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PHARMACO-EPIDEMIOLOGY OF DRUGS USED IN POST CATARACT SURGERY PATIENTS IN TERTIARY CARE HOSPITAL IN NORTH INDIA - A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Drug utilization studies aim to provide feedback to the prescriber and to create awareness among them about rational use of medicine hence we planned this study through evaluating the prescriptions in post cataract surgery patients in tertiary care hospital in north india**.** This prospective study was carried in the department of ophthalmology & Pharmacology over a period of 6 months. The data collected for post cataract surgery patients included the patient's demographic details and the drugs prescribed. Data were analyzed for drug use pattern and cost of drugs. In a total 674 prescriptions (1700 drugs) were analyzed; all drugs (100.0%) were prescribed by topical route as eye drops. Moxifloxacin (77.40%) and Prednisolone (77.40%) were found to be the most frequently prescribed drugs. Out of 674 prescriptions, 352 (52.22%) contained three drugs, the most common triple combination being Moxifloxacin, Prednisolone and Ketorolac (21.36%). Dexamethasone plus Ofloxacin (19.88%) being the only prescribed

Fixed dose combination (FDC). FDC Dexamethasone plus Ofloxacin treatment strategy was found to be the cheapest among all combination therapy. Moxifloxacin, prednisolone and Bromofenac combination was remain on highest cost. Our study shows that Fluoroquinolines and corticosteroids were the most frequently prescribed drug groups in post cataract surgery patients. Irrational prescribing among clinicians existed mainly in form of higher cost of treatment. It should be clear among prescribers that rational therapy can play an important role for convenience of patients as well as society in terms of disease burden, adverse events and treatment cost.

KEYWORDS: Cost analysis, Drug use pattern, Post cataract surgery, North-India.

INTRODUCTION

Cataract surgery is one of the most frequently performed elective surgical procedures in developed countries. The surgical methods have improved significantly over the years, thus lowering the risk of complications and raising patients' and surgeons' expectations of a successful visual outcome. In patients without other eye diseases, 20/20 visual outcome is a realistic expectation. Like other types of surgery, cataract surgery induces a surgical inflammatory response. Uncontrolled inflammation may lead to serious side effects, such as posterior synechia, uveitis, and secondary glaucoma. Management of inflammation is thus a mainstay in modern cataract surgery. Currently, 2 drug groups are available to control ocular inflammation: Steroids and Non-steroidal anti-inflammatory drugs (NSAIDs). Steroids are potent anti-inflammatory agents that work by acting on a number of intercellular inflammatory mediators, and NSAIDs work by inhibiting the cyclo-oxygenase enzymes. The cyclooxygenase enzymes catalyze the formation of prostaglandins (PGs) and thromboxanes. Prostaglandins mediate inflammatory reactions. Preventing the formation of prostaglandins reduces the inflammatory process. Production of PGs causes local vasodilation and increased vascular permeability resulting in a number of symptoms including hyperaemia, miosis, pain, photophobia and diminished visual acuity secondary to Cystoid Macular Oedema (CMO) – the most common complication of cataract surgery and potentially the most adverse ocular outcome of PG production.[1]

Pseudophakic cystoid macular edema (PCME, also termed "Irvinee Gass syndrome") is a swelling of the fovea due to fluid accumulation occurring a few weeks to months after cataract surgery. It is the most common cause of visual decline after cataract surgery. The

prevalence of PCME varies from study to study depending on how PCME is defined. By using fluorescein angiography, a prevalence of PCME of up to 20% has been reported.[2-3]

Topical NSAIDs have a number of important roles in the treatment of inflammation following ophthalmic cataract surgery. These include prevention of intra-operative miosis during cataract surgery; management of post-operative inflammation; reduction of pain and discomfort following cataract surgery; and prevention and treatment of CMO following cataract surgery.[4] Advantages of NSAIDs over corticosteroids include a reduction in post-operative pain and photophobia, decreased itching in allergic conjunctivitis, decrease in ocular pressure and reduction of intra-operative miosis.[5]

Periodic evaluation of drug utilization patterns need to be done to enable suitable modifications in prescription of drugs to increase the therapeutic benefit and decrease the adverse effects. The study of prescribing patterns seeks to monitor, evaluate and if necessary, suggest modifications in the prescribing behaviour of medical practitioners to make medical care rational and cost effective.[6]

Irrational drug use is a common problem in many countries of the world.[7] The assessment of drug utilization is important for clinical, economic and educational purposes.[8] Drug utilization studies aim to provide feedback to the prescriber and to create awareness among them about rational use of medicines.[9] There are many studies of ocular drug utilization pattern have been conducted in india which were conducted mainly on outpatient department patients. Data are not available in terms of inpatient department of ophthalmology specially post cataract surgery patients in prospective manner. Hence present study was planned to analyze the drugs used in ophthalmology department of tertiary care hospital in post cataract surgery patients.

