Surveillance of Adverse Drug Reaction in Hospitalized Children, A Cross Sectional Study from Qom Province, Iran

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Abstract: Prevalence of drug reactions in childhood is rising. This study was performed in hospitalized children. The main goal of this study was determination of drug reactions prevalence in childhood, evaluation of drug type, identify risk factors associated with adverse drug reactions (ADRs) and also onset time of reaction. **Materials and methods:** This study was performed as descriptive cross-sectional survey among 180 children hospitalized children in Qom Children Hospital from January 2005 to October 2010. The data were extracted from medical files. **Results:** The prevalence of adverse reaction to penicillin, cephalosporin, other antibiotics, corticosteroids, metoclopramide, anticonvulsants were16.7%, 11.1%, 16.1%, 1.1%, 21.7%, 10.6% respectively. 6.1% of them had unknown origin, and prevalence of adverse reaction against other drugs was 16.7%. Type of drug reaction was related with age and reaction time ($P < 0.05$). **Conclusion:** Overall, according to the results in comparison to other studies, it may be concluded that drug reactions are common among childhood and there is a need for planning to reduction of its frequency. For diminishing the risk of ADRs in children, close communication between clinicians and pharmacologist and knowledge about higher ADR risks in some drug groups is needed.
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Introduction

Appropriate drug use is a main factor in the economy and treatment process. The role of culture and medical groups was seriously considered as a major factor in drug utilization and prescription[1, 2]. According to the statistical record, drug production in Iran is very high. The rates in Europe and America is about half this number. Definitely consequences of inappropriate use of drugs develop low satisfaction of the patient, prolonged and severe illness, need for hospitalization, dangerous side effects, and eventually increase health care costs for individuals, government agencies, and more perennial problem of inadequacy of medicines in the country. According to statistics, the rate of drug reaction in this country is increased about 11.5%. Wearer rising rates of 7% in developing countries and global 9% worldwide have been reported [1]. Thus, reduction of medical complications is important. Understanding the epidemiology and risk factors of ADRs is important in order to develop appropriate prevention strategies. Children are thought to be at a higher risk of adverse drug events including medication errors and ADRs than adults due to their physiology and immature mechanism of drug metabolism [1, 2].

Drug sensitivity can be divided into two groups: Type A and Type B. The pharmacological effects of type A drug reactions are predictable and depends on the doses of drug that the patient is taking. Type A reaction reported about 80% of ADRs includes poisoning, side effects, secondary drug effects [3]. The pharmacological effects of type B drug reaction are not predictable and isn't dose dependent. The reactions of the type B included 15-10% of ADR, these reactions consisted of IgE mediated or T cell mediated reaction or rarely immune cytotoxic complex. In 10-5% of cases the mechanism of ADR, is unknown. This type of reaction, called non-immune or non-allergic [3]. The most important risk factor for drug sensitivity is the molecular weight. Drugs that have a complex chemical structure (such as specified non-human protein) are immunogenic. Another factor route of using. Intramuscular, intravenous and locally used drug are main ways to create a sensitive reaction [3, 4]. Whenever ADR is diagnosed in every major organ, these questions should be answered. What is the relationship between dose and response, how long after starting the drug , reaction response has been created, is the drug reaction observed for the first

time?, what is the reaction? This study aimed to identify risk factors associated with ADRs in hospitalized children and recommend strategies to minimize ADRs. We studied the cases of drug reactions among admitted children in Children Hospital in Qom city from 2005 to 2012.

Materials and Methods

A cross sectional study was performed in 180 patients. We studied the cases of drug reactions among admitted children in Children Hospital in Qom between April 2005 to October 2012. Data were collected over a 60-month period from medical files. All children admitted during the study period were initially included. Children with a hospital stay of less than 24 h were subsequently excluded. ADRs were defined according to the World Health Organization (WHO) as any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function [3]. ADRs were identified by the intensive chart review and evaluated by the research team, which consisted of at least one clinical pharmacist and one pediatrician / pediatric pharmacologist. The data were analyzed by SPSS version 13 soft wares. $P<0.05$ showed the statistical significance.

Results

The study population consisted of 180 patients, 103(57.2%) male and 77 (42.8%) female, at a mean age of 3.52±2.4 months. Baseline characteristics are shown in Table 1. There was no association between drug allergy history and type of drugs (P=0. 788). Data analyze showed that there was no significant correlation between gender and type of drugs (P=0. 757) (Table 2).

Table 1. Some characteristics of Patients

Data	Frequency	Percent
Gender		
Male	103	57.2
Female	77	42.8
clinical manifestation		
Cutaneous	101	56.1
CNS	56	31.1
Respiratory	2	1.1
Gastrointestinal	5	2.8
Allergic	14	7.8
Other	2	1.1
History of drug allergy		
Positive	21	11.6
Negative	159	88.3

Table 2. Correlation between gender and type of drugs

		ADR Drug								
		Penicillins	Cephalosporines	Other ABs	Corticosteroids	Metoclopramide	Anticonvulsants	Unknown	etc	Total
Sex	Male	19	9	15	1	20	12	7	20	103
		18.4%	8.7%	14.6%	1.0%	19.4%	11.7%	6.8%	19.4%	100%
	Female	11	11	14	1	19	7	4	10	77
		14.3%	14.3%	18.2%	1.3%	24.7%	9.1%	5.2%	13.0%	100%
Total		30	20	29	2	39	19	11	30	180
		16.7%	11.1%	16.1%	1.1%	21.7%	10.6%	6.1%	16.7%	100%

