing indicators)	Data
Average number of drugs per encounter	4.41
Percentage of drugs prescribed by generic name	
Percentage of total drugs prescribed by generic name	41.5%
Percentage of antimicrobial prescribed by generic name	11.92%
Percentage of encounters with an antibiotic prescribed	100%
Percentage of encounters with an injection prescribed	0.67%
Percentage of drugs prescribed from essential medicines list or formulary	34.24%

AMA: antimicrobial agent; WHO: World Health Organization; INRUD: International Network for Rational Use of Drugs

According to modified Kunin's criteria, categories 1 and 2 are considered appropriate, while categories 3 and 4 are considered inappropriate. About 57.67% cases belonged to category 1, 8.67% cases belonged to category 2, 4.11% cases belonged to category 3, and 29.56% cases belonged to category 4. About 66.33% use of AMAs was as per guidelines [All India Ophthalmic Society, National Treatment Guidelines for Antimicrobial Use in Infectious Diseases (2016), and Standard Treatment Guidelines, Health and Family Welfare Department, Gujarat, 2014]. However, 33.67% AMAs were prescribed inappropriately. Out of 33.67% which were prescribed inappropriately, the most common condition for its use was for postoperative prophylaxis for cataract surgery (n = 148, 16.44%).

It was observed that 537 of 900 patients were prescribed multiple AMAs, of which 240 (44.69%) were justifiable for conditions such as blepharitis, dacrocystitis, infiltrating trauma, endophthalmitis, severe conjunctivitis, and meibomitis according to the standard guidelines, while the rest 297 (55.31%) were not justifiable for conditions such as spring catarrh, superficial punctate keratitis, staphyloma, corneal abscess, corneal ulcer, and postoperative prophylaxis following cataract extraction surgery.

Discussion/Conclusion

In India, the infectious disease burden is among the highest in the world. However, AMAs used to treat these infections are used inappropriately and irrationally. This has led to increased incidence of development of antimicrobial resistance.[4]

This study was aimed to evaluate the pattern of use of AMAs in outdoor patients of ophthalmology department at a tertiary care teaching hospital where patients from four different states are drained giving us a very good idea of antimicrobial usage and resistance pattern in these areas.

The mean age of our study population was 45.04 ± 17.09 years (mean ± standard deviation). About 20% of patients belonged to age group of 51–60 years as older patients generally attended the department for cataract surgery. A majority of the patients in our study belonged to low socioeconomic class which might be because study site is a government hospital providing health services at negligible cost. The most common chief complaint was diminution of vision followed by pain, redness, and so on which are all signs of ocular infections and cataract.

The most common indications of use of AMAs were for treating ocular infections (50.22%), followed by postoperative prophylaxis (25.89%) followed by prophylaxis post foreign body removal or ocular trauma (11%). The common infectious diseases in our study were conjunctivitis followed by corneal abscess. In our study, a majority of the infections were bacterial. Similar findings were reported by Hemavathi *et al.*[5] This may be because the current study was conducted in the rainy season when bacterial infections are high. The second and third most common use of AMAs was for prophylaxis after cataract surgery and after foreign body removal/trauma, respectively. The main reason patients attend ophthalmology department is for surgical procedures such as cataract.

FQs were the most common group of antibiotics prescribed which were similar to reports of Jadhav *et al.*[6] This may be because of their broader spectrum of activity and slow development of resistance.[7] The most commonly prescribed AMA was moxifloxacin in our study, while it was gatifloxacin in the study by Jadhav *et al.*[6] This may be because prescribing

Table 3: Combinations of AMAs prescribed as concomitant drug therapy

Combination of AMAs prescribed as concomitant therapy	No. of prescriptions
≥2 FQs (oral + topical)	162
FQ+another broad-spectrum AMA (both topical)	141
2 FQs (oral + topical) + other* broad-spectrum AMA (topical oint.)	20
2 FQs (oral+topical) + antifungal (topical)	5
FQ (topical) + 1/2/3 antifungal (topical)	40
FQ+antifungal + other* broad-spectrum AMA (all topical)	23
FQ+antiviral (both topical)	96
Tobramycin (topical eye drops) + FDC chloramphenicol and hydrocortisone (topical oint.)	16
Tobramycin (topical) + FDC amoxiclav (oral)	4
Tobramycin + antifungal + antiviral + vancomycin+cephalosporin (all topical)	8
Tobramycin (topical) + azithromycin (oral)	1
Antiprotozoal (intravenous) + FDC amoxiclav (intravenous) + cephalosporin (topical) + aminoglycoside (topical)	5
2 Antivirals (topical and oral)	10
2 Antifungals (topical and intravitreal)	2

*Other broad-spectrum AMA – tetracycline, chloramphenicol, cephalosporin, azithromycin, tobramycin; AMA: antimicrobial agent; FQ: fluoroquinolone

patterns differ from prescriber to prescriber and antimicrobial resistance vary from area to area. However, both studies had a newer generation FQ as the most commonly prescribed AMA.

