Original Article

Fluoroquinolone utilization among inpatients in a teaching hospital in Western Nepal

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Abstract

Objective: To obtain information on the prescribing patterns of fluoroquinolones among hospitalized patients, other antibiotics and drugs co-prescribed, calculate fluoroquinolone utilization using defined daily dose (DDD), calculate mean cost of drugs and detail the sensitivity patterns of isolated microorganisms.

Methods: The study was carried out over a five-month period (1st November 2003 to 31st March 2004) at the Manipal Teaching Hospital, Pokhara, Nepal. Demographic details and duration of hospitalization was noted. The percentage of patients prescribed parenteral antibiotics and fluoroquinolones were recorded. The cost of drugs was determined using the price list supplied by the pharmacy. Fluoroquinolone utilization was measured in DDD/100 bed-days.

Results: Fluoroquinolones were prescribed to 263 patients during the study period; 160 females and 103 males. Mean ± SD number of drugs prescribed and duration of hospitalization were 6.5 ± 3.3 and 6.2 ± 5.4 days respectively. Fluoroquinolone utilization was 7.76 DDD/100 bed-days. Ciprofloxacin was the most commonly prescribed drug (6.83 DDD/100 bed-days). Fluoroquinolones were used for prophylaxis in 110 patients (41.8%). Other indications were urinary tract infections and acute gastroenteritis. E.coli, S.aureus and P.aeruginosa were common organisms isolated. The mean cost of drugs was 13.1 US$ and fluoroquinolones contributed to 36.7% of the total drug costs.

Conclusion: The use of fluoroquinolones was high compared to that reported previously (JPMA 57:78;2007).

Introduction

The study of prescribing patterns seeks to monitor, evaluate and if necessary, suggest modifications in prescribing practices of medical practitioners so as to make medical care rational and cost effective.[1] Antibiotics are among the most commonly prescribed group of drugs in hospitals today.[2] In acute care hospitals, 20 to 30% of inpatients receive antibiotics everyday and antibiotics constitute about 40% of drugs prescribed.[3,4] Emergence of antimicrobial resistance is being accelerated by inappropriate use of antimicrobials.[5] Infectious diseases, maternal and prenatal ailments, nutritional deficiencies and skin diseases are the leading causes of illness and death in Nepal.[6]

Previous studies in Nepal have shown that antimicrobials are a commonly prescribed group of drugs.[7,8] The costly category of broad-spectrum antibiotics were commonly used and their misuse or overuse is associated with the emergence of resistant bacteria.[9,10] In developed countries, fluoroquinolones are a commonly prescribed group of antibiotics.[11,12] In a Canadian province there was a significant increase in the use of ciprofloxacin, a fluoroquinolone over a period of three years.[13]

Studies have shown a link between increased utilization of fluoroquinolones and increasing resistance among bacterial pathogens.[14,15] The anatomic-therapeutic-chemical (ATC) classification assigns code letters and numbers to drugs.[16] The defined daily dose (DDD) concept was developed to overcome objections against traditional units of drug consumption and provides a fixed unit of measurement independent of price and formulation and enables the researcher to perform comparisons between population groups. DDD/100 bed-days provide a rough estimate of drug consumption among hospital inpatients.

Information on the utilization of fluoroquinolones, the diseases for which the drug is prescribed and the DDD/100 bed-days of fluoroquinolones are lacking in hospitals in Western Nepal. Hence the present study was carried out to:

1) Obtain information on the demographic pattern of inpatients who were prescribed fluoroquinolone/s during the study period

2) Obtain information on the prescribing patterns of fluoroquinolones, drugs coprescribed and measure utilization in DDD/100 bed-days

3) Calculate the mean ± standard deviation (SD) cost of drugs and the percentage of the total cost constituted by antibiotics (including fluoroquinolones) and by fluoroquinolones alone

4) Obtain information on organisms isolated on culture and sensitivity testing and their antibiotic sensitivity patterns.

Patients and Methods

The study was conducted over a five-month period (01.11.2003 to 31.03.2004) at the Manipal Teaching Hospital, a tertiary care hospital in Pokhara, Western Nepal. Inpatients prescribed a fluoroquinolone during the study period were taken up for analysis.

The age and sex of the patients, place of residence and the department of admission were noted. The condition for which fluoroquinolone were prescribed was recorded. The mean ± SD for number of drugs and duration was calculated. For noting the duration, the day of admission was included while the day of discharge was excluded.

The different drugs and the fluoroquinolones prescribed were recorded. The antibiotics and other drugs co-prescribed during hospitalization were also written. Only the prescriptions containing one or more fluoroquinolones were taken up for further analysis. The number of patients who were prescribed parenteral antibiotics and parenteral fluoroquinolones was recorded. Specimens sent for culture and sensitivity testing, organisms isolated and their sensitivity patterns were detailed. The use of fluoroquinolones was classified as for prophylaxis, bacteriologically proven infection (BPI), non-BPI and others.

