MIHARI Project Year 5

Medical Information for Risk Assessment Initiative

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Abstract

- Background: PMDA, the Japanese regulatory agency, is being in a process of reinforcing and enhancing its post-marketing safety measures as stated in its second mid-term (FY 2009-2013) plan. MIHARI project has started in PMDA since FY 2009 to develop a new safety assessment system for post-marketing drugs using Japanese medical databases and the update of MIHARI in the last year of the second mid-term is reported.
- Objectives: To develop a new safety assessment system for post-marketing drugs using Japanese medical databases.
- Methods: The following 5 steps were applied to multiple Japanese medical databases. 1) Establishment of accessibility to multiple databases. 2) Evaluation of each database by characterization studies, validation studies, and other pilot studies. 3) Development of skills to select appropriate study designs and statistical analysis for each characterized database. 4) Practice about real drug safety issues using the developed safety assessment system. 5) Implementation of this system.
- Results: In the fifth year, MIHARI was at the fourth and the fifth steps described in the methods. Some pilot studies about risk assessment and drug utilization using claims data were performed in this year. Based on the accumulated findings, knowledge, and experiences from the previous pilot studies in the last 5 years, we summarized features of each database available in Japan in order to make efficient use of those databases for the purpose of drug safety assessment. We have started using these databases as invaluable sources of information for pharmacovigilance.
- Conclusion: We established the framework to commence operations of the novel safety assessment system for post-marketing drugs using Japanese medical databases. We have achieved the goal of MIHARI project successfully over this 5 years, and consequently we will apply this framework to risk management of drug safety in PMDA and make the system more advanced in the next mid-term (FY 2014-2018).

Conflict of Interest: All PMDA members involved in MIHARI project have no dealings or transaction with any vendor, pharmaceutical companies or any other party which could result in benefit to us.

Background

- PMDA started reinforcing and enhancing its post-marketing safety measures as stated in the second mid-term (FY 2009-2013) plan. In addition to existing spontaneous adverse drug reaction report data, other data sources are required to collect more information for drug safety assessment.
- Recently, electronic medical record (EMR) system has been widely implemented in hospitals and clinics in Japan, which enables us to use medical information as database. Ministry of Health, Labour and Welfare (MHLW) is developing a national claims database called NDB. In addition, PMDA is developing a standardized EMR network collaborating with MHLW and hospitals, which is called MID-NET. And also there are several commercial databases.
- Pharmacoepidemiologic studies are expected to be performed if these medical information data are available, and such studies would help PMDA promote science-based drug safety assessments.
- In order to utilize these data, MIHARI project started at PMDA in FY 2009. MIHARI has already achieved to secure access to claims databases and EMR databases, and been developing methodologies for pharmacoepidemiologic studies using medical information data. The update from MIHARI in the fifth year – FY 2013 is reported.

Objective

To develop a new safety assessment framework for post-marketing drugs using medical information databases in Japan.

Methods

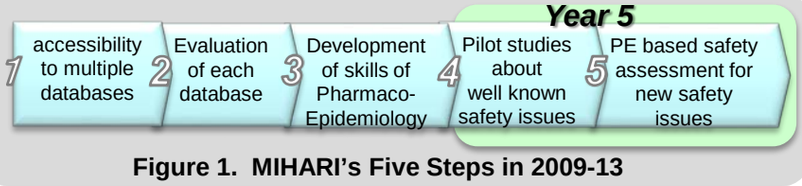

Figure 1. MIHARI's Five Steps in 2009-13

In the fifth year, MIHARI was at the fourth and the fifth steps. We conducted the followings:

- ☐ Some pilot studies using a new design or a new data sources
- ☐ Summary of characteristics of databases and pharmacoepidemiologic methodologies used in MIHARI project
- ☐ Practice in real drug safety issues and publish of the PMDA guideline for pharmacoepidemiologic study using electronic medical database in Japan.

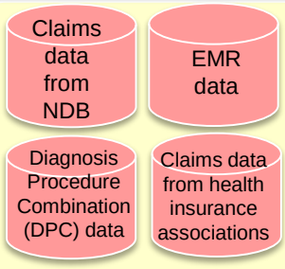

Figure 2. Data sources used in MIHARI in 2009-13

NDB: National claim database
EMR: electronic medical record

Results

Pilot studies: We conducted more than 40 pilot studies in the past 5 years. In fifth year, we conducted the following pilot studies:

1. The assessment of the risk of acute asthmatic attacks associated with non-steroidal anti-inflammatory drugs using claims data from health insurance associations with the SCCS design. *Some results from the study are shown in the poster presentation (poster no. 526).*
2. Drug Use Study about Heparin or Amiodaron using DPC data. *Some results from the study are shown in the poster presentation (poster no. 240).*

Table 1. Summery of characteristics of databases used in MIHARI Project

Data sources	Patients	Pros	Cons
Claims data from health insurance associations	2005-2012 190M patients Inpatients & out patients	✓ All patients in the medical claim information are includes unless the patient changes the health insurance association. ✓ Long-term follow-up is possible	✓ Elderly people are not included. ✓ Only medial information covered by health insurance ✓ Unable to link to the EMR data ✓ Luck of date information (only year & month information) before April 2012
Diagnosis Procedure Combination (DPC) data	2011-2012 128 hospitals Inpatients only	✓ Rich information about patient background (including BMI, smoker, etc)	✓ Frequent change of table format (uneasy to combine several years data) ✓ Only inpatient data covered by DPC system ✓ Luck of data from other hospitals ✓ Unable to follow up for long time ✓ Unable to link to the EMR data
Electronic Medical Record (EMR) data	2007-2011 6 hospitals Inpatients & out patients	✓ Include detailed medical information (ex. lab test data) ✓ Include insurance uncovered data ✓ Able to be used for validation study	✓ Small population ✓ Some contents need data cleaning ✓ Luck of data from other hospitals

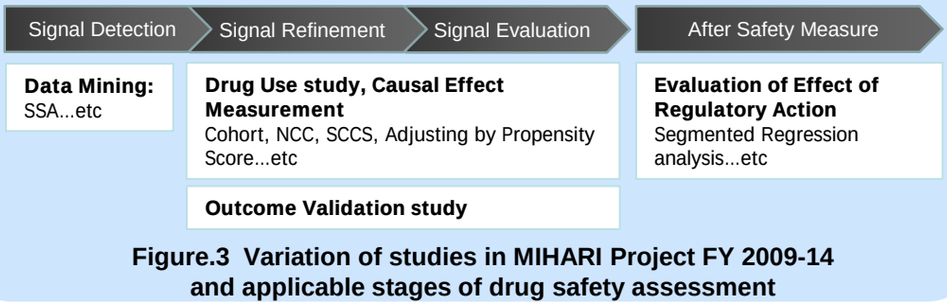

Figure.3 Variation of studies in MIHARI Project FY 2009-14 and applicable stages of drug safety assessment

Acknowledgement: We appreciate the cooperation of the hospital staff in this study. We also appreciate useful suggestions from all members in PMDA Experts Committee on Use of Electronic Medical Information for Drug Safety.

Conclusions

MIHARI Project has established the new safety assessment framework in PMDA. We believe that accumulated findings, knowledge, and experiences form the last 5 years contribute to decision making for drug safety issues. MIHARI Project will be continued for further improvement of safety assessment for drugs using medical information databases in Japan.