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CLINICAL USEFULNESS OF THE DATABASE PREDICTING DRUG-DRUG INTERACTIONS USING METABOLIC INFORMATION OF CYTOCHROME P-450 EVALUATED BY THE DOSAGE AND ADVERSE EVENTS OF THE HMG-COA REDUCTASE INHIBITOR ATORVASTATIN

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In addition to the usual database for detecting drug-drug interactions, we created a new database (the CYP database) to predict drug-drug interactions on the basis of the metabolic information of Cytochrome P-450 (CYP) on the package insert, and then evaluated the clinical effects caused by the concurrent administration of drugs that are not noted as contraindicatedor cautioned combination on the package insert, but are listed as cautioned combination in the CYP database (CYP database cautioned combination), according to the dosage and adverse events of atorvastatin. We investigated the CYP database cautioned combination situation for 10,018 patients who visited during a period of 16 months, and gathered information about the mean dosage and adverse events on the basis of the record for the digital medication history for 142 patients taking atorvastatin. There are 71 hazardous drugs for concurrent use in the CYP database among 647 drugs handled; and of those, the CYP database cautioned combination rate of 29 drugs amounts to 32.8%. The mean administered dosage of atorvastatin is 8.3mg. This value is low compared with 9.2mg, the mean dosage of the group without cautioned combination. When comparing the drugs used with atorvastatin to the CYP database cautioned combination group, the atorvastatin dosage with etizolam and zolpidem were significantly low, 6.6mg and 7.2mg, respectively. The major adverse events experienced by the patients who stopped taking atorvastatin due to these adverse events were feelings of weariness, muscular aches, colored urine and rash, prevalent in this order. Ninety percent of these are characteristic symptoms of myotoxicity. Compared with the rate of 2.7% of the atorvastatin dosage group without cautioned combination, the rate of occurrence of adverse events of atorvastatin among the group taking cautioned combination listed in the package insert, and the CYP database cautioned combination group are 8.3 and 8.5%, respectively, and the relative risks are 3.07 and 3.15 respectively.

Moreover, the rate of adverse events is 22.2%, and relative risk is 8.22, which are high values among the patients who concurrently use both the cautioned combination in the package insert and those in the CYP database. By examining the risk odds ratio of atorvastatin adverse events, both cautioned combinations were independently attributed to an increase in risk. On the basis of the above results, the information about cautioned combination in concurrent administration predicted by the CYP database is as clinically efficient as that using package insert.

Keywords: cytochrome P450, drug-drug interaction, atorvastatin, adverse events, the CYP database