The cost of drugs prescribed was calculated using the price list supplied by the hospital pharmacy. The percentage of the total drug cost constituted by antibiotics (including fluoroquinolones) and fluoroquinolones alone were calculated.

The use of individual fluoroquinolones and of the group as a whole was measured using the defined daily dose (DDD)/100 bed-days using the following formula:[17]

DDD/100 bed-days = No. of units delivered during the study period x 100 beds Assigned DDD for the drug/dosage form x No. of days in the study period x No. of beds x Occupancy index.

Our study was for a time period of 152 days, the total number of inpatient beds was 300 and the occupancy index was 0.4.

Results

Two hundred and sixty-three patients, 160 females and 103 males were prescribed fluoroquinolones during the study period. The age distribution was fifteen patients (5.7%) below the age of 14 years, 59 (22.4%) in the age group 40-50 years and 50 patients (19%) were greater than 59 years of age. Fifty-five patients (20.9%) were between 20-30 years. Considering the place of residence eighty-eight patients (33.5%) were from Pokhara city while 62 (23.6%) were from Kaski district. Thirty-five (13.3%) and 19 (7.2%) patients were from the neighbouring districts of Syangja and Tanahun respectively.

The maximum number of patients (82) were admitted in the department of Obstetrics and Gynaecology (OBG) followed by the department of Medicine (80 patients). Thirty-eight patients were admitted in the Otorhinolaryngology (ORL) ward while 35 were in the general surgical ward. The number of drugs prescribed per patient is shown in Table 1.

A total of 1710 drugs were prescribed. The mean ± SD was 6.5 ± 3.3. For an individual patient, a particular drug prescribed by different routes or by different brand names was taken as a single drug for the purpose of calculation. One hundred and one patients were admitted for a time period between 1 to 3 days, 72 for 4 to 6 days, and 39 for 7 to 10 days. Fifty-one patients were admitted for a period greater than or equal to 10 days. Mean ± SD duration of hospital stay was 6.2 ± 5.4 days.

Table 1. Number of drugs prescribed during the period of hospitalization.

Number of drugs prescribed	Number of patients (percentage)
0	0
1	4 (1.52)
2	13 (4.94)
3	27 (10.27)
4	46 (17.49)
5-10	124 (47.15)
≥ 10	49 (18.63)

Table 2. Antibiotics commonly co-prescribed with fluoroquinolones.

Name of antibiotic	Number of patients (% of total)
Metronidazole	93 (35.4%)
Gentamicin	35 (13.3%)
Ampicillin	15 (5.7%)
Cloxacillin	14 (5.3%)
Amikacin	10 (3.8%)
Ceftriaxone	10 (3.8%)
Ampicillin + Cloxacillin	9 (3.4%)

Table 3. ATC code and DDD/100 bed-days of fluoroquinolones prescribed to inpatients during the study period.

Drug Name	ATC Code	DDD/100 bed-days
Ciprofloxacin oral	J01M A02	3.92
Ciprofloxacin parenteral	J01M A02	2.91
Ofloxacin	J01MA01	0.49
Norfloxacin	J01MA06	0.44
Total		7.76

Ciprofloxacin was prescribed to 239 patients, norfloxacin to 20 patients and ofloxacin to 6 patients. Two patients received both ciprofloxacin and norfloxacin. Fluoroquinolones were prescribed for surgical antibiotic prophylaxis (SAP) in 110 patients (41.8%). Other indications were urinary tract infections (UTI) (15 patients), acute gastroenteritis (15 patients) and acute exacerbation of chronic obstructive pulmonary disease (COPD) (15 patients). The common antibiotics co-prescribed with fluoroquinolones are shown in Table 2.

Of the 1710 drugs prescribed from all groups, there were 213 (12.4%) intravenous fluids, 176 (10.3%) antiulcer drugs and 142 (8.3%) non-steroidal anti-inflammatory drugs (NSAIDs). Other common groups were 54 (3.1%) antiasthma drugs and 52 (3%) vitamin and mineral preparations. The five most commonly prescribed individual drugs were ranitidine, 129 (7.5%) diclofenac sodium, 80 (4.7%) and intravenous fluids comprising of ringer lactate 69 (4%), dextrose saline 62 (3.6%) and 5% dextrose water, 55 (3.2%).

Injections were prescribed in 171 patients (65%). Antibiotics were given by the parenteral route to 150 of the 263 (57%) patients while fluoroquinolones were administered in 131 (49.8%) patients. The ATC code and the DDD/100 bed-days of the prescribed fluoroquinolones are shown in Table 3.

