BUILDING A STRUCTURED MONITORING AND EVALUATING SYSTEM OF POSTMARKETING DRUG USE IN SHANGHAI

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ABSTRACT

In order to understand a drug's full profile in the post-marketing environment, information is needed regarding utilization patterns, beneficial effects, ADRs and economic value. China, the most populated country in the world, has the largest number of people who are taking medications. To begin to appreciate the impact of these medications, a multifunctional evaluation and surveillance system was developed, the Shanghai Drug Monitoring and Evaluative System (SDMES). Set up by the Shanghai Center for Adverse Drug Reaction Monitoring in 2001, the SDMES contains three databases: a population health data base of middle aged and elderly persons; hospital patient medical records; and a spontaneous ADR reporting database. Each person has a unique identification and Medicare number, which permits record-linkage within and between these three databases. After more than three years in development, the population health database has comprehensive data for more than 320,000 residents. The hospital database has two years of inpatient medical records from five major hospitals, and will be increasing to 10 hospitals in 2007. The spontaneous reporting ADR database has collected 20,205 cases since 2001 from approximately 295 sources, including hospitals, pharmaceutical companies, drug wholesalers and pharmacies. The SDMES has the potential to become an important national and international pharmacoepidemiology resource for drug evaluation.

Key Words: *Post-marketing, record linkage, Shanghai*

Limitations of pre-marketing drug studies can result in a failure to predict adverse clinical effects in the post-marketing environment. It is a problem known for decades and still persists today, from the thalidomide experience to the more recent problems with cyclooxygenase-2 Inhibitors.[1,2,3]

As well, some drugs, like clopidogrel, may have a changing risk to benefit ratio depending up the type of patient population receiving the drug in the post-marketing environment.[4] Spontaneous adverse drug reaction (ADR) reporting systems are a first line in post-marketing surveillance; however, they are limited to generating signals and many of the reported events are of uncertain validity and relevance.[5] These signals can lead to formal epidemiological evaluation but typically the focus of the analyses tends to be limited to issues of drug safety.

To fully understand a drug's entire post-marketing profile, data analyses regarding utilization patterns, benefits, ADRs and economics are required. Many countries have developed large

databases or systems in primary healthcare and use them for post-marketing drug evaluation and surveillance.[6,7,8] The evaluation and surveillance of post-marketed drugs may be difficult as linkages can be problematic due to the uniqueness of the healthcare systems they were designed to serve. China, the most populated country in the world, also has the largest population of people who are taking medications. Since 2001, the State Food and Drug Administration (SFDA) has promoted a spontaneous adverse drug reporting system and the number of ADR cases reported annually increased to over 170,000 in 2005.

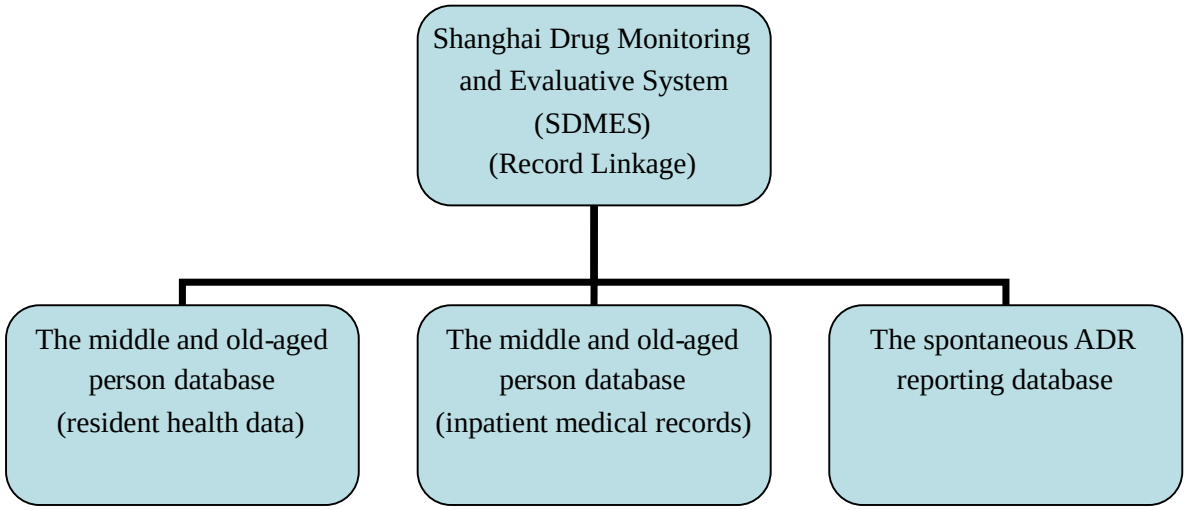
Evaluating signals generated from the ADR reporting system was difficult in the absence of a large healthcare database suitable for conducting epidemiological studies. To resolve this problem, a multifunctional evaluation and surveillance system was developed in Shanghai, the largest city in China, with a concentrated population of over 17,000,000 people. The Shanghai Drug Monitoring and Evaluative System (SDMES) were set up by the Shanghai Center for Adverse Drug Reaction Monitoring and has been in operation since 2001. The aim of the SDMES is broader than ADR evaluation; and includes structured monitoring and comprehensive evaluation of post-marketed drugs.

Three databases contribute data to the SDMES:

1. A population health survey database of middle-aged and elderly persons,
2. a hospital medical records database, and
3. the spontaneous ADR reporting database (Figure 1).

