Iranian J Publ Health, Vol. 38, Suppl. 1, 2009, pp.162-165
A supplementary Issue on:
Iran's Achievements in Health, Three Decades after the Islamic Revolution

Ten Years Pharmacovigilance Activities in Iran

*G Shalviri[1], M Valadkhani [2], *R Dinarvand [2,3]*

[1] *Iranian ADR Monitoring Centre, Food and Drug Deputy Ministry, Ministry of Health and Medical Educations, Tehran, Iran*
[2] *Food and Drug Deputy Ministry, Ministry of Health and Medical Educations, Tehran, Iran*
[3] *Faculty of Pharmacy, Tehran University of Medical Sciences, Iran*

Abstract
The Adverse Drug Reaction Monitoring Center (ADRMC) in Iran started its activities as a full member of WHO International Drug Monitoring Program in 1998. The Center has followed pharmacovigilance activities in the country with the main goal of increasing drug safety and preventing drug-related morbidity and mortality. To achieve its main goals, ADRMC has developed and implemented spontaneous ADR reporting system by health care professionals. In this article we have tried to elaborate on the achievement of the ADRMC in Iran. A total number of 17967 adverse drug events has been collected and evaluated by the Center. Evaluation of registered reports has led to 86 drug safety alerts to health care professionals, recall of 23 pharmaceutical products and labeling changes of 30 others, suspension on distribution for 8 medicines and withdrawal from national drug list of 4 different products.

Introduction
The Adverse Drug Reaction Monitoring Center (ADRMC) in Iran started its activities as a full member of WHO International Drug Monitoring Program in 1998. The WHO program was developed in 1967, following thalidomide disaster in early 60s, in order to coordinate implementing individual national Adverse Drug Reaction (ADR) centers in member countries. These national centers are responsible for gathering data on adverse drug events occurred in the country through yellow cards designed for reporting ADRs by health care professionals. Today, more than 80 countries are involved in this program as full or associate members.

Studies show that up to 40% patients in the community experience at least one ADR (1). The percentage of hospital admissions due to drug related events in some countries is at least 10% (2, 3). In the UK, Non Steroidal Anti-Inflammatory Drugs use alone accounts for 65,000 emergency admissions, 12,000 ulcer bleeding episodes and 2,000 deaths per year (4). A published report by Lazarou et al in 1998 showed that adverse drug reactions are the 4th to 6th largest cause of mortality in the USA (5). It was also estimated that annual death of drug related problem was more than annual death of breast cancer, AIDS and highway accidents in the United States(6). A report on July 2006 revealed that medication errors injure 1.5 million people a year in the USA (7). It has been reported that drug related morbidity and mortality expenses exceeded US$ 177.4 billion in the USA in 2000, exceeding the cost of the medications themselves (8). During 1960-1999 there were 121 safety related withdrawals worldwide in which market life was less than 2 yr for 31% and less than 5 yr for 50% of known 87 ones (9).

Results and Discussion
To ensure that drugs in the market are safe, several activities have been followed by ADRMC in Iran. These activities can be categorized into two different levels, pre and post marketing of drugs:

Pre-marketing Review of drugs

Safety of medicinal products applied to be included in the national list, are reviewed by the ADRMC. The center reviews published data in national and international ADR databases on safety of products, and gives the result of its assessment besides comparing safety of alternative products to the drug regulatory office.

***Corresponding author:** Fax: +98 21 66959055, E-mail:dinarvand@tums.ac.ir

Post-marketing vigilance of ADRs

In order to receive most data on drug related problems in the country, it is necessary to have regulation for reporting adverse drug events and to educate people on reporting them, besides facilitating means for submitting reports. Also it is highly important to improve methods for identifying, analyzing and responding to emerging safety issues and communicating those results to health care professionals and patients. The following procedures have been conducted to achieve these objectives:

a. Implementing Spontaneous Reporting System in Iran
b. Training over 30000 health care professionals through Drug Safety workshops
c. Developing easy methods for reporting
d. Issuing guideline for reporting ADRs and medication errors
e. Intensive hospital monitoring
f. Issuing guideline for reporting safety issues by manufacturers
g. Improving Medication Error reporting and developing preventive programs
h. Communication to heath care professionals
i. Improving data analysis by applying signal detection methods to our database

