EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 8
327-330
Year: 2017

ADVERSE DRUG REACTIONS ASSOCIATED WITH CEPHALOSPORINS USE IN PAEDIATRICS

Anand Gupta[1]*, Virendra Kushwaha[1] S. P. Singh[1], Pooja Agrawal[1], Arpita Singh[3] and Yashwant K. Rao[2]

[1]Department of Pharmacology and Therapeutics, GSVM Medical College Kanpur (U.P), India.
[2]Department of Paediatrics, GSVM Medical College Kanpur (U.P), India.
[3]Department of Pharmacology, Dr. Ram Manohar Lohia Institute of Medical Science, Lucknow.

***Corresponding Author: Pooja Agrawal**
Department of Pharmacology and Therapeutics, GSVM Medical College Kanpur (U.P), India.

Article Received on 12/06/2017 **Article Revised on 02/07/2017** **Article Accepted on 23/07/2017**

ABSTRACT
Cephalosporins are broad spectrum beta lactam antibiotics which have activity against both gram negative and gram positive bacteria. Cephalosporins are the most prescribed antibiotic now a days in paediatric patients. A prospective, observational study was conducted where data of adverse drug reaction related to cephalosporins group was collected over a period of twelve months from department of paediatrics of a tertiary care hospital, Kanpur. In the study 76 ADRs were observed in 53 patients receiving cephalosporins. Ceftriaxone was associated with 84.5% ADRs. Most common reaction caused by cephalosporins was rash followed by nausea and vomiting. 12% cases were of serious type. On causality assessment by naranjo's scale 53% were of probable causality.

KEYWORDS: Cephalosporins, Paediatric, ADRs, Ceftriaxone, Rash.

INTRODUCTION
WHO defines Adverse Drug Reactions (ADRs) as ''any response to a drug which is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function".[1,2] ADRs are important causes of mortality and morbidity.[3] Early detection, evaluation, monitoring and reporting of ADRs are essential to make drug treatment safe, efficacious and cost effective.[4]

ADRs are of major health concern affecting children with varying magnitudes. While a large number of pattern of adverse drug reaction studies are available for adults and geriatric age group all over the world, only a few studies provide information on pattern of adverse drug reactions in paediatrics. Paediatric age group is among the most vulnerable population susceptible for adverse drug reaction due to altered susceptibility to drugs because absorption, distribution, metabolism and excretion (ADME) pathways in children are completely different than in adults, and dosing cannot simply be extrapolated on a weight basis.[5]

The capacity of the liver to metabolize drugs is lower at birth since the metabolic pathways and enzymes are in various stages of maturation[7,8], and the rate of development of the various metabolic pathways is highly variable and may be influenced by exposure to drugs *in utero* and post-nataly.

Antimicrobials are the most common prescribed drug in paediatrics. For treating various infection and associated condition of GIT, respiratory, skin, those involving nervous system are being treated by antimicrobials through oral as well as parenteral route. Antimicrobials exert their effect by different mechanism of actions. Along with desired effect they also possess threat of adverse drug reaction leading to increased morbidity, permanent damage to organ system or even mortality. Cephalosporins constitute a major group among antimicrobials which are being used for various infectious conditions. Monitoring of these ADRs is very important to reduce this additional burden of morbidity and mortality on the health care system.

Thus aim of our study is to evaluate the pattern of adverse drug reactions occurring due to cephalosporins use in paediatric patients.

MATERIAL AND METHOD
A prospective, observational study was conducted at LLR hospital, GSVM, Medical College, Kanpur. The study was conducted over a period of twelve months from august, 2015 to September, 2016. Spontaneous ADRs reporting technique was used for data collection. "Suspected Adverse Drug Reaction Reporting Form" provided by Indian Pharmacopeia Commission (IPC) were used for ADRs reporting. All patients reporting to pediatric department, who developed an ADRs during the above mentioned time period were included in the

study. Patients who developed an ADRs due to intentional or accidental poisoning, ADRs due to the fresh blood / blood products, patients with drug abuse and intoxication were excluded. Reported ADRs were analysed with respect to patient's demographics, ADR pattern (causality, severity, seriousness and predictability), organ system involved characteristics of the drugs involved and, nature of the reactions.

OBSERVATION AND RESULT

Table 1: Demographic Details of patients

S.NO	PARTICULARS	NO. OF PATIENT (N=53)	NO. OF ADRs (n=76)
1	*Gender*		
	Male	27 (51%)	38 (50%)
	Female	26 (49%)	38 (50%)
2	*Age*		
	0-1 year	13(24%)	15 (20%)
	1-5 year	19 (36%)	26 (34%)
	5-18 year	21 (40%)	35 (46%)

In our study male and female patients equally encountered the ADRs. As per age groups are concerned maximum 35 ADRs (46%) cases were seen in age group 5-18 years followed by 26 in age group 1-5 years and 15 in age group 0-1 year.

