A STUDY OF CLINICAL PATTERN OF ANTIBIOTICS INDUCED ADVERSE CUTANEOUS DRUG REACTIONS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Abstract: Adverse cutaneous drug reactions (ACDRs) are caused by a wide variety of agents. Antibiotics are one of the commonest drug groups to cause ACDRs and clinical pattern of cutaneous ADR changing every year. Aims: Our objective was to evaluate clinical pattern of adverse cutaneous drug reactions of antibiotics in a tertiary care hospital. Methods: fifty five patients with adverse cutaneous drug reactions were recruited for this study during 2013-2014. Results: The Most of ACDRs belonged to the age group of 21-30 years (36.36%) with male predominance. The most common eruptions observed were maculopapular rash (36.36%) followed by fixed drug eruption (27.27%), SJS/TEN (18.18%) and Erythema multiforme (9.09%). Conclusion: The pattern of ACDRs And the drugs causing them is remarkably different in our population. Knowledge of these drug eruptions, the causative drugs and the prognostic indicators is essential for the clinician.

KEYWORDS: Cutaneous drug reactions, antibiotics.

INTRODUCTION

Drugs are the most common medical interventions, primarily used to relieve sufferings. But it has been recognized long ago that drug themselves can prove fatal; as the saying rightly goes “Drugs are Double Edged Weapons”. When a new drug reaches the market, patients expect it to be safe and effective. During drug development, preclinical and clinical studies usually
provide sufficient evidence of the product’s effectiveness, but this is not the case for safety.
Indeed, several examples serve to prove that pre marketing clinical trials may fail to detect side effects that later manifest themselves as adverse drug reactions. Thus, drug safety assessment should be considered an integral part of the day to day clinical practice.

An adverse drug reaction (ADR) is defined by the WHO as ‘A response to a drug which is noxious and unintended and which occurs at doses which are normally used in man for the prophylaxis, diagnosis or the therapy of a disease or for the modification of the physiological functions’. Antibiotics are used commonly in routine practice for treatment and prophylaxis of various disease conditions. Over half of all hospitalized patients are treated with antimicrobial agents and their use account for 20–50% of drug expenditures in hospitals. More than 70% of ICU patients receive antibiotics for therapy or prophylaxis, with much of this use being empiric and over half of the recipients receiving multiple agents. The total costs associated with antibiotics are not only related to antibiotic use itself, but also to co-medication and adverse drug events. In Darchy’s report, antibiotics accounted for 11% of iatrogenic disease. As more drugs are marketed and as more individuals take multiple drugs, the occurrence of Adverse Drug Reaction will probably continue to increase. Therefore, better approaches must be devised for reporting and assessment and management of individuals who present with drug induced diseases.

The pattern of cutaneous reactions differs among various drugs. Hence, understanding the precise nature of ACDR may help narrow down the search for the offending agent. Knowledge of drugs that can cause ACDR can help physicians in choosing safer drugs and therefore can be helpful to society at-large.

Keeping these observations in the background, this study was undertaken in our hospital to evaluate the clinical pattern of antibiotics induced cutaneous adverse drug reactions.

**MATERIAL AND METHODS**
The study was a prospective hospital based observational study. After getting approval from the institutional ethical committee, the study was jointly conducted in the Department of Pharmacology and Department of dermatology, NSCB medical college, Jabalpur over a period of one year (October 2013 to September 2014). The patients attending dermatology OPD with suspected ACDRs and the in-patients referred from other department with suspected ACDRs were enrolled. The participants had given the informed written consent
before they were enrolled in the study. The diagnosis of the ACDRs was based on detail drug history and a thorough clinical examination done by consultant dermatologist. The patient who consume medicines other than allopathic medications (like Ayurvedic/Homeopathic etc) & who are not able to recall the name of suspected medicine consumed (improper drug history) were excluded from the study. Detailed history of the patient including present illness, past or concurrent systemic illness & drug history were taken. The criteria for the diagnosis of ADRs\[4\] were as follows

1. The time interval between the introduction of the drug and the onset of a reaction should be within a specific time.
2. Improvement in the condition of the patient after dechallenge/withdrawal of the suspected drug.
3. Drug rechallenge producing similar reaction again.

The clinical pattern of ACDRs was assessed on local examination by consultant dermatologist on the basis of its site, nature, extent, colour & distribution of lesion, and pattern was recorded in form of maculopapular rash, urticaria, angioedema, fixed drug reaction, purpura, photosensitivity etc.

To establish the etiologic agents for ACDRs, attention was paid to the drug history, temporal correlation with the drug, duration of the rash, pattern of lesion, improvement of lesion on withdrawal of drug & recurrence of lesion on rechallenge if possible. Rechallenge was not undertaken in any of our cases because of the possible associated risks.

If more than one drug was thought to be responsible, the most likely offending agent was noted and the impression was confirmed by subsidence of the reaction with time or on withdrawing the drug. Finally data was recorded in CDSCO form\[5\] and was compiled and analysed.

