Evaluation of genetic polymorphisms of related enzymes to establish individualized warfarin therapy

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Warfarin is one of the most widely prescribed anticoagulant to prevent and treat thromboembolic disorders in venous, artery, and pulmonary artery. Warfarin has a very narrow therapeutic index—too much leaves a patient at risk for bleeding, too little leaves them at risk for thromboembolic disorders such as heart attack or stroke. In addition, warfarin exhibited large interindividual and interethnic differences in the dose required for its anticoagulation effect. It is challenge to determine quickly adequate dosage for each patient within optimal PT-INR range.

To propose an adequate initial warfarin dosage for each patient, we studied correlation between warfarin sensitivity and genetic polymorphisms in initial warfarin therapy. We developed that a *VKORC1* -1639G>A polymorphism influenced warfarin sensitivity. We suggest that lower warfarin dosage than 5 mg/day may lead stable warfarin therapy more quickly in Japanese patients.

We also study a correlation between warfarin sensitivity and *CYP4F2* polymorphism (a new genetic factor which may influence warfarin sensitivity) in maintenance warfarin dosage. Although there is not significant difference, warfarin maintenance dosage of mutant type patients is 1.3 times higher than that of hetero and wild type patients and warfarin sensitivity (PT-INR / WF dosage) of mutant type patients is 0.8 times lower than that of other patients.

In conclusion, we studied a correlation between warfarin sensitivity and genetic factor in initial and long treatment period. In initial warfarin therapy, Japanese patients should start warfarin dosage lower than 5 mg/day to reach adequate dosage more quickly and to avoid risk for bleeding and thromboembolic disorders. In long treatment period, we revealed that CYP4F2 polymorphism may be newly factor to establish personalized warfarin therapy in addition to genetic polymorphisms of VKORC1 and CYP2C9, body weight, age, serum albumin.