

Active pharmacovigilance in a hospital pharmacy department

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ABSTRACT

Introduction: A survey of voluntary reporting of adverse drug reactions (ADRs) showed that the reason for patient hospitalisation was an ADR in 8.4% of the cases and concluded that 14% were reported voluntarily. Hospital pharmacists are the professionals most willing to participate in active pharmacovigilance programmes in order to reduce under-reporting of ADRs. The objective of the project presented here was to increase the rate of ADR reporting in a general hospital by using an active ADR notification system.

Methods: For three months, the clinical history of patients treated with drugs that could lead to an ADR or whose diagnoses led to suspicion of an ADR was reviewed. The patients' hospital discharge diagnoses were also determined. Patients were included if they had a diagnosis that corresponded to the WHO's International Statistical Classification of Disease and Related Health Problems 9th Edition [1], codes referring to potential ADRs (ICD-9 E codes) either during their hospital stay or as a reason for admission.

Results: Twenty-seven ADRs were identified in 85 patients: 66.66% during review of their clinical history in accordance with ICD-9 E codes and 14.81% after the identification of alerting drugs. The ADR reporting rate was 11 times higher than during the same period the year before. Of the 27 ADRs identified, 11 fulfilled the criteria for being reported under the pharmacovigilance programme. The identification method was mainly adopted from ICD-9 E codes (54.55%).

Conclusion: The active pharmacovigilance system increased reporting of ADRs. Most ADRs were identified by the review of patients' clinical history in accordance with ICD-9 E codes.

KEYWORDS

Adverse Drug Reactions, alerting diagnosis, alerting drugs, pharmacovigilance

INTRODUCTION

Drugs are intended to cure, prevent or diagnose diseases and signs or symptoms, but their downside is that proper or improper use can be the cause of patient morbidity and even mortality. Despite the increasing interest in Adverse Drug Reactions (ADRs) after the thalidomide disaster of the 1960s, this issue has not attained real importance until recently [2].

WHO defines ADR as "any response to a drug which is noxious and unintended, which occurs at doses normally used in man for prophylaxis, diagnosis or disease therapy, or for the modification of physiological function" [3].

Nowadays, ADRs are considered an important health hazard in many countries. About 120,000 people die every year because of ADRs in the US alone. Deaths from ADRs rank between the fourth and sixth causes of mortality in the US. The economic costs derived from drug-related problems are approximately US\$76.6–177 billion (Euros 59.83–138.2 billion) per year [4].

In Spain, an exhaustive study on voluntary ADR reporting showed that ADRs could be the cause of hospital admission in 8.4% of patients. In the past 10 years, 4.8% of ADRs reported have been a threat to patients' lives, with fatality in 0.72% [5]. Recently, a national study conducted by the Sistema Nacional de Salud (SNS - Spanish national health

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system) in Spanish hospitals showed that the main cause of an adverse event is drug use (37.4%), and 9.3% of patients had an adverse event while under hospital care [6].

In our country, a final report after five years of surveillance concluded that only 14% of ADRs were voluntarily reported. All pharmacists and clinical physicians must remember that reporting all suspected ADRs is their responsibility and professional obligation [7, 8]. ADR notification in Spain is based on spontaneous voluntary reporting [9]. Although active pharmacovigilance programmes have shown excellent results in increasing the rate of ADR reporting, unfortunately such programmes are not common in Spanish hospitals [8].

Many incidents of ADRs go unreported, owing to a variety of factors involved in understanding and recognising ADRs. Hospital pharmacists are the most suitable professionals to participate in active pharmacovigilance programmes in order to reduce under-reporting of ADRs, because of their knowledge of pharmacotherapy and safe use of drugs, their efficient information system and training in using specific tools to correlate ADRs and drugs.

Hospital Juan Ramón Jiménez is the main hospital in Huelva, which is one of the eight provinces that comprise Andalusia in southern Spain. The hospital takes care of 250,000 citizens out of the total Spanish population of 40 million citizens. The aim of this report is to describe the active ADR notification system developed in the hospital to increase the ADR reporting rate in this area.

