Survey Analysis

ASSESSMENT OF RATIONAL USE OF THIRD GENERATION CEPHALOSPORINS IN LADY READING TERTIARY CARE TEACHING HOSPITAL OF PESHAWAR, PAKISTAN

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Submitted on: 18.04.2015 Revised On: 11.05.2015 Accepted on: 17.05.2015

ABSTRACT:

Objectives: To analyze the rational use of third generation cephalosporins (TGCs) including cefexime, cefotaxime and ceftriaxone in warded patients using WHO INURD indicators.
Methods: A cross-sectional, descriptive study was conducted at the Lady Reading Teaching Hospital, Khyber Pakhtunkwa (KPK), Pakistan during the time period from April 10th to May 30th 2014, collecting total 400 complete patient medication profiles for analysis which contained cefixime, cefotaxime and ceftriaxone being co-prescribed with other drugs.
Results: No drugs were prescribed by generic names however all were part of Essential drug list (EDL) of Pakistan. Dose adjustment based on age, gender, hepatic or kidney impairment was not the practice except in paeds ward (based on body weight). Cefixime, cefotaxime and ceftriaxone was prescribed without indication by 12.5%, 10 % and 20 %, respectively. No Pharmacists allocation was made in wards.
Conclusion: In order to attain rational use of TGCs, proper intervention in form of restrictive policy regarding use of TGCs and its implementation is required.

KEY WORDS: Third generation cephalosporins, Rational use,Tertiary care hospitals, Bacterial resistance

KEY MESSAGE:

- Resistance is a global problem, drug resistance leads toward the failure of therapy. In USA annually $5-24billion expending on this problem.
- In this study we have point outed the irrationality which leads toward the resistance problem.

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Indian Research Journal of Pharmacy and Science; 5(2015) 135-142;
Journal home page: https://www.irjps.in

INTRODUCTION

Irrational and liberal use of TGCs like prophylactic and use without indication may result in development of bacterial resistance with the emergence of extended-spectrum beta- lactamases (ESBLs). This may result in ineffectiveness of antimicrobials in severe infection increasing prescription cost, drug interactions and toxicity. The widespread use of third generation cephalosporin antibiotics has resulted in development of ESBLs in Gram-negative bacteria globally that may lead to therapeutic failure (1). Therefore, development and adherence to hospital antibiotic guidelines to control antibiotic misuse is highly important (2). The practice adopted by many hospitals has increased appropriate prescribing of TGCs over last few years (3). The prescriber and pharmacist both are responsible for rational prescribing and use of drugs in order to attain maximum therapeutic effectiveness, safety (4) and to enhance its cost effectiveness.

Concept of rational use of drug is though not quite a new in developing countries like Pakistan, however, the role of pharmacist being the last personnel of the health care team to advice the patients before they take the drug has always been ignored. Role of qualified pharmacists is extremely important for dispensing and counseling the patients on safe and effective use of drugs. However, in Pakistan where the irrational use of antibiotics along with other drugs is common, role of pharmacist is highly ignored at the same time. Necessary amendments in pharmacy act in this regard are highly important. Intermittent assessments of prescriptions might be a good tool to evaluate the rational use of drugs in terms of prescribing, dispensing and to evaluate patient understanding regarding drug usage.

Current study is also based on the assessment of rational use of antibiotics (Third Generation) in randomly selected wards of a tertiary care hospital setup.

METHOD

The study was conducted at the paeds, males/females medical wards (where patients being treated by medicine and no surgery involved) of Lady Reading Teaching Hospital (LRTH), Peshawar, Pakistan, a 550-bedded tertiary care teaching hospital. The data for this study was collected over the time period from April 10th to May 30th 2014 (6 weeks). Patients being hospitalized in the mentioned wards of the hospital were enrolled in the study. In order to evaluate rational use of TGCs, three drugs cefixime, cefotaxime and ceftriaxone were selected, as these were frequently prescribed medicines among TGCs in the hospital. Three main categories of WHO recommended drug use indicators were checked including prescribing, patient care and facility specific indicators.