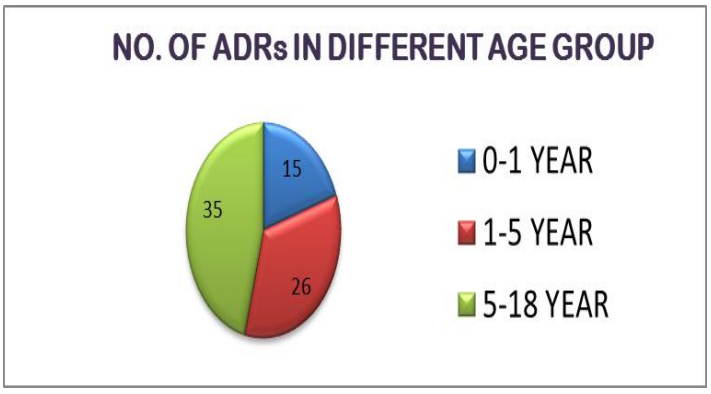

Figure 1: ADRs Reported In Different Age Group

Table 2: ADRs Assessement-Type (Expanded Rawlins & Thomsons classification), Severity (Modified Hartwig scale), Seriousness (WHO), Predictability (CIOMS guidelines), Causality (Naranjo's scale).

S.NO	PARTICULARS	NO. OF ADRs (n=76)	% OF ADRs
1	*Type*		
	A	25	33
	B	51	67
2	*Severity*		
	Mild	60	79
	Moderate	15	20
	Severe	1	1
3	*Seriousness*		
	Non-Serious	67	88
	Serious	9	12
4	*Predictability*		
	Predictable	74	97
	Un-Predictable	2	3
5	*Causality*		
	Probable	40	53
	Possible	36	47

In ADRs assessment type B ADRs were more (67%) compared to type A ADRs(33%) and there were no type C,D,E or F type ADRs. Most of the cases were of mild (79%) type then moderate and only 1 case of severe type. In seriousness assessment 88% cases were non-serious type and as per predictability scale 97% were predictable type ADRs.

Table 3: Organ System Involved

S.NO	ORGAN SYSTEM INVOLVED	NO. OF ADRs	% OF ADRs
1	GIT	22	29
2	Dermatological	34	45
3	CNS	6	8
4	Musculo-Skeletal	10	13
5	Respiratory	2	2.5
6	Misc.	2	2.5
	Total	76	100

Dermatological system was affected most with 45% cases followed by GIT and musculoskeletal with 29% and 13% cases respectively.

Table 4: Drug Responsible For ADRs

S.NO	DRUG	NO.OF ADRs	% OF ADRs
1	Ceftriaxone	64	84.5
2	Cefexime	5	6.5
3	Cefotaxime	7	9
	Total	**76**	**100**

Ceftriaxone was the most common offending drug with 84.5% ADRs cases followed by cefotaxime (9%) and cefexime (6.5%).

Table 5: Type of Reactions With Cephalosporins

S.NO	TYPES OF REACTION	NO.OF ADRs	% of ADR
1	Abdominal Pain	5	6.57
2	Anorexia	2	2.63
3	Anxiety	2	2.63
4	Chest Pain	1	1.31
5	Constipation	1	1.31
6	Diarrhoea	5	6.57
7	Dizziness	1	1.31
8	Dyspnoea	2	2.63
9	Excess Sweating	2	2.63
10	Exfoliative Dermatitis	1	1.31
11	Fever	1	1.31
12	Headache	3	3.94
13	Itching	8	10.52
14	Joint Pain	3	3.94
15	Nausea & Vomiting	9	11.84
16	Parotid Swelling	1	1.31
17	Rash	22	28.94
18	Swelling	6	7.89
19	Toxic Epidermal Necrosis	1	1.31
	TOTAL	76	100

Rash was the most common reaction (28.94%) observed followed by nausea & vomiting (11.84%) and swelling (7.89%).