A total of 76 specimens were sent for culture and sensitivity testing. These comprised of urine 25 (32.9%) blood, 16 specimens (21%), sputum, 11 (14.5%) and pus, 1 (14.5%). E.coli (12 isolates), S.aureus (6 isolates) and P.aeruginosa (5 isolates) were the most common organisms isolated. E.coli and S.aureus were resistant to some of the commonly used antibiotics. Resistance to norfloxacin among E.coli was seen in 50% of isolates. E.coli was resistant to ciprofloxacin also. Fluoroquinolones were used for prophylaxis in 110 (41.8%) cases, for BPI in 47 (17.9%) patients and for non-BPI in 61 (23.2%) cases. In 45 patients antibiotics were used in predominantly viral infections or in fever under investigation. This was included in 'others'.

The mean ± SD cost of drugs was 967.1 ± 723.8 Nepalese rupees (13.1 ± 9.8 US$). The median cost incurred on drugs was 405.4 Nepalese rupees (5.48 US$) and the interquartile range was 948 Nepalese rupees (12.8 US$). The mean ± SD cost of antibiotics was 550.4 ± 284.8 Nepalese rupees (7.4 ± 3.8 US$). The median cost of antibiotics was 212 Nepalese rupees (2.86 US$) and the interquartile range was 428.3 Nepalese rupees (5.8 US$). Antibiotics contributed to 56.9% of the total cost incurred on drugs. The mean ± SD cost of fluoroquinolones was 4.8 ± 2.3 US$ and contributed to 36.7% of total drug costs. The median cost of fluoroquinolones was 128 Nepalese rupees (1.73 US$) with the interquartile range being 203.17 Nepalese rupees (2.74 US$).

The use of fluoroquinolones was inappropriate in 110 patients (41.8%) of these 5 cases had viral infection and fever which was being evaluated. The use for prophylaxis was prolonged in 65 patients.

Discussion

In our study 15 patients below the age of 14 years were prescribed fluoroquinolones (fqs). In a study from Kathmandu valley, fluoroquinolones constituted 6% of total antibiotics whereas it was advised that ciprofloxacin and other fluoroquinolones deserve continuous monitoring.[18] Fluoroquinolones have also been prescribed in children in a hospital in France.[19] However, a review concluded that ciprofloxacin was safe and efficacious in children in developing countries.[20] Despite these suggestions it is better to be cautious while using fluoroquinolones in children due to conflicting reports in literature. In our hospital, the paediatricians sometime, prescribe fqs especially ciprofloxacin for chronic disease. However, there are no set criteria for prescribing and the decision whether or not to use a fq is left for the individual paediatrician.

In the study, fluoroquinolones were most commonly prescribed in OBG, followed by Medicine, ORL and surgery. In an American study, fluoroquinolones were most commonly used by the specialties of family practice, internal medicine and urology.[11] However, the study was on ambulatory patients and comparisons with hospitalized patients may be difficult. The mean ± SD number of drugs prescribed was 6.5 ± 3.3. The mean number of antimicrobials and fluoroquinolones prescribed were 1.74 and 1 respectively. In a study in district hospital of Nepal, the mean number of drugs and antimicrobials were 4.26 and 1.55.[21] In another study from Bharatpur, Nepal the mean number of drugs was 4.34.[7] The reasons for the high number of drugs prescribed in our study should be investigated. The excessive use of intravenous fluids (IVFs), antiulcer drugs and NSAIDs may be partly responsible. Formulation of criteria for use of IVFs should be considered. This may reduce their inappropriate and excessive use. We had not looked at the rationality of use of IVFs in individual patients as our study was retrospective.

Ciprofloxacin, norfloxacin and ofloxacin were the common fluoroquinolones prescribed as only these are licensed for use in Nepal by the department of Drug administration, the National drug control authority. The broader spectrum agents were not used in our hospital. This is a welcome sign as the newer agents are expensive and the organisms isolated in general continue to be sensitive to the older fluoroquinolones. This is in contrast to the increasing use of newer fluoroquinolones reported in an earlier study in America.[11] A study in south-western France had reported that older fluoroquinolones were more commonly prescribed.[2] A previous study in Nepal had also reported ciprofloxacin as a commonly prescribed antibiotic.[21]

The commonest indication for fluoroquinolones was SAP. Other indications were urinary tract infection (UTI), acute gastroenteritis and acute exacerbation of COPD. In an American study among ambulatory patients, fluoroquinolones were most commonly prescribed for UTI, sinusitis, skin, bone and joint infections and upper respiratory tract infections.[11] In a previous study, ciprofloxacin was used for the treatment of UTIs, chest infections, bacterial gastroenteritis and bacteraemia.[1] The use of fluoroquinolones in gastroenteritis, a predominantly viral infection is to be discouraged. The use to prevent secondary infection in COPD should also be carefully investigated. In many cases, no organisms were isolated from the sputum. At the time of the study there were no guidelines for SAP. Recently, the Department of General Surgery has framed guidelines for SAP and cephalosporins are recommended for prophylaxis. This may have reduced the use of fqs.

