Cutaneous Drug Reactions in Children Attending a Tertiary Care Hospital

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Abstract

Background: Cutaneous drug reaction (CDR) is a growing health hazard in the world. Adverse drug reactions are common complications in drug therapy. About 3-8% of all hospital admissions are the results of adverse drug reactions, among them 2-3% are children and these can cause significant disability to patients. Early identification and management of adverse cutaneous drug reaction has both short term and long term prognostic significance.

Objective: To know the cutaneous reaction to drugs in children in a tertiary care hospital.

Study design: Hospital based descriptive, observational study.

Subjects: 50 children with cutaneous drug reactions were studied in the department of Dermatology and Pediatric respectively in Rajshahi Medical College Hospital, Rajshahi.

Methods: Data were collected by detailed history taking, physical examination and laboratory investigations in a prefixed data collection sheet and with the help of GOLD guideline after taken informed consent of the patient.

Results: This study showed a significant male predominance. Male: female ratio was 1.08:1. In this study prevalence was highest among 1-5 years age group. Cotrimoxazole, NSAIDs, anticonvulsant and quinolone were most offending medications. Maculopapular eruption, Stevens Johnson Syndrome, fixed drug eruption and urticaria were most common morphological types. Majority of CDRs were noted with oral route of administration. It was observed that almost all the CDRs that were reported involved mainly the skin. Majority of adverse cutaneous drug reactions reported were moderate in severity.

Conclusion: Frequency distribution of the offending drugs and the adverse reactions revealed that adverse cutaneous drug reactions occurred mostly by cotrimoxazole, NSAIDs and quinolones. Maculopapular rash and Stevens Johnson Syndrome were the most common morphological types. A better understanding of the mechanisms underlying CRDs is important in drug development and in patient care.

Key words: Cutaneous drug reaction, Stevens-Johnson syndrome, erythema multiforme, fixed drug eruption.

Introduction

A cutaneous drug reactions (CDRs) are undesirable change in structure and function of the skin, its appendages, or mucous membranes due to drugs.1 Several studies have found that CDRs to be the most prevalent adverse drug reactions in

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hospitalized children, with an estimated rate of 2-3%.\textsuperscript{2,3}

Drug reactions vary in their appearance, rapidity of onset, severity, and underlying immunopathological mechanisms. They can range from pruritus or rash to severe and life-threatening Stevens Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN). Cutaneous Drug Reactions (CDRs) are a major cause of morbidity and mortality, accounting for up to 7% of all hospital admissions and rank as the fifth leading cause of death in the western world.\textsuperscript{4}

Although most drug-induced skin eruptions are not serious, some are severe and potentially life threatening. Serious drug reactions include angioedema, erythroderma, SJS and TEN. Drug reactions can also occur as part of a spectrum of multi organ involvement, for example in drug induced SLE. A cutaneous drug reaction should be suspected in any patient who develops a rash during a course of drug therapy. The reaction may be due to any medicine the patient has been currently taking or has recently been exposed to, including prescribed and over the counter medicine, herbal or homeopathic preparations, vaccine or contrast media.\textsuperscript{5}

The most common morphological types of CDRs range from maculopapular, urticaria/angioedema to fixed drug eruptions, and the common incriminating drug groups remain antimicrobials, anticonvulsants and Non-Steroid Anti-Inflammatory Drugs (NSAIDS).\textsuperscript{6,7,8,9,10}

Certain risk factors for CDRs are (a) patient related, viz age of patients, female sex, viral infection, genetic variations in the metabolism of the drug and human leucocyte antigen (HLA) association and (b) drug related, viz number of drugs taken, route of administration, duration of intake, dose and variation in metabolism.\textsuperscript{11,12}

The analysis of the data by Chatterjee et al shows that urticaria and fixed drug eruptions were the most common morphological reaction types. The common offending drug groups as stated by the same group were antimicrobial (34.10%), anticonvulsants (32.88%), anti-inflammatory drugs (21.51%). Other less frequent ones were antipsychotics, antidepressants, anti hypertensives, oral contraceptives, antidiabetics, insulin, vaccines, radio contrasts, pancreatic enzyme supplements, homeopathic and ayurvedic preparations. The most common offending drugs were carbamazepine (16.23%), phenytoin (15.15%) and cotrimoxazole (13.53%); however, antimicrobials were the most common drug group implicated.\textsuperscript{13}