About 39.89% of patients were treated with single AMA, while 60.11% of the prescriptions had multiple AMAs in our study. In 26.67% of patients, AMAs from the same antimicrobial group were prescribed concomitantly but in different formulations. Some combinations of AMAs used at our setup were two FQs, two FQs + antifungal, FQ + chloramphenicol, FQ + aminoglycoside, and FQ + cephalosporin. However, some of these concomitant AMAs were administered through different routes as mentioned in Table 3. These were prescribed usually for postoperative prophylaxis, keratitis, corneal ulcer, abscess, and viral conjunctivitis to prevent the chance of secondary infection. However, the use of two drugs from the same class like two FQs is irrational. Also, use of two broad-spectrum AMAs concomitantly is also unjustifiable as per guidelines. The FQs were also prescribed concomitantly with antiviral and antifungal drugs, respectively. This is not justifiable because chances of getting viral or fungal infection with bacterial infection are unusual. But this prescribing pattern may be to prevent secondary infection in patients.

In the total 900 prescriptions, 212 FDCs were prescribed. A majority of the FDCs were rational as per approved list of Central Drugs Standard Control Organization (CDSCO). However, two FDCs were not included in the list which were gatifloxacin + dexamethasone and gatifloxacin + prednisolone. These FDCs are usually used in clinical setting for postoperative prophylaxis of infection and reduction of pain and inflammation. Combinations of antibiotics and steroid eye drops are undesirable for more than one reason. Antibiotic therapy where not indicated has the disadvantage that the patient may develop resistance to the drug and may not respond when antibiotic is urgently needed. Steroid therapy when not indicated can aggravate the infection particularly the viral infection and if indiscriminately used for long periods may cause steroid-induced cataract and glaucoma.[8]

More than two-thirds of the patients were prescribed AMAs as eye drops as they achieve rapid, high concentrations of the antibiotic at the local site of infection compared with systemic antibiotics. Oral AMAs were prescribed concomitantly with topical AMAs for the treatment of stye and for prophylaxis in penetrating trauma and after cataract surgery. As per the standard guidelines, this use of oral AMAs along with eye drops is justifiable only in advanced cases of infection or when the patients belong to high-risk category such as diabetics, immunocompromised, or patients on long-term corticosteroid therapy.[9] Analysis using WHO/INRUD prescribing indicators showed that the average number of drugs per encounter was 5.69 ± 2.38. The study by Prajapati and Yadav[10] had 2.23 drugs per encounter. As per the WHO, the average number of the drugs per prescription should be 1.6–1.8.[11] This indicates polypharmacy in both studies. The percentage of encounters with injectables prescribed was 0.67 which is higher compared to a study performed earlier in this area by Prajapati and Yadav[10] with 0.01. This may be because advanced and unresponsive cases are referred to tertiary care hospitals. The percentage of use of antibiotics was 100%. This is due to the inclusion criteria in this study. The study by Prajapati and Yadav[10] showed antibiotics in 59.5% of the prescriptions. Environmental conditions, poor education, lack of awareness, lower socioeconomic status, and poor sanitation of the patients increase the risk of secondary infections. The percentage of total drugs and AMAs prescribed by generic name was 41.5 and 11.92, respectively, in our study compared with Prajapati and Yadav[10] where it was a mere 1.14%. The reason for this might be the habit of prescribers to prescribe drugs by brand name. The percentage of antimicrobial drugs prescribed from essential drugs list was 34.24% in our study when compared with 61.84 in the study by Prajapati and Yadav.[10] The reason for such high amount of drugs prescribed from outside EML in our study is that AMAs such as moxifloxacin, gatifloxacin, and other newer AMAs which form a large chunk of the prescribed drugs are not included in the essential drugs list. This signifies that antimicrobial resistance is on the rise. The mean duration of antimicrobial therapy was 7.2 ± 4.54 days. This may be due to the fact that most ocular infections need 5–7 days of antimicrobial treatment as per standard guidelines. Infections such as corneal ulcer, dacryocystitis, keratitis, and severe conjunctivitis required longer treatment for complete healing and preventing recurrences.

Appropriateness of antimicrobial treatment was evaluated by modified Kunin's criteria.[3] About 66.33% of prescriptions were appropriate and belonged to categories 1 and 2. The rest

33.67% of prescriptions were inappropriate and belonged to categories 3 and 4. The most common inappropriateness in AMA prescriptions was use of AMAs for diseases such as iritis, vitritis, macular edema, subconjunctival haemorrhage, spring catarrah, pterygium, inflamed pinguecula, vascularised cornea, viral conjunctivitis, and chalazion which are noninfectious, and hence usage of AMAs for these conditions is not justified. The reason for this prescribing may be due to high risk of patients to get secondary infections due to their lower socioeconomic class and poor hygiene. Willemsen *et al.* observed that inappropriate choice and unjustified use of AMA is present only in 16% of patients.[12] This is because in developed nations there is a very stringent policy for AMA use and restricted availability of AMAs. A Turkey study has shown that appropriate use of AMAs was found to improve from 45.7% to 91.4% after implementation of antibiotic restriction policy.[13] This shows that implementation of antimicrobial policy, educational intervention, and availability of laboratory facilities and drugs may improve the appropriate antimicrobial treatment.

This study emphasizes that there is a need to implement antimicrobial restriction policy at all healthcare levels, especially at primary health centers where there is also an issue of poor laboratory facilities. It is also the first point of contact for the community; therefore, any unjustifiable AMA use can lead to increased resistance in the community. Educational interventions among doctors can lead to rational prescribing and safer use of AMAs.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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