

# Adverse Drug reactions - the Singapore Experience

**M**s Chan Cheng Leng heads the Pharmacovigilance Unit (PV) as well as the Information & Research Unit at the Health Sciences Authority. As the head of the PV Unit, she is responsible for monitoring the safety of marketed drugs and related health products in Singapore. Ms Chan spearheads efforts to improve the national level of adverse drug reaction reporting.



## **1. What is pharmacovigilance and what does the pharmacovigilance unit of the HSA do?**

Pharmacovigilance was a term coined in France in 1972 to describe a national system for maintenance of vigilance over toxic and unwanted effects of pharmaceuticals. Since then, Pharmacovigilance has evolved to encompass the postmarketing surveillance activities related to the detection, assessment, understanding and prevention of adverse drug reactions.

The Pharmacovigilance (PV) Unit at HSA is responsible for monitoring the safety of marketed drugs and related health products in Singapore and ensuring that appropriate regulatory action is taken to enhance the safer use of these products based on the signals that it obtains. It does this by conducting the following activities:

- Reviewing Adverse Drug Reactions (ADRs) reports submitted by local healthcare professionals, pharmaceutical companies, from the scientific literature and from information shared among its regulatory counterparts
- Assessing the risks & benefits of a drug and instituting appropriate regulatory action to enhance the safer use of these products
- Providing relevant safety information to advise and inform the clinical community and the public at large to ensure safer and more effective use of these products

## **2. How serious is the problem of adverse drug reactions in Singapore?**

The magnitude of adverse drug reactions in Singapore is uncertain, because of the limited incidence data. Nonetheless from the reports and signals that we receive from our healthcare professionals, it is definite that ADRs has a direct impact on patient's morbidity and mortality.

The US Institute of Medicine reported in January 2000 that about 44,000 to 98,000 deaths occur annually from medical errors. Of this total, an estimated 7,000 deaths occur due to ADRs.

The Pharmacovigilance Unit has been receiving an increasing number of ADR reports from our healthcare professionals over the last 6 years. There has been a 5-fold increase in the reports since 1997. The proportion of serious ADR reports has also increased from 4% in 1997 to 22% in 2002. However, this does not necessarily indicate an increasing number of serious ADRs experienced by our population per se but signifies the increase in participation of our healthcare professionals in reporting ADRs to us and the improved quality of reporting.

## **3. Why should doctors report adverse drug reactions?**

All drugs have the potential to cause adverse effects. The US General Accounting Office reported that in about 50% of drugs that are approved by the US FDA, the serious ADRs manifest only after the product is marketed and used

extensively in a large number of patients with the majority of them occurring within the first 3 years of marketing of a drug.

In addition, traditional and herbal medicines are gaining in popularity. They pose different toxicological problems, e.g. drug-herb interactions, and the potential for adulteration with western medicines for commercial reasons.

Reporting of spontaneous adverse drug reactions by healthcare professionals is recognized as one of the most powerful and cost effective tools for detecting serious adverse drug reactions associated with a product throughout its marketed life. Doctors are critical to this process, especially those who are working directly with patients as the first hint of a potential safety problem originates with the perceptive physician who then reports the case to the regulatory authority.

Your reports will allow us to detect serious ADRs or an increase in the trend of serious ADRs and enable us to take relevant regulatory action to protect public health and safety. These actions include updating the prescribing information of a product to reflect the new risks, re-evaluation of the earlier regulatory approval decision, suspension of particular batches of a product, and in rare cases, complete withdrawal of the product from the market, if the health risk is assessed to be too great.

## **4. What is the role of the family physician in monitoring adverse drug reactions?**

Adverse Drug Reactions represent a significant public health problem. Although we do not have the incidence data for our population, the overseas data suggests that ADRs account for 2-6% of all hospital admissions. Our family physicians being the first line of care for our patients would thus be in an ideal situation to be among the 1st to be alerted to a potential drug safety problem.

The Slim 10 incident was an exemplary case of the value of ADR reporting by our doctors. Slim 10 was approved for

marketing as a Chinese Proprietary Medicine in November 2001 and was tested free of adulterants at the time of marketing approval. The product was already sold freely in China before its introduction into Singapore.

Three months after its launch in the local market, a family physician was among the first to report to us of hyperthyroidism in her patients who were taking Slim 10 for weight loss. In addition, she was able to furnish us with relevant clinical laboratory results to support her suspicions of possible adulteration of Slim 10 with an exogenous source of thyroxine. In this instance, the high quality of our doctors' reports were powerful signals of a potential safety problem with Slim 10 and provided HSA with the stimulus to mandate a withdrawal of a harmful product.

Slim 10 was subsequently found to be adulterated with thyroid gland material, nitrosfenfluramine and fenfluramine. You can imagine the epidemiological disaster that could have followed if our doctors did not alert HSA to the ADRs.

#### **5. What should a doctor do when he sees a case of adverse drug reaction?**

I appreciate that the recognition of an ADR is quite subjective and imprecise. However, causality is NOT a pre-requisite for ADR reporting; suspicion that a health product may be related to a serious adverse event is sufficient reason for a doctor to lodge an ADR report to us.

In order to facilitate the reporting process, we have opened several channels for reporting. These include the following:

- Mail/Fax the yellow ADR reporting form (please contact PV Unit if you do not have access to this form).
- Call PV Unit (Tel no: 63252432/63255498)
- Email to [hsa\\_drugsafty@hsa.gov.sg](mailto:hsa_drugsafty@hsa.gov.sg)
- Online reporting at [http://www.hsa.gov.sg/ADR\\_Online](http://www.hsa.gov.sg/ADR_Online)

#### **6. Does reporting of adverse drug reactions really make a difference?**

Yes, most definitely! Local ADR reporting

allows us to develop our own signals which may or may not be the same as the other countries. We all are aware that most of the clinical trials are conducted in the American, European and Japanese patients with very little Asian exposure; active reporting of ADR allows us to detect adverse events unique to our population eg whether they be due to genetic differences, smaller body build of our patients and life-style differences eg concomitant use of complementary medicine.

Your reports will enable us to take the appropriate regulatory action to protect public health.

#### **7. How does Singapore compare to other countries in pharmacovigilance and what would be the ideal situation that we should all work towards?**

I think generally on the whole, we have come a long way since the unit was first established in 1993. We are slowly but surely building a brand name for ourselves as being efficient and responsive to the needs of our healthcare professionals in the area of pharmacovigilance.

There are of course, various areas in which we can improve, eg to leverage on IT such as electronic medication records for signal detection and communication and working more closely with GP groups and the national clusters to develop sentinel centres for ADR detection.

The ideal situation would be that when our doctors are confronted with what looks like an ADR matter at hand, their first instinct would be to alert the Pharmacovigilance Unit of their suspicions, whether it be to western or complementary medicine.

Ideally, the regulators and the healthcare professionals should work more closely together in order to bring about more quality signals and also the learned and professionals inputs from our healthcare professionals will refine our regulatory decisions.

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