Adverse drug reactions causing admission to a Pediatric Hospital in Hamedan – Iran: a 2 years study

MOJGAN SAFARI, ZAHRA ZANDIAN, SIMA VAKILI, and BAHMAN RASULI

ABSTRACT

Severe adverse drug reactions are an important cause of childhood morbidity and mortality. Despite this, few reports in the literature describe it. This study was designed to evaluate the admitted pediatric patients due to adverse drug reactions. This retrospective study was conducted at Pediatric ward of Besat Hospital. The records of hospitalized patients that admitted with diagnosis of adverse drug reactions enrolled in study over a 2 years period. The data collected on a data collection form using the records of the patients and included the patient demographic features (age, gender, allergy history, primary cause for drug administration) and drug information (name, duration of use, description of drug reaction, duration of drug reaction and concomitant use of drugs). Thirty-five patients were enrolled in study. Of them, 24 (68.6%) were male and 11 (31.4%) were female. Ages were under 1 years old in 5 (14%), between 1 to 5 years old in 22 (63%) and beyond 5 years old in 8 (23%) patients. Most patients (88.5%) had no known drug allergies. The primary cause for drug administration was upper respiratory tract infections (43%), diarrhea (26%), seizure (14%), gastroenteritis (8.5%) and vomiting (8.5%). Drugs most frequently cited included: Furazolidone (n = 9), Penicillin (n = 8), Amoxicillin (n = 7), Co-Trimoxazole (n = 4) and Phenobarbital (n = 4). Most frequent reactions were: skin rashes (83%), arthralgia (37%), fever (34%), pruritus (23%) and edema (11.5%). Understanding causality and preventability of adverse drug reactions will significantly aid in better therapeutic monitoring for children receiving the same therapy in future.

Keywords: Adverse drug reactions, Hospitalization, Pediatric, Antibiotic
Adverse drug reactions (ADRs) can lead to significant morbidity and death among children [4-11]. ADRs not only may result in hospital admission or prolonged hospitalization but also may lead to permanent disability or even death. Notably, in a meta-analysis by Lazarou et al. [4], fatal ADRs among both adults and children ranked as the fourth to sixth leading cause of death in the United States of America. Another study demonstrated that ADRs were associated with an average of 243 reported deaths among young children, from newborn to 2 years of age, each year [9].

The incidence of unwanted drug reactions is generally unknown. The treatment cycle could be interrupted by drug side effects; thus, in these cases changing the drugs sometimes may be necessary. Outcomes can extra costs for treatment and prolonged treatment period. Sometimes these side effects may cause new problems, therefore hospitalization and new treatment could be necessary [12]. Diagnosing the patient demographic features (age, gender, allergy history, primary cause for drug administration) and drug information (name, duration of use, and description of drug reaction, duration of drug reaction and concomitant use of drugs) can be helpful in determining the type, strategy and dosage of the prescribed drugs. According to the fact that epidemiologic studies are the basis of other studies, the incidence of unwanted drug reactions should be assessed. Due to lack of research findings about this problem in Hamedan, we evaluate the incidence of hospitalization due to ADRs in pediatric patients at Besat hospital in Hamedan city.

### Patients and Methods

The data collected on a data collection form by using the records of the patients and included the following information: patient demographic features (age, gender, allergy history, primary cause for drug administration) and drug information (name, duration of use, and description of drug reaction, duration of drug reaction and concomitant use of drugs). The records of hospitalized patients who were admitted with diagnosis of drug side effects, drug sensitivity, serum sickness, hives, rashes, Stevens-Johnson syndrome, and hypersensitivity syndrome were enrolled in study during 2 years. Their hospitalization folder had been checked and recorded. If the patient’s folder was incomplete, the patient was removed from the study. All the data were put into questionnaire and compared using one-way ANOVA test in SPSS.16 software.

### Results

Thirty-five patients were enrolled in this study. Of them, 24 (68.6%) patients were male and 11 (31.4%) patients were female. Ages were under 1 years old in 5 (14%) patients, between 1 to 5 years old in 22 (63%) patients and beyond 5 years old in 8 (23%) patients.

Most patients (88.5%) had no known drug allergies. More than one drug prescribed in 57% of patients. Duration of drug consumption in 19 (54%) cases was less than 7 days. In 15 (43%) of cases, duration of drug consumption was between 7-14 days and in 1(3%) case, it was between 14-21 days. The adverse reaction began during the first week after drug exposure in 17 (48%) cases, during second week in 14 (40%) patients and during third week in 4 (11%) patients.

Most frequent reactions descriptors include: skin rashes (83%), arthralgia (37%), fever (34%), pruritus (23%), edema (11.5%), claudication (8.5%), protuberant fontanel (2.8%) and combination of extrapyramidal symptoms, agitation, upward gaze and perioral rhythmic movement (2.8%) (Table 1).