The present study was undertaken to investigate the drug utilization pattern and current prescribing practices of the ophthalmologists in post cataract surgery patients.

MATERIALS AND METHODS

This prospective study was carried out in department of ophthalmology & Pharmacology in a tertiary care teaching hospital, Dehradun, India from 15 February 2014 to 15 August 2014. Study approval was obtained from Institutional Ethics Committee before initiating the study. The data was collected from patients of all age groups, of either gender who were diagnosed

with cataract by the ophthalmologist and agreed to give information. The data was recorded in a proforma containing patient's demographic details, final diagnosis and cataract surgery and the post cataract surgery prescription which included names of prescribed drugs, their dose, frequency, duration, and route of administration. Since many drugs were prescribed by their brand names, the generic names of drugs and generic contents of each formulation were obtained from commercial publications drug compendium Indian Drug Review (IDR) 2014 issue 4. Data was analyzed for drug use pattern and cost of medications. Average cost of drugs (eye drops) was determined by first calculating the cost per milliliter of the various brands mentioned in the IDR 2014 issue 4. The size of drop varies between 25 and 50 µl, so on an average 27 drops constitute 1 ml.[10] Assuming use in operated eye for each medication and number of drops required per day, the cost of therapy for 30 days was calculated. Data were analyzed using Microsoft Excel version 2010. All parameters were expressed in percentage. Chi-square test was used to analyze the data where appropriate and values with $P < 0.05$ were considered statistically significant.

RESULTS

Of 674 patients, 350(51.92%) were male and 324 (48.07%) were female. They were classified into three age groups i.e., less than 40, between 40 and 60, and more than 60. Maximum patients 377 (55.93%) were in age group above 60 years followed by 289 (42.87%) were in age group between 40 to 60 years. Phaco-emulsification or SICS was performed followed by implantation of intraocular lens (IOL) in posterior or anterior chamber. Irrespective of any type of surgery, drugs were prescribed pre and post operatively. All patients received Moxifloxacin eye drop preoperatively. Regarding the drugs prescribed postoperatively, total 1700 drugs prescribed, all (100.00%) were prescribed in combination therapy as eye drops. During the study the average number of drugs per prescription was 2.52 and the range of drugs per prescription varied from 2 to 3. Study also revealed that the drugs were prescribed only by brand name (100%). Only 31.76% drugs in the study are present in National List of Essential Medicine of India 2011. Average cost per prescription was 293.64 INR Cost range of prescriptions was between 140.00 – 367.00 INR (Table 1).

Moxifloxacin (77.44%) and prednisolone (77.44%) were found to be the most frequently prescribed drugs. Ketorolac (20.77%), FDC Dexamethasone plus Ofloxacin (19.88%), Tobramycin (17.21%) and Bromofenac (13.64%) were the least prescribed drugs. Fluoroquinolines and corticosteroid (97.32%) were the most frequently prescribed drug

group. These steroid therapy was given 6 times a day for initial first week, 4 times a day , 3 times a day ,2 times a day respectively for subsequent 3 weeks and lastly one time a day for another subsequent weeks till 6 weeks post operatively whereas the antibiotic therapy was given 6 times a day for initial first week then 4 times a day for subsequent weeks till 3 weeks post operatively. It was varied somewhere depending on patient condition on follow-up visits. Other groups included NSAIDs (34.42%) and Aminoglycoside (17.21%) for post cataract surgery patients. Combination therapy was prescribed to all patients including concurrent and fixed dose combinations (FDCs). Moxifloxacin and prednisolone (27.89%) was most commonly prescribed drug combination followed by Moxifloxacin, prednisolone and Ketorolac (21.36%), FDC Dexamethasone plus ofloxacin (19.88%), Moxifloxacin and prednisolone and Tobramycin(17.21%),Moxifloxacin, prednisolone and Bromofenac (13.65%). Out of 674 prescriptions, 352 (52.22%) contained three drugs, the most common triple combination being Moxifloxacin, Prednisolone and Ketorolac (21.36%). Out of 674 prescriptions, 134 (19.88%) received FDC. Dexamethasone plus ofloxacin (19.88%) being the only prescribed FDC (Table 2).

Written instructions to the patients regarding dose, dosing interval and duration of therapy were mentioned in all the prescriptions. Put only one drop of the drug was clearly written in all prescriptions.