A total number of 17967 reports of adverse drug events have been registered in our database in which 1094 reports are categorized as medication errors. The increasing trend of registered ADEs is shown in Fig. 1. Ceftriaxon and tramadol are the most frequent medicines reported as suspected drugs. Top ten medicinal products suspected to induce registered ADEs are listed in Table 1.

These reports are resulted in a wide variety of decisions and/or actions made by ADRMC and/or drug regulatory authority, some of them are listed below:

1. Issuing Alert letters

Whenever received information by IADRMC show that there are possibility of preventing adverse events, the points are submitted through alert letters. Eighty six different alert letters are issued by the center which has a beneficial role in improving drug safety knowledge.

2. Safety labeling change

Some data available through collected yellow cards and/or international information on drug safety indicate that there is a need to change the labeling of the product. In such cases ADRMC ask to change the labeling of the medicinal product so that new safety information can be obtained. There are 30 safety labeling change for different medicinal products based on ADRMC assessments.

3. Limitation on drug use

In case of injection form of diclofenac sodium, piroxicam and tramadol, there were serious and unusual adverse events reported to the center so that drug regulatory authority decided to limit distribution and administration of these products for hospital use only.

4. Recall of the product

There are several items that the quantity and/or quality of reported ADEs indicated that the product should be recalled from the market. These recalls are sometimes limited to some special batches of the final product; however it can be involved all batches available in the market. Also based on severity and level of importance of received data, it could be an emergency recall. For example one of the recent nationwide safety recalls is related to hydrocortisone phosphate due to much more frequency and severity of allergic reactions induced by this product compared to the literature and other forms available. 23 products have been recalled due to safety reasons recognized by ADRMC.

5. Drug distribution suspension

Some of the reported ADEs to the center led to suspension on drug distribution until the assessment of the problem were completed. As an example, the distribution of Bupivacaine was suspended following received data on sever reactions by intrathecal injection of the non-appropriate product for this route of administration. Eight products have been

suspended for distribution due to safety reasons recognized by ADRMC.

6. ***Drug withdrawal***

Four products terfenadin, phenylpropanolamin, iron dextran and cisapride suspension-have) beenwithdrawn from the market and removed from national drug list because of safety reasons, including terfenadin, phenylpropanolamin, iron dextran and cisapride suspension.

Table 1: Top ten medicinal products responsible for reported ADEs to ADRMC

Name of Drug	No. of ADEs
Ceftriaxone	755
Tramadol	617
Streptokinase	576
Co-trimoxazole	475
Diclofenac	419
Vancomycin	381
Penicillin	330
Cefazolin	300
Ciprofloxacin	251
Hydrocortisone	246