Sample size and data collection method

Prescribing indicators: In order to assess prescribing indicators, a total of 450 Encounters being collected during the period from April 10th to May 30th 2013 were included while recommendation to other hospitals or vaccinations was excluded (**Table 2)**. Therefore, a total of 400 prescribing encounters were included.

Patient care indicators: A total of 400 patients (representing a mix of health problems and age

groups) during the period of hospitalization were interviewed.

Patients included in the study were those who were examined by the physician, received treatment and were willing to participate.

(c) Facility-specific indicators: Pharmacist from stock/stores of hospital facility was interviewed. Ten nurses of relevant wards under investigation were also interviewed using a cross-sectional survey.

The collected encounter were assessed for the age and gender wise distribution of patients (**Table 1**), average number of drugs per prescription, therapeutic category of drugs prescribed, encounters with at least one injectable, cost effectiveness of the prescriptions and patient knowledge on proper use of drugs. Determined parameters were compared among three drugs of TGCs. One way ANOVA (analysis of variance) test was used to compare medication parameters between cefixime, cefotaxime and ceftriazone. A $p < 0.05$ was taken as statistically significant.

Table 1. Age and gender wise distribution of patients

	No. of patients using			No. & percentages
	Cefixime	**Cefotaxime**	**Ceftriazone**	
Age				
<1-10 years	28	20	32	
11-15 years	12	9	18	
16-30 years	14	8	8	
31-40 years	22	7	16	
41-50 years	10	10	18	
51-60 yeas	8	12	16	
61-70 years	22	22	30	
> 70	21	14	15	
Gender				
Females	71	52	85	218/400 = 54.5 %
Males	60	52	70	182/400 = 45.5 %

Table 2. Different drug use indicators obtained by processing Encounters of hospitalized patients collected from different ward (Prescription & Patient indicator)

	Cefixime containing prescriptions		Cefotaxime containing prescriptions		Ceftriaxone containing prescriptions		
Indicators	**No and percentages**	**Mean ± SD**	**No and percentages**	**Mean ± SD**	**No and percentages**	**Mean ± SD**	***p*-value**
Prescription Indicators							
No. of Prescriptions	63	-	40	-	297		-
Average drugs in one prescription	-	3.5 ± 0.84	-	3.2±0.46	-	3.7±1.1	0.8
Average cost per prescription and % age increase in cost as compared to low cost alternatives	65%	450 ± 1.8	85%	500 ± 2.8	80%	800	0.04
No. of oral drugs *	102/260 = 40 %	102 ± 2.9	60/160 = 37.5 %	60 ± 6.8	400/1010= 39.6 %	400 ± 11.7	0.003
No. of Parenterals*	90/260 = 35.4 %	90 ± 2.7	54/160 = 33.8	54 ± 3.7	320/1010= 31.6 %	320 ± 21.3	0.04
No. of Topicals*	68/260 = 26.2 %	68 ± 0.8	46/160 = 28.8	46 ± 2.3	290/1010 = 28.7 %	290 ± 14.7	0.01
Drug without indication	12.5 % n = 8/63	8 ± 0.2	10% n = 4/40	4 ± 0.03	20% n = 60/297	60 ± 5.2	0.06
No. of Generics prescribed	0	-	0	-	0		0
Single TGC	185/260 = 71.2	185 ± 11.8	110/160 = 68.8	110 ± 14.9	800/1010 = 79.2%	800 ± 56. 87	0.03
TGC in combination with other antibiotic	75/260 = 45	75 ± 6.9	50/160 = 31.2	50 ± 11.2	210/1010 = 20.8	210 ± 8.1	0.07
TGC prescribed in contraindication	0	-	0	-	56/297 = 18.9	56 ± 4.6	0.002
Patient indicators							
Knowledge of patient on use of drugs	4/63 = 6.34 %	-	5/40 = 12.5 %	-	10/297 = 3.4 %	-	-