MATERIALS AND METHODS

For three months (May, June and July 2006), the clinical history of patients who were receiving treatment was reviewed. Attention was paid to the following:

1. Drugs that could lead to ADRs (alerting drugs) including those that could be used for treating ADRs, such as dexchlorpheniramine, which are also considered as alerting drugs.
2. Drugs that require special control; these include drugs recently introduced to the market, such as ertapenem, linezolid, eplerenone, drugs used off-label but allowed by the SNS, such as sildenafil for pulmonary hypertension, and drugs under active pharmacovigilance, such as allopurinol in renal failure and levofloxacin, used long term and in the elderly.
3. Patients whose diagnoses, such as upper gastrointestinal tract haemorrhage or pseudomembranous colitis, led to suspicion of an ADR (alerting diagnoses).

The patient's hospital discharge diagnosis was also determined. Patients were included in the study if they had

a diagnosis that corresponded to International Statistical Classification of Disease and Related Health Problems 9th Edition (ICD-9 E) codes referring to potential ADRs (ICD-9 E codes) either during their hospital stay or as a reason for admission. Spontaneous reporting of ADRs was also considered. ADRs were reported when at least one of the following criteria was found:

1. Death or a severe reaction related to drugs.
2. Hospital admission or a prolonged stay produced by an ADR.
3. ADRs to drugs introduced into the market in the past five years.
4. Unknown ADRs.

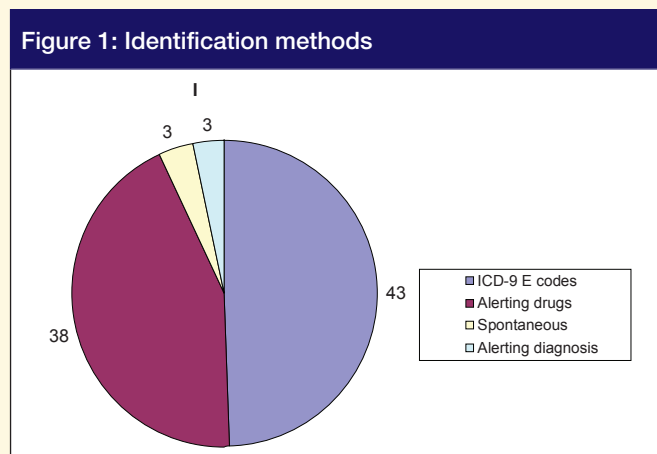
When hospital patients were identified, they were followed until the ADRs were evaluated. Having notified the national pharmacovigilance programme about all suspected ADRs, the Karch-Lasagna algorithm was used for establishing the relationship between the cause and effect.

RESULTS

Eighty-seven patients were selected over a 3-month period. Forty-three (49.43%) patients were selected using the ICD-9 E codes, 38 (43.68%) by alerting drugs through dispensing software, three (3.45%) because of an alerting diagnosis and three (3.45%) by spontaneous notification.

ADRs were identified in 27 (31%) patients, that included 18 (66.67%) based on ICD-9 E codes, four (14.81%) by alerting drugs through the dispensing software, three (11.11%) by spontaneous notification and two (7.41%) by alerting diagnosis (see Figure 1).

In most of the 38 patients identified by the dispensing software, the relationship between the drug and the effect could not be identified after the first clinical interview and review of patients' clinical histories, and therefore a follow-up was required.



The rate of ADR reporting during this review was 11 times higher than the same period in the year before. Of the 27 ADRs identified, 11(40.74%) fulfilled the criteria for being reported to the Spanish National Centre of Pharmacovigilance. The methods used to identify these ADRs are shown in Figure 2.

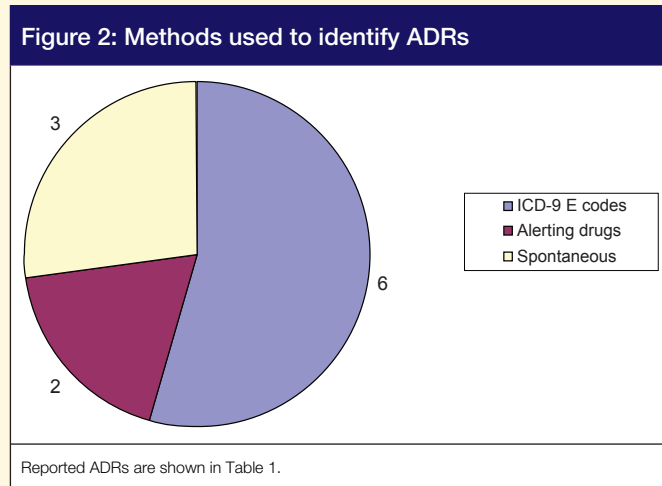


Table 1: ADRs notified

Drugs	ADRs	Causality
Ketorolac	Extrapyramidal disorder	Probable
Infliximab	Non-Hodgkin's lymphoma	Possible
Eplerenone	Erythema	Probable
Emtricitabine	Hepatorenal syndrome	Unlikely
Ibuprofen	Upper gastrointestinal tract haemorrhage	Definite
Amiodarone	Interstitial lung disease	Probable
Oxcarbazepine	Hyponatraemia	Possible
Fluconazole	Myoclonia	Possible
Vancomycin	Toxicodermia	Possible
Lamotrigine	Rash	Possible
Efalizumab	Aseptic meningitis	Probable