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### Table 1. Adverse drug reactions in hospitalized pediatric patients

<table>
<thead>
<tr>
<th>Medicine(s) used</th>
<th>Adverse drug reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furazolidone</td>
<td>Fever, Rash, Urticaria, Arthralgia, Erythema multiforme, ,Erythema marginatom, Swelling and redness of limbs and joints</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Extrapyramidal effects, Dystonia or tremors, Agitation, Perioral rhythmic movement, Upward gaze</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Injection type: Prominent Fontanel, Maculopapular rash, Stevens-Johnson syndrome, Erythema multiforme, Joint swelling, Swelling of limb, Urticaria</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Maculopapular rash, Morbilliform exanthema</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Fever, Pruritus, Abdominal pain, Erythema multiforme</td>
</tr>
<tr>
<td>Hyocine</td>
<td>Fever, Rash</td>
</tr>
<tr>
<td>Co-Trimoxazole</td>
<td>Arthralgia, Urticaria, Pruritus, Acute generalized exanthematous pustulosis</td>
</tr>
<tr>
<td>Cefalexin</td>
<td>Pruritus, Papules and plaque in combination therapy with co-TMX</td>
</tr>
<tr>
<td>Cefixime</td>
<td>Pruritus, Claudication, Urticaria, Fever, erythema marginatom, Drug induced arthritis</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Fever, Pancytopenia, Maculopapular rash</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Fever, Urticaria</td>
</tr>
<tr>
<td>Na-valproate</td>
<td>Fever, Rash</td>
</tr>
<tr>
<td>Liskantina Primidona</td>
<td>Fever, Rash</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Fever, Rash</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Fever, Rash</td>
</tr>
</tbody>
</table>
administration was upper respiratory tract infections (43%), diarrhea (26%), seizure (14%), gastroenteritis (8.5%) and vomiting (8.5%). Drugs most frequently cited include: furazolidone (n = 9), penicillin (n = 8), amoxicillin (n = 7), co-trimoxazole (n = 4) and phenobarbital (n = 4) (Table 2).

**DISCUSSION**

The aim of this study was to determine the frequencies of drug reactions in pediatric patients who were hospitalized because of drug reactions at Besat Hospital in Hamedan city over a 2 year period. We have shown that the frequencies of drug reactions are more common in 1-5 year old boys. The majority of these patients had no history of allergy and drug reactions. The most common signs of drug reactions reported were: rash followed by artheralgia and fever. The most common used drugs resulted in drug reactions were antibiotics and anticonvulsive drugs.

In the retrospective study conducted by Carleton and his colleagues [13], 1193 patients were evaluated in Canada during 1998-2002; 59% of the patients were beyond 13 years old. The most frequently drug reactions were: psychological disorders, nervous system disorders and rashes. The most commonly-used drugs associated with these reactions were: isotretinoin (56 case), paroksetin (42 case), Methylphenidate (41 case), amoxicillin (40 case), valproic acid (32 case), bupropion (26 case) and carbamazepine (25 case). Drug reactions have been resulted in death in 42 patients and irreversible sequel in 14 cases. Death and disability were not reported in our study. The number of our cases was significantly less than the patients of this study, our cases were generally between 1-5 years old and the most common drug reactions announced were due to antibiotic consumption. Excessive use of antibiotic can be assumed as the reason of these differences.

The prospective study on 512 children who were 2 years old and under was conducted by Martinez and his colleagues [14] in Spain. Drug reactions were seen in 4.3% of pediatric patients. The drug reactions often reported in these children were: convulsion, vertigo, vomiting, tremor, fever and itching. The systems most commonly affected were: the central nervous system (40.5%), the gastrointestinal system (16.7%), and the skin (14.3%). The main drug groups concluded were: respiratory drugs (35%), antibiotics (25%), drugs affected the central nervous system (15%) and the used drugs in dermatology (10%). The differences between this study and ours are the affected organisms, drug groups and drug reactions. This study was also evaluated broad spectrum of pediatric patients who were 2 years old and under, therefore the unequal conclusions can be explained by paying attention to the differences in number and age groups.

The other study was conducted in Brazil by Santos and his colleagues [15]. The skin (49%) was the most commonly affected organism in the hospitalized pediatric patients. Antibiotic consumption (53.2%) was the main cause of the problems occurred and damaged the organisms. Risk of drug reactions got increased to 3 times and more by using more drugs, being male, having prior history of hospitalization. Conclusions of this study are close to ours, as it has been demonstrated, rash was the most common sign due to using drugs and antibiotics were more responsible for drug reactions. Also the majority of the patients were male.

To best of our knowledge, the only study conducted in Iran was done by Mir Saeed Ghazi and his colleagues [1]. Icterozoin (56 case), phenobarbital (14 case), amoxicillin (13 case), metronidazole (12 case), furazolidone (11 case), cefixime (10 case), cefixime (9 case), metronidazole (8 case), amoxicillin (7 case), and phenobarbital (6 case) were used in these patients.

The most common sign of drug reactions reported in these children were: convulsion, vertigo, vomiting, tremor, fever and itching. The systems most commonly affected were: the central nervous system (40.5%), the gastrointestinal system (16.7%), and the skin (14.3%). The main drug groups concluded were: respiratory drugs (35%), antibiotics (25%), drugs affected the central nervous system (15%) and the used drugs in dermatology (10%). The differences between this study and ours are the affected organisms, drug groups and drug reactions. This study was also evaluated broad spectrum of pediatric patients who were 2 years old and under, therefore the unequal conclusions can be explained by paying attention to the differences in number and age groups.
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