P < 0.05 is taken to be significant. No.; number, TGC ; thirg generation cephalosporin, - ; no value

RESULTS

In 400 encounters comprising cefixime, cefotaxime and ceftriazone, 1430 drugs were prescribed. Among these 1430 drugs, 12 different drugs were co-prescribed along with cefixime, cefotaxime and ceftriazone in various combinations according to

diagnosis. The mean ± SD number of drugs prescribed was 3.4 ± 0.84 (cefixime containing prescriptions), 3.2 ± 0.5 (cefotaxime containing prescriptions) and 3.7 ± 1.1 (ceftriazone containing prescriptions) out of them only 50/ 1430 (3.5%) drugs were dispensed from the hospital pharmacy. The remaining drugs were either not available in the pharmacy or the poor socioeconomic condition of patients was a problem to buy them. The drugs were not prescribed by their generic names. All the drugs (n = 12) including third generation cephalosporins were from essential drug list of Pakistan (EDL).

Proportion of female patients was higher (54.5%) as compared to males (45.5%). Highest proportion of patients was found in age range of <1- 10 and 61-70 years of age **(Table 1).**

Out of 1430 prescribed drugs, 35 % of drugs were antibiotics followed by anti-gastric secretary medicine (25 %), anti-diuretics (20 %), anti-parasitic drugs (11 %) and hypnotics (9 %). The cost of the prescription was also assessed in the study and is listed in **Table 2**. The average cost per prescription comprising ceftriaxone was 800 PKR showing 80 % rise in average price compared with a low price alternative while for cefotaxime and cefixime containing prescriptions it was 550 PKR and 450 PKR, sowing 65 % and 85 % increase as compared to low price alternative, respectively.

Higher proportion of drugs prescribed was oral followed by parenteral and topical was significantly higher for ceftraixone as compared to cefixime and cefotaxime containing prescriptions. The use of injectables was associated with ceftriaxone and cefotaxime as both drugs are available as I/V, I/M and I/V injectables, respectively. However, cefixime was administered orally. Moreover there was no significant difference between male and female patients and patients belonging to different age groups with regard to their knowledge of correct use of drugs. The patient knowledge regarding proper use of drugs is displayed in the **Table 2**.

Among facility indicators, 3.5 % drugs were supplied within the hospital premises. Only four pharmacists were there in order to resolve drugs related issues.

DISCUSSION

Evaluation of prescribing pattern of drugs using WHO drug use indicators reflects the effective therapy by rational use of drugs. Previously, many studies have been conducted in various parts of the world, in order to assess rational use of antibiotics (generally) (3, 5-6) and TGCs (specifically) (7). The average number of drugs per prescription was found to be 3.5 ± 0.84 (cefixime), 3.2 ± 0.46 (ceotaxime) and 3.7 ± 1.1 (ceftriaxone) in our study which is almost at equal level with studies conducted in Ghana (3.6) (8), West Bengal and India (3.2) (9). However, the mentioned studies were not specified for TGCs rational use assessment. A comparatively higher number of drugs is an alarming signal as poly pharmacy may lead to DDIs (drug drug interaction), increased chances of hospitalization, adverse drug reactions and patient non-compliance (10). Though, few diseased conditions may require more than one use of drug like cardiovascular complications like Treatment of High Blood Pressure (11). Therefore number of drugs per prescription was not an issue at all however, the tendency to use fixed dose combinations (FDCs) was disappointing in current study being not prescribed at all. FDCs are helpful in

reducing the number of pills to be administered, moreover proves to be cost effective and increase the patient adherence (12). However, special care is required while prescribing FDCs to avoid irrational combination. Pharmacist can play a very important role here by suggesting rational combinations.

