Chapter V

Discussions and conclusions

This chapter included discussions, conclusions, policy recommendations, limitations, and further studies. Twelve issues were discussed including unique data recording, proxy variables for data coverage of key variables in database, appropriate time frame foe data collection, suitable cut point of key variables, data completeness, easy to understand algorithm of DUE by using CAAT, conventional DUE method as a reference standard, effect of date of data recorded and accuracy, different of DUE results in pattern analysis among Atorvastatin and Rosiglitazone, using more specific guidelines more finding irrational use of DUE, excess Atorvastatin expenditure, high rosuvastatin expenditure.

The study concluded that CAAT can be applied for monitoring the use of high cost drugs efficiently. However, assessing acceptability and applicability among health care providers and assessing policy acceptance of the Comptroller's General department are recommended for further studies.

Discussions

5.1 Unique data recording

This study was conducted in four regional hospitals having different data records and database system. Thus, it took more time for data management especially at the beginning, but for hospitals that recorded the data in the same system, the unique database reduced workload in data management. The results of this study consistent with the former study related to data management of Limwatananont & et al confirming the unique data recording is necessary. They reported that in each hospital, there were some differences in data recorded of the frequency of drug use per day with alphabet character or alphanumeric which has difference codes. Data transformation is needed to make the unique data recording of these data ready to analyze. The studies conducted by Graber & et demonstrated that the primary key was needed in data structure because this key variable will be used to link or match other data table and the primary key among each data tables must be unique.

5.2 Proxy variables for data coverage of key variables in database

Some key variables might not be in the records. Proxy variables are needed for more coverage of data. For examples, CHD diseases equivalent can be retrieved form ICD-10 database. However, it has some arguments about incomplete disease recording in database. Drug use related to the interest diseases from dispensing database would be retrieved. Patients who had been using drugs related to diseases of interest were diagnosed as having that diseases. Such as, patients who had history of nitrate drug group use were assumed that they had got angina pectoris which was one of CHD equivalent diseases. According to the CAAT guidelines for Atorvastatin use, these patients were classified in Secondary CHD prevention group which suitable LDL-cholesterol level should be $\leq$ 100 mg/dl.

5.3 Appropriate time frame for data collection

This study collected retrospective data related to the guidelines for 1 year from the date of initiating the use of Atorvastatin and Rosiglitazone. Because there were not unique duration for interest drug dispensed to the patients which vary from 1 month to 6 months. LDL_cholesterol were checked after interest drug use after 3 or 6 months or more than that. Therefore, retrospective data collection for 1 year should be appropriate especially from the beginning of drug use evaluation program. It might not follow the international guidelines recommendation. For example, HbA1C or LDL-cholesterol should be checked after dose titration or using new drugs at 3months. In real practice these activities were done vary from 3 to more than 6 months.

5.4 Suitable cut point of key variables

Cut point of key variables for Atorvastatin use evaluation of this study are revealed not only from the literature but also the experts. This study employed the cut point from CGD guidelines set up by working group for drug use in CSMBS. Cut point only from literature reviews might not be suitable in real practice.

5.5 Data completeness

Data completeness must be highly concerned because it would effect the results in analysis process which could lead to wrong interpretation. Based on this study, repeating data must be checked along with data management. Different codes of

data in the same variable must be transformed to the same character. If not transformed, it might get lost in the data analysis process.

5.6 Easy to understand algorithm of DUE by using CAAT

For the guidelines which is composed of many key variables, the algorithm of DUE could be started with any key variables. However, an algorithm that starts with the appropriate key variable and followed by another suitable key variable in the correct order would make an easy algorithm to understand and to follow with clear directions.

5.7 Conventional DUE method as a reference standard

To validate CAAT guidelines, the Conventional DUR method was used as a reference standard. By checking data retrieved from database against the data collected from patient records it was confirmed by related study of Graber & et al that the accuracy of each replicate extract data for DUE is verified monthly by manually comparing a sample (approximately 40 records) of the prescription data against the original data. However, there were some data which might have not been recorded in the patients record. Computer database will be used as patient records, laboratory data was searched case by case by the staffs. In this study, most of key variables available in patients record were available in CAAT. Some key variables which disappeared in the database were also unavailable in the patients records, such as smoking behavior. In this study, the guidelines used for Conventional DUE were the same as guidelines used for CAAT.