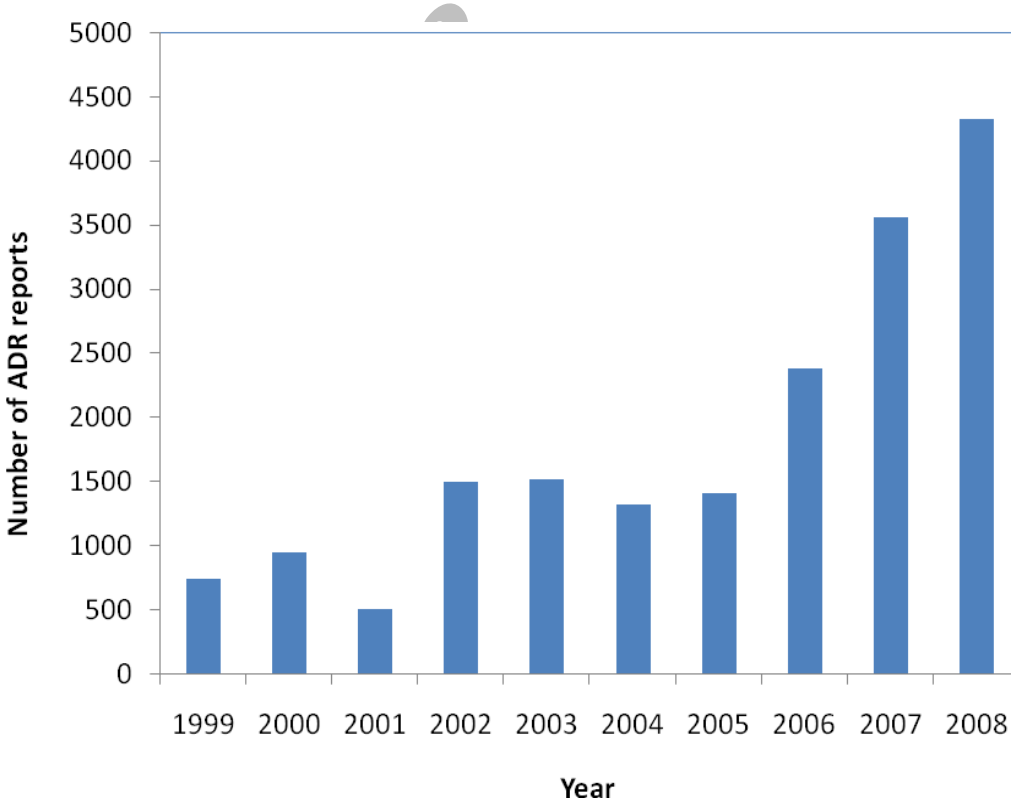

Fig. 1: The ADE reports registered by ADRMC, Food and Drug Dept, Ministry of Health and Medical Education, Islamic Republic of Iran in 1999-2008 period

Conclusion

In conclusion, pharmacovigilance is a new but very important activity developed in Iran with a high impact on reducing drug related morbidity and mortality. Therefore it is very important that all people involved in health system network, ranging from regulatory decision makers to health care professionals in the field support the activities of ADRMC in Iran.

References

1.Martyrs C (1979). Adverse reactions to drugs in general practice. *BMJ*, 2: 1194-97.

2.Imbs JL, Pouyanne P, Haramburu F, Welsch M, Decker N, Blayac JP, et al. (1999). Iatrogénie médicamenteuse: estimation de sa prévalence dans les hôpitaux publics français. *Therapie,* 54:21–7.

3.Bhalla N, Duggan C, Dhillon S (2003). The incidence and nature of drug-related admissions to hospital. *Pharmaceutical Journal*, 270 (7246): 583-86.

4.Blower AL, Brooks A, Fenn GC, Hill A, Pearce MY, Morant S, Bardhan KD (1997). Emergency admissions for upper gastrointestinal disease and their relation to NSAID use. *Aliment Pharmacol Ther*, 11: 283-91.

5.Lazarou J, Pomeranz BH, Corey PN (1998). Incidence of Adverse Drug Reactions in Hospitalized Patients. *JAMA*, 279: 1200-205.

6.Kohn LT, Corrigan JM, Donaldson MS (2000). To err is human: building a safer health system. 1st ed. National Academy Press. Washington, D.C.

7.Cohen MR (2007). Preventing medication errors: The Institute of Medicine report. *AJHP*, 64(14) Supplement 9:S1-S2.

8.Ernst FR, Grizzle AJ (2001). Drug-related morbidity and mortality: updating the cost-of-illness model. *J Am Pharm Assoc*, 41(2): 192-9.

9.Fung M, Thornton A, Mybeck K, Wu J, Hornbuckle K, Muniz E (2001). Evaluation of the characteristics of safety withdrawal of prescription drugs from worldwide pharmaceutical markets-1960 to 1999. *Drug Information Journal*, 35: 293-317.