FDC Dexamethasone plus ofloxacin treatment strategy was found to be the cheapest among all combination therapy. These were mainly prescribed for those patients who were poor and operated in free cataract surgery camps. The treatment cost varies from INR 140 to 367. Moxifloxacin, prednisolone and Bromofenac combination was remain on highest cost. (Table 3)Side by side comparison of cost of prescribed brand drugs with other different brands revealed that Prednisolone was the only drug which cost lies in lower side. Rests of the drugs were costly. (Table 4)

Table-1 Demographic characteristics and drug use indicators

Patient Characteristics	**N (%)**
Age (Years)	
<40	8 (1.18%)
40-60	289 (42.87%)
>60	377 (55.93%)
Total number of patients	674
Sex	
Male	350 (51.92%)

Female	324 (48.07%)
Prescribing indicators	
Total drugs prescribed	1700
Average number of drugs per prescription	2.52
Percentage of drugs prescribed by Brand names	100.00%
Percentage of drug prescribed by eye drop	100.00%
On essential drug list	31.76%
Average cost per prescription	293.64 INR
Cost range of prescriptions	140.00 – 367.00 INR

INR-Indian Rupee (One Dollar ~ 60 Indian Rupees)

Table- 2: Combination therapies (concurrent and FDCs) used in a tertiary care hospital after Post cataract surgery

Sr. no.	Name of drug combinations	No. of patients (n= 674) N (%)
1	Moxifloxacin 0.5% and Prednisolone 1%	188 (27.89%)
2	Moxifloxacin 0.5%, Prednisolone 1% and Ketorolac 0.4%	144(21.36%)
3	Dexamethasone 0.1% plus Ofloxacin 0.3% (FDC)	134(19.88%)
4	Moxifloxacin 0.5% and Prednisolone 1% and Tobramycin 0.3%	116(17.21%)
5	Moxifloxacin 0.5%, Prednisolone 1% and Bromofenac 0.1%	92(13.65%)

INR-Indian Rupee (One Dollar ~ 60 Indian Rupees)

Table 3: Cost Analysis of prescriptions of different drug combinations

Sr. No.	Name of drug combinations	Cost per 5 ml eye drops	Number of 5 ml eye drops	Total cost of treatment (INR)
1	Moxifloxacin 0.5% and Prednisolone 1%	77+16= 93	3+3=6	279
2	Moxifloxacin 0.5%, Prednisolone 1% and Ketorolac 0.4%	77+16+74= 167	3+3+1=4	353
3	Dexamethasone 0.1% plus Ofloxacin 0.3% (FDC)	28	5	140
4	Moxifloxacin 0.5% ,Prednisolone 1% and Tobramycin 0.3%	77+16+42=135	3+3+2=8	363
5	Moxifloxacin 0.5%, Prednisolone 1% and Bromofenac 0.1%	77+16+88=181	3+3+1=5	367

INR-Indian Rupee (One Dollar ~ 60 Indian Rupees)

Table-4: Cost effective analysis of prescribed drugs after post cataract surgery in tertiary care hospitals

Sr. No.	Drugs prescribed	Brand name (Manufactured by)	Cost per 5 ml eye drop (INR)	Cost range of different brand (Lowest to highest) in INR Including Brand name (Manufactured by)	Prescribed brand drug cost
1	Moxifloxacin 0.5%	Moxifax (Optho Remedies)	77.00	Contromax-M(Neiss)-39.00 MoxicipDPS(Cipla)-108.50	Higher side
2	Prednisolone 1%	P-lone (Syntho Pharma)	15.95	Predmet-DPS(Sun)-13.00 Vepred(Adley)- 40.55	satisfactory
3	Tobramycin 0.3%	Tocin (Optho Remedies)	42.00	Tozen (FDC)- 23.75 Toba (Sun)- 63.00	Higher side
4	Dexamethasone 0.1% plus Ofloxacin 0.3% (FDC)	Deflox (Syntho Pharma)	27.50	Miflox-DM (Sun pharma)(Dexamethasone plus Ciprofloxacin)- 16.00 Dexamehasone plus Moxifloxacin (FDC)-9.03	Higher side
5	Ketorolac 0.4%	Acular LS (Allergan India)	73.43	Oculac(Svizera)-31.00 Ketoeye(Eyecare)-46.50	Higher side
6	Bromofenac 0.1%	Bromifen (Optho Remedies)	88.00	NSAID Eye(Syntho pharma)- Dicofenac- 15.00 I-gesic(Centaur)-Diclofenac-22.71	Higher side

INR-Indian Rupee (One Dollar ~ 60 Indian Rupees)