5.8 Effect of date of data recorded and accuracy

Validating CAAT with Conventional DUE of Atorvastatin and Rosuvastatin showed the accuracy of results more than 95%. The other 5% of inaccuracy was mainly effected from the difference of laboratory checked date recorded in the database and in the patient records when comparing set of data from database to the data from patient records. Findings showed that number of patients who had laboratory checked date in the patients records were more than number of patients who had laboratory checked in laboratory database. It is possible that patients really had laboratory checked date as same as laboratory checked date in documented in laboratory

database, but they visited hospital to see doctor on the day after laboratory checked date. Thus, the laboratory result would be recorded in the patient records on the visiting date instead of the real laboratory checked date. Another reason that caused the difference of the laboratory checked date was patients might have been laboratory checked outside the hospital. Thus, laboratory results would be recorded in only patient records. This differences have main effect on the patterns or steps needed before initiating of Atorvastatin and Rosiglitazone use for rational evaluation. Thus, the difference of laboratory checked date had effect not only on the accuracy but also on the sensitivity and specificity of CAAT. However, sensitivity and specificity of CAAT were more than 80% according to rational use of these two drugs evaluation based on pattern analysis.

5.9 Different of DUE results in pattern analysis among Atorvastatin and Rosiglitazone

Using CAAT to evaluate rational Atorvastatin use in four regional hospitals and Rosiglitazone in two hospitals, the results showed 13% (n = 76) Atorvastatin use rational evaluated following SLA pattern (initiating Atorvastatin after Simvastatin used and LDL-check respectively) and 17.2% (n =15) Rosiglitazone use rational evaluated which follow by MHR pattern (initiating Rosiglitazone after Metformin used and HbA1C check respectively). Irrational use of these drugs were high, being more than 80%. However, there were some differences of irrational drug use patterns between two drugs. The majority of irrational use of Atorvastatin (73.8%) were in LA and A patterns which patients had not used Simvastatin before initiating Atorvastatin. Mainly of irrational use of Rosiglitazone (63.2%) were in MR pattern which patients had used Metformin before initiating Rosiglitazone. It might be observed that the use of recommended drug before initiating studied drugs for Rosiglitazone was higher than for Atorvastatin. It might be explained that diabetic drugs have different groups which has different pharmacologic action, and side effects. In this study, Metformin is a biguanide group and Rosiglitazone a thiazolidinedione. Therefore, it could not be substituted. But both Atorvastatin and Simvastatin are Angiotensin converting enzyme inhibitors drugs. The pharmacologic action and side effect are alike. There is little difference in the potency where Atorvastatin is more potent than Simvastatin when using the same dose. Besides, CSMBS patients can reimburse form the government. For these two reasons,

Atorvastatin was prescribed instead of Simvastatin. This results agree with the report of Medical Audit that Atorvastatin was used as a fist line drug in CSMBS outpatients in stead of Simvastatin. Recent study of Munkratok supports this study that Atorvastatin was highly prescribed in CSMBS at the rate of 20.08 per 1000 patients in aging group but only 0.05 per 1000 patients in aging group in Universal Coverage (UC).

5.10 Using more specific guidelines, findings more irrational DUE

Using more specific guidelines to evaluate Atorvastatin and Rosiglitazone use, patients initiating the use of Atorvastatin and Rosiglitazone following SLA and MHR pattern were recruited. Results showed that only 2 patient (0.3%) and 12 patients (13.8%) were rational evaluated Atorvastatin and Rosiglitazone use.respectively. It should be noticed that the rational use of Atorvastatin evaluation based on specific guidelines was less than rational use evaluation based on pattern analysis by 75 cases (12.7%). The rational use of Rosiglitazone evaluated based on specific guidelines was less than rational use evaluated based on pattern analysis by 3 cases (3.4%). It might be effected from the number of criteria use in the guidelines. For Atorvastatin, the specific guidelines add up more criteria before initiating Atorvastatin in SLA group including maximum dose of Simvastatin use, duration of Simvastatin use and required LDL-cholesterol level according to type of CHD risk prevention. But the criteria added up to specific guidelines for Rosiglitazone use evaluation was less than criteria added up to specific guidelines for Atorvastatin use evaluation. It added only duration of Metformin use and HbA1C check. Maximum dose of Metformin and the type of patients were not included. Thus, it might be concluded that less specific criteria led to less irrational drug use.

It was observed that Simvastatin 10-20 mg was commonly used in patients who had used Simvastatin before initiating Atorvastatin. It might be possible that prescribers worry about rhabdomyolysis. However, earlier study reported that Atorvastatin were mainly used in CSMBS who can reimburse all of their expense. Thus, guidelines of the use of Atorvastatin and monitoring were not much concerned.