Each person has a unique identification or Medicare number, which permits record-linkages within and between databases. Analyses can address issues of utilization, clinical benefit, ADRs and health economics. The Shanghai Food and Drug Administration (SHFDA) and the Shanghai Municipal Science and Technology Commission (program number: 04dz19218) support this program. The following is a description of the features and potential benefits of this program.

FIG. 1 The three databases of the Shanghai Drug Monitoring and Evaluative System (SDMES) can be linked by a common patient ID or Medicare number, which can facilitate long-term tracking of patients.



Shanghai Drug Monitoring and Evaluative System (SDMES) Databases

The population health survey database of middle-aged and elderly persons was set up in 2002. Participants were women older than 45 years of age and men older than 50 years of age (i.e., ages that are older than the earliest permitted retirement age in Shanghai). This age group was felt to be at significant risk for chronic disease. This study identifies persons within each of the 19 districts of Shanghai. A trained investigator goes to the participant's home to determine eligibility. Eligible persons are then asked to complete a questionnaire. Data collected includes: demographic data, health care service use, quality of life, health status and current medications. There are now data for more than 320,000 residents that are included in the database.

The second database includes hospital inpatient medical records. Hospitals using different Hospital Information Systems (HIS) presented a problem for integration to the SDMES. A program was designed to automatically collect data from the different hospitals and merge it into a common database, which can provide access to long-term medical records for post-marketing drug evaluation and surveillance.

To create a common database, all the variables that were intended to be retrieved from the individual HIS were identified. Variables include demographic data, clinical and diagnostic information (including laboratory values) and drug information. Then, database and software program were designed to automatically retrieve and house HIS computer files, which contain the desired variables. On an ongoing basis, files are sent to the main computer server through the Internet, e-mail or by disk. These files are automatically entered into the patient specific medical record in the main computer server. The inpatient medical records database would generally represent the more severe illnesses. The database has been accumulating records for two years and currently contains the inpatient medical records from five hospitals. The database continues to develop and by the end of 2007 will contain records from ten hospitals.

The third database is the spontaneous adverse drug reaction reporting database. This database collects ADR cases identified by the traditional spontaneous ADR reporting system. Reports come from 295 units, including hospitals (almost 95% of reports), pharmaceutical companies, drug wholesalers and drug stores. From 2001 to April 30 2006, the database has collected more than 20,000 ADR reports (potential signals). There have been 669 severe ADR reports, 417 new ADR reports and 53 reports that represent both new and severe events.

DISCUSSION

Due to the limitations of data obtained from pre-marketing studies for predicting the consequences of drug use after regulatory approval, post-marketing drug evaluation and surveillance studies are required.[9] According to the World Health Organization (WHO), most countries have set up spontaneous ADR reporting systems[10] and many perform important actions in drug safety, including the USA[11], Australia[12], the UK[13] and Canada.[14]

But, spontaneous ADR reporting systems represent only a fraction of the actual adverse drug-related events[15] and therefore, cannot provide an accurate estimate of the true ADR rates.[16] In view of the shortcomings of the voluntary spontaneous adverse drug reaction (ADR) reporting, other approaches are needed for the evaluation of drugs[7], including Prescription-Event Monitoring[17], the UK General Practice Research Database and The Tayside Medicines Monitoring Unit (MEMO) in UK[18]; Group Health Cooperative[19], Kaiser Permanente Medical Care Program[20], The HMO Research Network[21], United Health Group[22], Medicaid Databases[23] in USA, Health Services Databases in Saskatchewan, Canada[24] and Automated Pharmacy Record Linkage in The Netherlands.[25] Many of these post-marketing drug surveillance systems have been designed to adapt to the particular type of healthcare systems in which

they operate. In China, there are a variety healthcare delivery systems, including traditional Chinese medicine (Chinese herbs). China requires a post-marketing drug evaluation and surveillance system to systematically collect data of the medicines being used, including Chinese traditional medicines. To this end the Shanghai Drug Monitoring and Evaluative System (SDMES) has been designed to meet the needs of the Chinese population, but it may also have value to other populations.

The inclusion of three different databases in the SDMES allows for the evaluation of post-marketing drug effects from three perspectives, a natural residential population, a hospital inpatient population, and ADR reporting. Further, the system can longitudinally track a patient by record linkage using patient identification cards or Medicare numbers. But there are limitations with these data.

The community-based survey database is not dynamic and is not automatically updated. The data for each individual are collected only once. As a result, studies that only use data from the residential data base are cross sectional in design.[6] Further, the population for which the data has been collected thus far is limited to middle and old-aged persons, although the hope would be to eventually develop a complete residential database.

The inpatient medical records database is dynamic and automatically updated. All hospitals in Shanghai use the ICD10 coding system for diagnosis. With unique patient identification numbers the data are linkable to other databases allowing either cross-sectional or longitudinal outcome studies to be conducted. In addition, inpatients are more likely to be using medications and more ADR reporting takes place.[27] Limitations of this database are that it only represents the ill (hospitalized) patient population and that it contains inpatient but not outpatient data.

The SDMES Spontaneous Adverse Drug Reaction Reporting Database is similar to other traditional spontaneous ADR reporting systems. Like many other systems, adverse drug event reporting from hospitals is good, but more will need to be done to increase reports from the health care practitioners in the community. The additional ability to link these reports with the hospital data in the SDMES is an important feature of this system.

In summary, the Shanghai Drug Monitoring and Evaluative System (SDMES) consist of three different databases, which have record linkage capability. Initially designed for conducting post-marketing drug evaluation and surveillance in Shanghai, it is an important development for China as a whole. The system may also be of particular interest to pharmacoepidemiologists in other countries because of the potential to investigate a whole drug profile (including safety, therapeutic benefit and economic consequences) in the post-marketing environment.

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