**Materials and Methods**

**Study design:** Hospital based observational descriptive study.

**Study period:** 06 months (July 2011-December 2011.)

**Study place:** Department of dermatology, Rajshahi medical college hospital, Rajshahi.

**Sample size:** Sample size 50 who fulfilled the inclusion and exclusion criteria were enrolled in this study.

**Inclusion criteria:**
- Patient who agreed to be included in this study
- Patients with cutaneous adverse drug reactions who have documented evidence of having taken the suspected drug recently.
- Age range : 1 months to 12 years
- Sex: Patients of either sex.

**Exclusion criteria:**
- Patient who did not agree to be included in this study
- Age less than 1 month and more than 12 years
- Rash without history of taking any offending drugs recently.
• Patients having alternative etiologic candidates like infections, food allergy, and other skin morbidity which can cause acute onset of skin rash.

• Patients on non-traditional medicine. e.g: homeopathy, herbal, ayurvedik.

Results

This study was intended on cutaneous reaction to drugs in children in a tertiary hospital. 50 children aged between 1 month to 12 years of both sexes, who had clinical symptoms of cutaneous drug reactions were selected. They were diagnosed through complete history taking, physical examination and laboratory investigations.

Among the reported CDRs, 40 were directly from dermatology department and 10 cases from pediatric department. Dermatology department reported maximum number of CDRs because majority of the reactions were of cutaneous in nature. Other departments referred the patients to dermatology department for evaluation upon noticing an CDR (Table 1). Out of 50 patients, 26 (52%) were males and 24 (48%) were females, with a male to female ratio of 1.08:1 (Table 2).

Among the 50 reported CDRs, the patient age group was categorized as 0-12 months, 1-5 years and 6-12 years. Age, as a predisposing factor, plays an important role in the occurrence of CDRs. In this concern pediatrics were more prone to CDRs when compared to adults. From the reports, we observed 1-5 years age group children predominance over others in CDRs occurrence during study period (Table 3).

Majority of CDRs were noted with oral route accounted 44 cases (88%) and parenteral route accounted for 6 cases (8%) of CDRs (Table 4). Drugs can affect any organ system but to which system is mostly affected depends on drug and its nature. It is observed that almost all the CDRs that were reported involved the skin (Table 5).

The severity of the reported reaction were analysed as mild, moderate and severe upon the Hartwig scale. The severity of reported CDRs are shown in table below. There were 10 reports in which patient’s clinical condition was severe and in 5 cases it was mild. Majority of CDRs (35 cases) reported were moderate in degree of severity (Table 6).

Out of all offending drugs, 10 cotrimoxazole (20%), 8 NSAIDs (16%), 7 anticonvulsant (14%), 6 quinolone (12%), 6 penicillins (12%), 5 tetracyclines (10%), 4 cephalosporin (8%), 3 metronizazole (6%) and 1 antitubercular (2%) group of drugs (Fig 1).

Among affected children, 14 had maculopapular eruption (28%), 10 had Stevens - Johnson syndrome (20%), 8 had fixed drug eruption (16%), 6 had urticaria (12%), 5 had exfoliative dermatitis (10%), 5 had erythema multiforme (10%), 1 had purpura (2%) and 1 had acneform eruption (2%) (Fig 2).

Table 1: Number of CDRs reports received from different departments

<table>
<thead>
<tr>
<th>Department</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatology</td>
<td>40</td>
<td>80%</td>
</tr>
<tr>
<td>Pediatric</td>
<td>10</td>
<td>20%</td>
</tr>
</tbody>
</table>
### Table 2: CDRs categorized based on gender of the patients

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>26</td>
<td>52%</td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
<td>48%</td>
</tr>
</tbody>
</table>

### Table 3: CDRs categorized based on age group of patients

<table>
<thead>
<tr>
<th>Age group of patient</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-12 months</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>1-5 years</td>
<td>20</td>
<td>40%</td>
</tr>
<tr>
<td>6-12 years</td>
<td>18</td>
<td>36%</td>
</tr>
</tbody>
</table>

