Role of active surveillance in improving hospital adverse drug event monitoring

Clinical trials allow only limited assessment of adverse drug events (ADEs) due to their restricted number of patients, short duration and narrow inclusion criteria. About half the drugs which enter the market have serious adverse effects that are detected only after approval. Post marketing surveillance (PMS), through spontaneous reporting (SR) and cohort event monitoring, has an important role in the identification of the side effects which are not seen during pre-marketing trials. It also forms the basis for regulatory and public health decisions. In most hospitals throughout the world, including India, PMS is done through SR. Active monitoring of post-prescription events to newly marketed drugs is not usually done. SR is a well-accepted method, but some of the drawbacks include its selective nature and under reporting. To improve the hospital-based adverse event monitoring, active surveillance of post-prescription events has been suggested.

This proposal was followed up by conducting a six month-descriptive study of ADE occurrence and evaluation. This study compared the SR system with the active surveillance system among in-patients in a tertiary care hospital, Christian Medical College (CMC), Vellore, between July and December, 2004.

Three newly marketed drugs, i.e. the diuretic, torsemide; the vasodilator, cilostazol; and the antihyperlipidemic, rosuvastatin, were randomly selected for the study. All drugs were approved by the Drugs Controller General of India in 2003 and introduced in our pharmacy from July 2004.

In the SR system, ADE reporting cards were kept in each ward. The treating physicians and nurses were requested to enter the cards whenever they suspected ADEs in their patients. The cards were then collected, on a regular basis, and evaluated by pharmacologists associated with the hospital ADE monitoring centre. All spontaneously reported ADEs, associated with study drugs, were selected for the study.

In the active surveillance system, all 176 in-patients, consuming any one of the above mentioned drugs, were continuously enrolled from the hospital intranet computer, based on the in-patient prescriptions dispensed by the hospital pharmacy. A pharmacology resident doctor, associated with the hospital ADE monitoring centre, followed up these in-patients on alternate days until their discharge. Physician’s notes, nurse’s notes and investigational reports attached to the patients’ charts were reviewed. To detect incidents not recorded in the medical records, direct patient interviews were conducted by a pharmacology resident, using a structured questionnaire. Questions pertaining to the incidence of similar complaints prior to drug use were included in the questionnaire. Information regarding the patient’s age, sex, address, height, body weight, associated illness, use of concomitant drugs was also collected.

Naranjo’s algorithm score was used to assess the causality of each suspected ADE. Only definite (>9) and probable (5-8) events were taken into consideration. ADEs were classified as serious and non-serious, based on the ICH (International Conference on Harmonization) guidelines. Treating physicians and nurses were kept unaware of the study, to avoid reporting bias, though they were consulted while evaluating the ADEs.

Adverse events listed in the summary of product characteristics, enclosed with the drug package at the time of the study, were considered labelled and events not listed were classified as unlabelled.

Statistical evaluation was done using two sample tests of proportion. The total number of ADEs, number of labelled and unlabelled ADEs and number of serious and non-serious ADEs, detected through each of the two ADE reporting systems, were used for comparison. P values less than 0.05 were considered significant.

A total of 176 patients were followed up, of which 130 (73.9 %) were males and 46 (26.1%) females. A total of 102

Table 1

Comparison of adverse drug events (ADE) detection systems used in the study

<table>
<thead>
<tr>
<th>Group</th>
<th>Type of ADEs</th>
<th>Causality of ADEs</th>
<th>Severity of ADEs</th>
<th>Source of ADEs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Labelled</td>
<td>Unlabelled</td>
<td>Probable</td>
<td>Definite</td>
</tr>
<tr>
<td>Spontaneous reporting</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>Nil</td>
</tr>
<tr>
<td>Active surveillance</td>
<td>44* (85%)</td>
<td>8 (15%)</td>
<td>52</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Data are represented as the number of ADEs reported. *P<0.05 in comparison with spontaneous reporting.
In the present study, a dry cough (4)* and nausea and vomiting (1) were identified through active surveillance. The labelled ADEs shows that a significant number (15%) of unlabelled ADEs were identified through active surveillance. The labelled ADEs are the extension of the pharmacological activities of the drugs and resources available for ADE monitoring.

In conclusion, we suggest supplementing SR-based hospital ADE monitoring systems with an active surveillance system to monitor the safety profile of newly marketed drugs at all tertiary care hospitals. This will help in providing better patient care as well as offer substantial data support to the recently initiated National Pharmacovigilance Programme in India.

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