DISCUSSSION

In our study among cephalosporins antibiotic, ceftriaxone was the most common drug causing ADRs 84.5% followed by cefotaxime 9%. This is comparable to study done by *Issac AJ et a.l*[9] who reported maximum cases of ADRs by ceftriaxone (99%) followed by cefixime 1%, *Anjan Adhikariet et.al.*[10] also reported maximum no. of ADRs with Ceftriaxone 26.7% among other antibiotics, *Baniasadi S et al.*[11] also shows that 80% of ADRs among cephalosporins are with ceftriaxone & rest 20% with cephalexin. Similarly *Jianquan Lu et.al.*[12] also showed that 46% case of ADRs are with ceftriaxone followed by cefoperazone 15% cases, *Qing shi et.al.*[13] study also prove maximum ADRs with ceftriaxone 16% followed by cephalexin 13% among cephalosporins. This could be due to the fact that ceftriaxone was most commonly prescribed drug in in-patient setting among cephalosporins due to its broad spectrum activity against various type of

microorganism.hence reported ADRs were also more with ceftriaxone.

In our study the most frequent ADRs observed were rash (28.94%), followed by nausea & vomiting (11.84%) and swelling (7.89%). This finding is similar to studies conducted by *Qing shi et.al* showed rash-30.60%, anaphylactic reaction (15%)–body as whole, nausea & vomiting (12%). In our study rash is most common ADRs encountered, it could be because it is an immediate occurring reaction and easily visible and hence more reported.

In our study most frequently involved organ systems were dermatological system (45%) followed by GIT (29%), musculo-skeletal system (13%). This finding is comparable with the study conducted by *Qing shi et.al* that also shows the major involvement of dermatological system (skin-43.50%, Body as whole -21% & GIT-20%). Since in our study most common offending drug class is cephalosporins and they give bizarre type hypersensitivity reactions causing serious damage to skin and the digestive system, visible easily & noticed by healthcare provider / patient / care taker hence reported more as compared to other system.

In our study on ADRs assessment for type, seriousness, severity, predictability & causality- type B ADRs (67%) followed by type A ADRs (33%), mostly Non serious (88%), Mild severity (79%), severe (1%), predictable (97%) & mostly of probable causality (53%) followed by possible (47%).Similar study by *Qing shi et.al* showed Causality as probable (61%) followed by possible (27%), severity-mild (52%) & moderate (47%), severe (0.9%).

CONCLUSION

Cephalosporins is an important group among antibiotics, having broad spectrum antibacterial action. Out of cephalosporins; Ceftriaxone is most prescribed antibiotic in paediatric tertiary care hospital. Ceftriaxone is associated with dermatological ADRs, so while prescribing ceftriaxone clinician should give special attention to monitor dermatological ADRs(rash) specially in 5-18years age group.

AKNOWLEDGEMENTS

Authors are thankful to the Department of pharmacology and Department of paediatrics, GSVM Medical College Kanpur (UP) India for providing suitable facilities for the successful completion of our study.

REFERENCES

1. World Health Organization. International drug monitoring: the role of the hospital. Geneva, Switzerland: world health organization, technical report series, 1966; 425.
2. Khraenbuhl-MA, Schlienger R, Lampert M, et al. Drug – related problems in hospitals. A review of the recent literature. Drug Safety, 2007; 30: 379-407.
3. Dhar et al. Pattern of adverse drug reactions to antibiotics commonly prescribed in department of medicine and pediatrics in a tertiary care teaching hospital, Ghaziabad Jou of App Pharma Sci., 2015; 5(04): 078-082.
4. Munir P, Alasdair MB. Clinical review adverse drug reaction. Bri Med Jou, 1998; 316(25): 1295–1298.
5. Suzanne S. Pediatric drug market finds its own pathway. Pharmaceutical Commerce Nov/Dec 2015.
6. McLeod HL et.al. Disposition of anti-neoplastic agents in the very young child. Br. J. Cancer, 1992; 18: S23–S29.
7. Anderson GD, Lynn AM. Optimizing pediatric dosing: A developmental pharmacologic approach. Pharmacbookapy, 2009; 29: 680–690.
8. Issac AJ et al. Assessment of prescription pattern & monitoring ADR of antibiotic in paediatric inpatients. Int J Contemp Pediatr, Aug, 2016; 3(3): 1071-1075.
9. Anjan A et.al. Ceftriaxone related adverse drug reactions in children in a tertiary care hospital, kolkata, west bengal, India. Explor Anim Med Res., 2014; 4(1): 44-47.
10. Baniasadi S et al. Increasing the number of adverse drug reactions reporting: the role of clinical pharmacy residents. Iranian Jour Phar Res., 2014; 13(1): 291-297.
11. Jianquan L et.al. Analysis on 113 cases of adverse reactions caused by β-lactam antibiotics. Afr J Tradit Complement Altern Med., 2013; 10(4): 83-87.
12. Qing-PS et.al. Adverse drug reactions and pattern use of cephalosporins: A retrospective review of hospitalized patients during 5 years. *Int Jou of Pharma*, 2013; *9: 66-73.*