### Table 4: CDRs categorized based on routes of administration

<table>
<thead>
<tr>
<th>Routes of administration</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>44</td>
<td>88%</td>
</tr>
<tr>
<td>Parenteral</td>
<td>6</td>
<td>12%</td>
</tr>
</tbody>
</table>

### Table 5: Organ systems affected due to CDRs

<table>
<thead>
<tr>
<th>Organ systems</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>42</td>
<td>84%</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Eye</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Genital mucosa</td>
<td>2</td>
<td>4%</td>
</tr>
</tbody>
</table>

### Table 6: Severity assessment of the CDRs

<table>
<thead>
<tr>
<th>Severity</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>35</td>
<td>70</td>
</tr>
<tr>
<td>Severe</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Fatal</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Cotrimoxazole=Cot
Anticonvulsant=Anticon
Tetracycline=T/C
Metronidazole=Metro

Non-Steroidal Anti Inflammatory Drug=NSAID
Quinolone=Quin, Penicillin=Peni
Cephalosporin=Cepha
Antitubercular=AntiTB

Fig. 1: Pharmacological classes of drugs implicated to cause CDRs

Maculopapular Eruption=ME
Stevens-Johnson Syndrome=SJS
Fixed Drug Eruption=FDE
Urticaria=Urti
Exfoliative Dermatitis=ED
Erythema Multiforme=EM
Purpura=Purp
Acneform Eruption=AE

Fig. 2: CDRs categorized based on morphologic pattern of the patients
Discussion
As seen from the data, CDR seems to be a common problem in patients getting drugs of all types. The distribution indicates fairly uniform trend of occurrence of CDR in males. CDRs were common in 1-5 years age group in this study.

As predicted the bulk of CDRs are reported from dermatology department. It is a department that relies on drug therapy to the maximum. All the patients reported to dermatology department may be permanently attending OPD or may be referred from other departments.

Psychopharmacological agents are being increasingly used and recent drugs are being tried. Data reveals a large number of CDR due to these agents. Skin seems to be most common organ system affected intensive monitoring strategies regarding any medication errors, patient factors and underlying cause of these CDR. It is well known that oral route is commonest and hence CDRs were also commonest with oral route.

This study reflects the need to carefully assess safety, monitoring, preventability and treatment of CDR of conventional drugs. It may a beginning of more serious efforts on part of physicians to report each and every CDR they come across while administering the drugs in a tertiary care hospital where patients are exposed to large spectra of drugs.

Many studies carried out in this respect but very few are compatible to the period of our study. The pattern of CDRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere. It provides a database of CDRs due to common drugs used in our hospital, which will help clinicians for optimum and safe use of these drugs. Hence strict vigilance is required for the use of these likely drugs and their safety assessment.

This descriptive type of cross sectional study was undertaken to observe the cutaneous manifestations of drug reactions. Out of 50 patients studied 52% were males and 48% females with a male female ratio of 1.08:1. Age varied from 1 month to 12 years. 40% of the patients were of 1-5 years age group, 36% were from 0-12 months age group. The remaining 24% were from 6-12 year age group.

Vervloet and Durham had reported similar findings. Drugs most frequently involved were cotrimoxazole 20%, NSAIDs 16%, quinolones 14%, anticonvulsants 14% and cephalosporin 12%, penicillins 12%, tetracyclines 10%, metronidazole 6% and antituberculous drugs 4%. In the Boston collaborative drug surveillance programme almost similar results were obtained by Shear.

Noel et al. reported maculopapular rash in 35%, followed by Stevens-Johnson syndrome 15%, urticaria and erythema multiforme 7% each, and exfoliative dermatitis and fixed drug eruption 4% each. Jhaj et al. also reported maculopapular rash as the most common reaction in 50% patients, urticaria 21.5%, Stevens-Johnson syndrome 13.9% and toxic epidermal necrolysis in 10% cases. Other reactions included pruritus without a rash, contact dermatitis, purpura, erythema multiforme, fixed drug eruption and acneiform eruption.

Conclusion
Maculopapular rash and Stevens Johnson Syndrome were most common morphologic types of adverse cutaneous drug reactions noted in our study. Cutaneous adverse reactions occurred mostly with sulphamides, NSAIDs, anticonvulsant and quinolones. A better understanding of the mechanisms underlying CRDs is important in drug development and in patient care.

References


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