DISCUSSION

Spontaneous ADR reporting is the core data-generating system of international pharmacovigilance, and relies on healthcare professionals (or consumers in some places) to identify and report any suspected ADR to their national pharmacovigilance centre or the drug manufacturer. Spontaneous ADR reports are almost always submitted voluntarily. One of the major weaknesses of this system is under-reporting, as this varies greatly between countries

and there is also a difference in reporting minor and serious ADRs.

For hospital pharmacists, reporting of suspected ADR is not only a responsibility, but a professional obligation [10], and even a duty according to Spanish legislation [11]; it is also an opportunity for improving patient safety. The active pharmacovigilance programme described here provides hospital pharmacists with the opportunity to be part of a multidisciplinary team, share their knowledge in ADR recognition, evaluation and reporting, and to make healthcare professionals aware of the importance of pharmacovigilance. This experience has also led the hospital pharmacy team to provide possible pharmacotherapeutic alternatives.

Pharmacists at Hospital Juan Ramón Jiménez were most concerned about the importance of ADR under-reporting, and it was therefore decided to consider pharmacovigilance as the duty of the hospital pharmacy department. An active pharmacovigilance system was developed and established to increase identification and reporting of ADRs. The significant increase in the reporting rate is undoubtedly a successful outcome. The ICD-9 E codes were found to be the most efficient tool for identifying potential ADRs; these codes are direct registers of potential ADRs based on hospital discharge reports. Other Spanish hospital pharmacists confirmed that the ICD-9 E codes are undoubtedly the main tool for ADR identification [11,12].

Obvious limitations commonly seen in a retrospective study are: difficulty in interviewing patients, lack of important information for evaluating the event and non-uniformity of some diagnosis codification. Prospective tools, such as alerting diagnosis or alerting drugs, allow clinical pharmacists to interview patients and identify data which are not included in clinical histories, but are necessary for evaluating ADRs.

The use of dexchlorpheniramine as an alerting drug is especially useful because it often leads to an ADR among all the other drugs in the formulary, and thus should be monitored first. The injectable form is used mainly for the treatment of anaphylactic reactions, angioedema, urticaria and other dermatological ADRs, and it is easy to monitor because only a few patients are treated with dexchlorpheniramine. Other alerting drugs, such as IV corticosteroids, could also be monitored but with lower effectiveness.

Recently, an informatics tool was introduced to identify all the diagnoses on hospital admission and soon realised that it had increased the number of ADRs identified by the alerting diagnosis method. One Spanish hospital found that ADRs were the cause of 2.5% of hospital admissions.

However, the percentage of patients identified depends on the alerting diagnosis that each hospital decides to consider. The more effective alerting diagnoses are for gastro-intestinal haemorrhage, hydro-electrolytic disorders and brain or heart attack [13,14].

Spontaneous ADR reporting increased three times from the baseline in this hospital. The dissemination of an active pharmacovigilance programme among nurses, medical staff and pharmacist teams has encouraged them to report any suspected ADR to the hospital pharmacy.

A significant number of ADRs are identified in this hospital now. Additionally, in the future, pharmacists also want to prevent ADRs. May et al. [15] used an educational programme in a quasi-experimental study and found a 70% decrease in the incidence of upper gastro-intestinal haemorrhage caused by non-steroidal anti-inflammatory

drugs. Educational programmes, rational use of drugs and promotion of the patients' follow-up with inclusion criteria could be good tools for preventing ADRs in any hospital.

Unfortunately, there is no report from other hospital pharmacy departments giving data about an active pharmacovigilance programme. This suggests low activity on active pharmacovigilance in most hospitals.

This methodology is commonly used in most European hospitals, because of the establishment of a dispensing software system, and the informatics databases of hospital discharge reports.

CONCLUSION

The active pharmacovigilance system increased reporting of ADRs, which were mostly identified from a review of the patients' clinical history in accordance with ICD-9 E codes.

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