In the study IVFs, antiulcer drugs and NSAIDs were commonly prescribed. In an Indian study, cardiovascular drugs, NSAIDs and anti-ulcer drugs were most commonly prescribed.[1] In a teaching hospital in Nepal, antimicrobials, analgesics and drugs for acid-peptic diseases were commonly used.[7] The use of drugs depends on the morbidity patterns and other factors and may not be comparable between different studies.

In our study, 65% of patients received injectable drugs, 57% were prescribed an injectable antibiotic while fluoroquinolones were prescribed parenterally in 49.8% of patients. In many cases therapy was initiated with parenteral ciprofloxacin and was later switched over to oral fluoroquinolones. In a previous study, 26% of fluoroquinolones were administered parenterally.[19] Injections are expensive in terms of usage of trained manpower and carry the risk of transmission of infections and their use should be minimized. An antibiotic use policy for the hospital can be helpful in reducing excessive and inappropriate use. Early switchover from parenteral to oral antibiotics can be considered. In our hospital patients are usually discharged once the parentral antibiotics are discontinued. The retrospective nature of our study prevents us from making more concrete recommendations.

The use of fluoroquinolones was inappropriate in 110 of the 263 patients (41.8%) with prolonged use for SAP and use of antibiotics in predominantly viral infections being the major problems. In a previous study in 40% of patients the use of a fluoroquinolone was not felt to be clinically justified.[1] A drug use evaluation identified inappropriate use of ciprofloxacin in 40% of patients.[22] In an American study, only 58% of fluoroquinolones prescriptions were for FDA-approved diagnoses.[11] Patient age, male sex, and prescribing by urologists, otorhinolaryngologists rather than family practice physicians were factors associated with prescription of fluoroquinolones for unapproved diagnoses.[11] In our hospital, the use of fluoroquinolones for viral infections and prolonged use for SAP are problems to be addressed.

The utilization of fluoroquinolones in DDD/100 bed-days (DBD) was 7.76. This is higher than 4.29 DBD reported in a Czech study.[14] In France the mean DBD of fluoroquinolones in 49 hospitals was 3.7.[2] In our hospital the utilization of fluoroquinolones was nearly twice that reported in the literature. Prolonged use for SAP and use of fluoroquinolones in viral infections may be partly responsible. These problems may be addressed to a large extent by framing guidelines for SAP and formulating an antibiotic use policy for the hospital. Steps have been taken in this direction.

The organisms isolated were sensitive to ciprofloxacin in most cases but E.coli was resistant to norfloxacin and ciprofloxacin. In United States teaching hospitals decreased susceptibility of P.aeruginosa, P.mirabilis and E.coli which was significantly related to increase in fluoroquinolone use.[15] In Germany, consistently high use of fluoroquinolones in haematology-oncology services in a hospital was associated with higher fluoroquinolone resistance of E.coli.[23] The sensitivity of bacteria to older antibiotics is a welcome sign but the resistance pattern of ?E.coli is a matter of concern.

The mean ± SD cost of fluoroquinolones was 4.8 ± 2.3 US$ and contributed to 36.7% of the total drug costs. Parenteral fluoroquinolones contributed to 66.9% of the total fluoroquinolone cost. In the UK, a sustained reduction in the use of intravenous (iv) ciprofloxacin was obtained by a combination of education and restriction, which reduced the expenditure on iv ciprofloxacin to 34% of original levels.[24] Similar programs can be implemented in our institution.

Our study had many limitations. The use of fluoroquinolones was studied over a five-month period and seasonal variations were not considered. The number of patients was small. The total cost incurred by the patient during hospital stay was not calculated. The reasons behind the inappropriate use of fluoroquinolones were not investigated. The number of organisms isolated on culture and sensitivity testing was low and it would be difficult to extrapolate the findings.

Conclusion

The mean number of drugs prescribed in our hospital was high. The older fluoroquinolones were commonly used and this is to be welcomed. The fluoroquinolones were being used in predominantly viral infections and this has to be discouraged. Parenteral fluoroquinolones were commonly used and the use for surgical prophylaxis was prolonged. Fluoroquinolones use in DDD/100 bed-days was higher than that reported in previous studies. Resistance was noted among E. coli and S. aureus. An antibiotic use policy for the hospital is mandatory. Guidelines for SAP are also urgently required.

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