DISCUSSION

WHO has been introduced drug utilization research with the goal towards rational prescribing through audit methods.[11] The study was a part of prescription audit which is intended to rationalize the prescription on pharmacological basis in future perspective. We audited prescriptions of post cataract surgery patients prospectively to make more effective without any error. Usual prescription pattern was one anti-inflammatory mainly steroids and one antibiotic mainly fluoroquinolones. All drugs are prescribed topically as eye drops. Almost similar results were obtained in a study conducted retrospectively in india earlier.[12]

FDC Dexamethasone plus ofloxacin treatment strategy was found to be the cheapest among all combination therapy. These were mainly prescribed for those patients who were poor and operated in free cataract surgery camps. Prescribing under generic name is considered economical and rational but not a single prescription was written under a generic name. As per IDR, one of the most cheapest combination of antimicrobial plus NSAID plus steroid may be one FDC of Ofloxacin plus Dexamethasone (brand name OXOP-D manufactured by

Centaur) cost around 10.51 INR and Diclofenac sodium (brand name NSAID-Eye manufactured by Syntho pharma) cost around 15.00 INR hence total cost of treatment would not be more than 50 INR .means it will be more cost effective as well as more compliant to the patient especially in developing country like India. Private hospitals should take some initiatives to make availability of cheap alternative medicines in their pharmacy and conduct some awareness program for the prescribers for achieving the goal.

Prescribed antibiotics were different type of fluoroquinolones and aminoglycosides used to prevent endophthalmitis. FQs are good efficacious against the causative organism of endophthalmitis. Moxifloxacin is more potent newer fourth generation FQs with broad spectrum of activity which is most frequent prescribed antibiotics in our study. Ofloxacin is more cost effective and it was the most frequent antibiotic prescribed in post operative patient in one retrospective study.[12] Systemic antibiotics were not prescribed in our study .It is good thing as benefit of systemic antibiotic therapy to prevent endophthalmitis remains controversial.[13] Optimum antibiotic concentration in aqueous humour can be achieved with topical application.[14] A authentic Indian document Vision 2020: The Right to sight publication - guideline for management of cataract in India (Vision 2020) clearly denies the need of systemic antibiotics on routine basis after post cataract surgery.[15]

Only 35.01% prescriptions contained NSAIDs however several trials have established that topical NSAIDs have a number of important roles in the treatment of inflammation following ophthalmic cataract surgery and somewhere more advantageous over steroids.[4, 20] As per Vision 2020, there is no inclusion of NSAIDs in both definitive and optional drug therapy after cataract surgery. Hence there is need to proper investigation of role of NSAIDs in management of post cataract surgery patients over and above the steroids and should be included in guideline accordingly.

Essential medicines are those that satisfy the priority healthcare needs of majority of the population. Moreover it is country specific, addressing the disease burden of the nation and the commonly used medicines at primary, secondary and tertiary healthcare levels. In our study, we found that only 31.76% drugs in the study are present in National List of Essential Medicine of India 2011. There is a need to adhere the prescription drugs to the Essential drug list of particular country as it does not only promote rational use of medicines considering the three important aspects i.e. cost, safety and efficacy but it also promotes prescription by generic names.[16]

In this study, written instructions regarding dose, dosing interval and duration of therapy were mentioned in all the prescriptions which is higher than that reported in earlier study of drug use pattern in ophthalmology from India.[17-18]

Put only one drop of the drug was clearly written in all prescriptions. Patients usually have the habit of applying 2-3 drops in the eye resulting into the wastage, increased cost and poor compliance.[19] The instructions regarding drug instillation is important aspect of ocular therapy.[20]

Dosing intervals and duration of therapy of combined topical antibiotic and steroid treatment postoperatively were match with Indian document Vision 2020. This is a positive phenomenon towards rationalization and homogeneity in the treatment part. It also increases the quality management of cataract in India.

Our study had some limitations. The study was carried out over a six-month period and also included the free cataract surgery camp patients in which surgeons generally write low cost prescription drugs. The patients' knowledge of the correct dose, proper time to take the medicine and the proper method of applying topical preparations were not ascertained.

CONCLUSIONS

To conclude, Fluoroquinolines and corticosteroids were the most frequently prescribed drug groups in post cataract surgery patients. Rational prescribing is an important criterion for convenience of a patient in terms of disease, adverse events and treatment cost. Study data may be helpful to understand the need of writing generic name in prescriptions, adherence with the National essential drugs list policy and availability of chief alternative medicines in hospital pharmacy. Health care providers have to take initiative for rational prescribing keeping in mind that it is not only a matter of national policy but also to wellbeing of individual patient.

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