Using CAAT to evaluate rational use of Rosiglitazone in 2 hospitals, the results showed 17.2% rational evaluated which followed MHR pattern (initiating Rosiglitazone use after Metformin used and HbA1C check respectively). Irrational use of this drug was 82.8% of patients initiating Rosiglitazone evaluated according to using pattern of

its use as a guidelines was high. In contrast to Atorvastatin, the majority of Rosiglitazone irrational evaluated (65..8%) had used Metformin but they did not have HbA1C check before initiating Rosiglitazone.. It might be possible that the prescribers considered Fasting Plasma Glucose instead of HbA1C. When using more specific guidelines to evaluate Atorvastatin use, it was found that only 2 patient (0.3%) was rational evaluated. Irrational evaluation was at 99.7% which is higher than using the pattern of Atorvastatin use as a guidelines. Because the specific guidelines add up more criteria before initiating Atorvastatin in SLA group which include maximum dose of Simvastatin (40mg) use together with duration of Simvastatin use and required LDL-cholesterol level according to type of CHD risk prevention.

5.11 Excess Atorvastatin expenditure

This study assumed irrational use of Atavastatin was based on pattern analysis subsidized by 40 mg of Simvastatin (4generic Simvastatin 10 mg) for 1 tab of irrational Atorvastatin use. The maximum price of generic Simvastatin 10 mg retrieved from 4 hospital was used in the calculation of the expense for Simvastatin use to substitute the use of irrational Atorvastatin expense. Thus, the results of excess Atorvastatin expenditure caused by irrationale use was minimum.

5.12 High Rosuvastatin expenditure

The results showed that new CSMBS outpatients and the expenditure for Rosuvastatin (newer than Atorvastatin) use were higher than Atorvastatin. This effect might come from being more potent in the same dose that Rosuvastatin claimed.

Conclusions

The results of this study showed that CAAT development for high cost drug use evaluation composed of two main parts, CAAT algorithm and data management. Results of the study confirmed that CAAT with sensitivity, specificity, and accuracy ≥ 80% can be used for monitoring HCD use. By using CAAT to evaluate the use of Atorvastatin based on pattern analysis, only 13% were found rational. For Rosiglitazone, only 17.2% were found rational. Base on specific guidelines, rational use of Atorvastatin were only 2.6%. For Rosiglitazone, only 13.8% were reported rational. Considering the evaluation of pharmaceutical spending among anti- lipid drugs, Atorvastatin consumed 39.9%. Rosuvastatin consumed 44.8% of all anti-lipid drug spending. Considering the evaluation of pharmaceutical spending among anti-diabetic drugs, Rosiglitazone consumed 20.4%. Pioglitazone consumed 21.1%. Glagine insulin consumed 20.3% of all anti-diabetic drug spending.

Policy recommendations

Applying CAAT to control HCD use expenditure in many levels will have recommendations as follows;

1. For health care providers, CAAT can be used for HCD use evaluation. The organization should control the use of HCDs. Monitoring the use of Atorvastatin should be done together with Rosuvastatin. The intervention might include implementation clinical practice guidelines, and restriction of prescribing to increase the efficient of drug use evaluation.

At the beginning of DUE program in population, it is recommended that clinical practice guidelines for initiating the use of Atorvastatin and Rosiglitazone should base on pattern analysis to get more participation in real practice.

2. For CGD to monitor the use of HCD for reimbursement reason, CATT should be applied to evaluate the rational use of HCDs of interest by medical or pharmaceutical auditors.

3. For the government, CAAT can be applied to monitor the policy implementation on controlling HCD use.

The national coding system of drugs, laboratory, and patient characteristics should be established.

Limitations

Several limitations were described in the following :

First of all, samples for validating CAAT for Rosiglitazone use evalution were less than the calculated samples (139). First use of Rosiglitazone CSMBS outpatients in the study time were 80 patients. Only 76 patient records were found..

Secondly, the evaluation of Rosiglitazone use could be done in only two hospitals because the other two hospitals did not have this drug in the hospital drug lists.

Thirdly, the present study was concentrated on drug use evaluation using data from the database. Software program implementation for alerting high cost drug use was not included. More knowledge will be needed to create such software programs.

Finally, drug interaction between the other drugs and studied HCDs were not included in the development of CAAT algorithm for rational HCD use evaluation To develop CAAT for other HCDs, drug interaction should be considered.

Further Studies

Further investigation should be conducted including:

1. Assessing acceptability and applicability of health care providers of using CAAT for monitoring HCD use evaluation and assessing policy acceptance of CGD.
2. Development of CAAT for other HCD use evaluation
3. Development of HCD use alert software programs
4. Evaluation of outcome of Statins and Dibetes drug use