**RESULT AND DISCUSSION**

A total of 58 cases of adverse drug reactions were identified. Out of these 3 cases had to be excluded from the final because they failed to state the names of the offending drugs or the data was insufficient to make reliable analysis. The remaining 55 cases of ACDRs were analyzed further. ACDRs were more common in males than in females (M:F ratio 1.75:1), which is similar to the other Indian studies where male preponderance was observed.\[6,7\]
Majority of the patients with ACDRs belonged to the age group of 21-30 years followed by 41-50 & 11-20 yrs. The ACDRs were more common in adult patients (68%) as compare to the children(32%).

NSAIDs (63.63%) were the most common drugs followed by antimicrobial agents(27.27%) in our study. But many different studies carried out elsewhere in India\[8,9,10\] have reported antimicrobial agents as the major group of drugs causing ACDRs followed by NSAIDs.

**Table-1 Table-1 clinical pattern of antibiotics induced ACDR**

<table>
<thead>
<tr>
<th>Type of reaction</th>
<th>Frequency</th>
<th>Present study (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maculopapular rash</td>
<td>08</td>
<td>36.36%</td>
</tr>
<tr>
<td>Fixed drug eruption</td>
<td>06</td>
<td>27.27%</td>
</tr>
<tr>
<td>Steven Johnson Syndrome/ Toxic Epidermal Necrosis</td>
<td>04</td>
<td>18.18%</td>
</tr>
<tr>
<td>Erythema multiforme</td>
<td>02</td>
<td>9.09%</td>
</tr>
<tr>
<td>Urticaria</td>
<td>01</td>
<td>4.55%</td>
</tr>
<tr>
<td>Serum sickness</td>
<td>01</td>
<td>4.55%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>22</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

ACDRs vary in their patterns of morphology and distribution. Of the various types of ACDRs the most common pattern observed was maculopapular rash (36.36%) followed by fixed drug eruption (27.27%), SJS/TEN (18.18) and Erythema multiforme(9.09%) Other types of ACDRs that were seen in our study included urticaria and serum sickness each of 4.55% (table-1) In previous studied from North India also the most common morphological patterns were exanthenatous rash, urticaria, and/or angioedema, fixed drug eruption and erythema multiforme.\[10,11\] maculopapular drug eruptions are usually begin within 1-2 weeks of starting a medication and gradually resolve 1-2 weeks following cessation.

**Table-2 Antimicrobial Drugs**

<table>
<thead>
<tr>
<th>Drug group</th>
<th>Individual drugs</th>
<th>No. of cases</th>
<th>Total no. of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobials</td>
<td>Ciplox-TZ(ciprofloxacin &amp; tinidazole)</td>
<td>5</td>
<td>(22cases)</td>
</tr>
<tr>
<td></td>
<td>Penicillins</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cephalosporins</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sulfonamides</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tetracycline/doxycycline</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolones</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazoles</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

The antibiotic classes affected with ADRs are shown in table 2 which revealed that ciplox-TZ(ciprofloxacin & tinidazole) were the most accounted antibiotic class 5(22.72%) followed
by penicillins, cephalosporins & sulfonamides 4(18.18%) each, others are 2(9.09%) doxycyclines & fluoroquinolones each and metronidazoles 1(4.54%).

There is no gold standard investigation for confirmation of a drug-induced reaction. Instead diagnosis and assessment of a drug cause involve analysis of a constellation of features such as timing of drug exposure and reaction time (the reaction was not considered as drug induced if the drug was administered after the onset of reaction), improvement in condition of patient after drug withdrawal or dechallenge, nature of a recurrent eruption on rechallenge, previous history of similar reaction to the same drug. On causality assessment, due to ethical issue rechallenge was not attempted deliberately and hence maximum number of ACDRs were labelled as probable cases.

During our study 4 cases of SJS/TEN due to Beta-lactam and sulfonamide were considered severe as they required immediate hospitalization and intensive medical care. Assessing the severity of ACDRs is an essential component in Pharmacovigilance studies as an ACDR may require intervention including the stoppage of the suspected drug(s) and even hospitalization in severe cases.

**CONCLUSION**

To sum up, the occurrence of ACDRs in the present study was similar in many ways to other studies conducted in India. A wide clinical spectrum of ACDRs ranging from mild maculopapular rash to serious SJS/TEN was observed. Majority of the patients with ACDRs belonged to the age group of 21-30 years followed by 41-50 & 11-20 yrs. Slight male preponderance was observed. Most frequent ACDRs reported were maculopapular rashes, fixed drug eruption, SJS/TEN and Erythema multiforme, urticaria and serum sickness in decreasing order of frequency. Considering individual drug, ciplox-TZ(ciprofloxacin & tinidazole) followed by penicillins, cephalosporins, sulfonamides, doxycyclines & fluoroquinolones.

On evaluation it is observed that, a proper evaluation and history taking would have prevented most of the ACDRs cases.
REFERENCES