Not any single drug was prescribed by generic name in current study. This is another alarming signal as less prescribing by generic names not only increases average cost of prescription but also affects inventory control of hospital pharmacy. Lesser number of brands is easy to keep intact in terms of their availability and price. The finding is also an indicator of interference by pharmaceutical companies at therapeutic level while at the same time role of clinical pharmacist becomes self-evident, and their allocation is extremely important in wards.

All the drugs including TGCs were part of EDL of Pakistan. This finding is really positive as it suggests that rational drug use exists in least form.

Among 1430 drugs, large number of prescribed medicines were oral products and the percentages were 40 % (cefixime), 37.5 % (cefotaxime) and 39.6 % (ceftriaxone), the parenterals were second most commonly prescribed dosage form while topical were on third placement.

The difference in dosage form distribution of drug may vary in different areas of the world however; current study reflected quite a reasonable and acceptable pattern. It may show disease prevalence in specific period of study or in that specific area. The dosage form affects patient compliance and therapeutic safety as well. Use of injectables is least preferable except emergency situation or certain situations necessarily associated with use of injectables. However, in elderly people oral products while liquid dosage form may be appropriate in paeds. Role of pharmacist in Patient counseling is also very important specially while taking specialized dosage forms. Involvement of pharmacist may be reflected by the written information provided by him on the medicines or prescription while dispensing the drugs. The situation was awful in this connection in the hospital understudy as the pharmacist were not involved at this level. The wards were without facility of pharmacist while their rounds were also not arranged or overall adequate labeling was not found in any of the dispensed medicine.

Several studies have acknowledged the improvement in patient knowledge about medications following counseling by pharmacists (13). The knowledge of patients on drug use was not satisfactory. Only 6.3 % (cefixime), 12.5 % (cefotaxime) and 3.4 % (ceftriaxone) were aware about proper way to use drugs. Here again the dispensing pharmacist is essential and key element in ensuring patient adherence.

The average cost per prescription was found to be 450 PKR (cefixime), 500 PKR (cefotaxime) and 800 PKR (ceftriaxone). The increase in average prices to be observed as compared to the low cost alternatives of TGCs was 65 % (cefixime), 85 % (cefotaxime) and 80 % (ceftriaxone). From a view point of developing countries cost is a very important factor. The hospital charges and expensive medicines prove a very important factor in affecting patient adherence (14). Lesser cost alternatives may be valuable in this connection.

The conclusion made from current study in the light of given facts and factors is that there must be a

hospital committee of antibiotic resistance control which makes sure rational use of antibiotics in hospital. Some notable irregularities which were found in current study in this connection were use of TGCs without indication, no generic prescribing, wards without allocation of pharmacist, poor status of knowledge of patients regarding proper use and adherence to therapy. All before mentioned problems need immediate addressing by allocation of pharmacists at proper places within the hospital in order to control all steps the ranging from inventory control, distribution, proper administration and then monitoring drug therapy.

LIMITATIONS

The study was limited to be conducted during a specific period of time so it was not assessed for seasonal variations. Seasonal variation may affect diseases prevalence and related drug use. The sample size may be increased. Only 400 prescriptions from 5 wards were selected which can't be representative of whole setup of hospital. Number of prescriptions and wards need to be increased.

CONCLUSION

Current study brings the fact in limelight that proper intervention in form of a restriction policy regarding use of TGCs in hospitals is required. Pharmacists need to be allocated in wards in order to assure rational use of drugs along with prescribers. The prescribers should be educated about generic prescribing which may bring lot of benefits with it.

The relevant Drug and Therapeutics Committee of the hospital should adopt better policy in order to attain rationalizion in the prescribing and dispensing practice in the hospital.

ACKNOWLEDGEMENT

We thank hospital administration for providing us opportunity to visit different wards and collect the required data.

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Conflict of Interest Reported: Nil; Source of Funding: None Reported