Table 3. Relationship between duration of hospitalization and reaction time of ADRs and type of drugs

ADR Drug		Age	Hospital Stay	Reaction Time
Penicillins	Mean	4.80	2.69	5.87
	Std. Deviation	6.949	1.466	3.829
Cephalosporines	Mean	3.26	1.84	4.30
	Std. Deviation	2.562	.765	3.028
Other ABs	Mean	3.03	2.62	4.28
	Std. Deviation	3.202	3.530	3.650
Corticosteroids	Mean	4.65	1.50	5.50
	Std. Deviation	6.152	.707	2.121
Metoclopramide	Mean	2.29	1.47	.89
	Std. Deviation	3.275	.893	3.329
Anticonvulsants	Mean	6.53	2.74	6.01
	Std. Deviation	3.339	1.447	3.330
Unknown	Mean	3.31	2.09	14.00
	Std. Deviation	2.816	1.921	7.000
etc	Mean	2.60	2.28	1.21
	Std. Deviation	3.301	2.026	2.187

Table 4. Drugs used for treatment of ADRs

Treatment

		Frequency	Valid Percent
Valid	Antihstamin	23	14.1
	Corticosteroids	65	39.9
	AB	22	13.5
	Biperiden	39	23.9
	etc	14	8.6
	Total	163	100.0

Also, there was no relationship between gender and type of complication. The complications were more common at lower ages, also association was found between age and type of drugs (P=0. 011). The mean duration of hospitalization was 2.2±1.2 days. There was no relationship between duration of hospitalization and type of drugs, but duration of reaction was correlated with type of drugs (Table 3). The mean age of metoclopramide side effect was less than other drugs, but in anti-convulsants was more than other drugs. Complications were seen in (3)16.7% of cases due to penicillin, 20(11.1%) in cephalosporin, 29(16.1%) in other antibiotics, 2(1.1%) in corticosteroids, 39(21.7%) in metoclopramide, 19(10.6%) in anti convulsants, 11(6.1%) unknown and 30(16.7%) in other drug. The drugs were used for treating side effects shown in Table 4.

Discussion

The early detection of ADRs is important to prevent unnecessary harm to patients. Knowledge of predisposing factor of ADRs is important to develop appropriate prevention strategies. Many factors can increase the likelihood of an adverse drug reaction including the simultaneous use of several drugs, very young or old age, and hereditary factors which make some people more susceptible to the toxic effects of certain drugs. Certain diseases can alter drug absorption, metabolism, and elimination and the body's response to drugs and also adverse drug reactions. Mechanisms of drug reactions are related to use of inappropriate drug doses that develop toxicity in the human body, but sometimes it can cause unwanted reaction in normal dosage. Sometimes interactions between two or more drugs using simultaneously can induce side effects. The drug may produce a classic allergic reaction to one of four types of dumping. Allergic reactions in the same person at different times may be different. Different individual response to medication may be different because of presenting imbalance in the ecological quality of abnormal sensitivity to medications by different drugs and changing the natural balance of microorganisms in the skin and the status of fetal defects, teratogenicity and other side effects were rare. This problem is well understood by using different kinds of drugs. This study revealed a correlation between age and kind of drugs. The mean age in reaction to metoclopramide was lower and in the cases of anticonvulsants was higher than other drugs, which shows a need for concerning about drug administration in children. There was no correlation among gender and ADRs compatible to Rose study (5). Previous studies have shown ARDs in very young children and very old person are more common because of their lower immunity status (6,7). In our review half of the patients were lower than two months. Although drug safety was better in children, according to French investigation (8). In our study the high ADRs rate was detected in metoclopramide(21.7%), the second rate was related to penicillin (16.7%) followed by 16% for other antibiotics (16.1%) and cephalosporin (11.1%), 10.6%in anticonvulsants and lower rate for corticosteroids (1.1%) in contrast to other studies with highest rate of ADRs for antibiotics (9 ,1-3). The most complication in our study was cutaneous reaction followed by CNS, respiratory and gastrointestinal complication respectively in comparison to American study with gastrointestinal predominance in adverse effect (10). Antihistamines were the most drugs used for treatment, compatible to another study from USA (11). This review confirms previous studies which have presented ADRs to be a major problem in children (12). The severity of symptoms were shown not related to drug dosage. The same result was reported in Kimland study from Sweden (13). Carleton's study in Canada 2009, showed the incidence of medical complications in people who have a history of drug allergy, is a little more than others but in the course of our study was not statistically significant in this area [14]. In our study the severity of most adverse reactions were

low, particularly in antibiotic using, in comparison to ADRs against anticonvulsants (15). According to previous investigation ADRs can increase the duration of hospitalization especially in CNS complication (16). This effect was found in CNS drug reaction in our study.

Conclusion

Overall, the results of this study and their comparison with other studies showed drug reactions in children is common and to reduce the burden of drug complications, health planning is needed. Further studies to confirm these findings is necessary. A limitation of this study was the small sample size from one hospital. Other studies with larger sample size are recommended.

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