P-55

Risk Factors for Out-of-Range International Normalized Ratio in Paediatric Patients Receiving Warfarin

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Introduction: Warfarin has a narrow therapeutic window; therefore, out-of range international normalized ratio (INR) often occurred in paediatric population. We aim to identify risk factors for out-of-range INR in paediatric patients receiving warfarin.

Methods: Study population was recruited from a database of 823 consecutive INR measurements (24 patients) which were performed for dose optimization of warfarin between 2004 and 2012. INR measurements which were performed <1 week after initiation of warfarin, those from patients who used combined medicines having an interaction with warfarin except aspirin and heparin and those from patients with liver dysfunction were excluded from the study. No patients experienced pharmacogenomics of warfarin. Age, gender, body weight, warfarin dose, Fontan physiology as an indication of anticoagulation and complications during anticoagulation were analysed. INR values were divided into 3 groups; optimal anticoagulation (INR from 1.5 to 3.0), under-anticoagulation (INR <1.5) and over-anticoagulation (INR >3.0).

Results: A total of 576 measurements were selected for additional study. Age, female gender, body weight, warfarin dose, INR values and Fontan physiology were 7 ± 3 years, 77%, 20 ± 8 kg, 1.86 ± 0.04 mg, 1.83 ± 0.54 and 82%, respectively. There were neither thrombotic nor haemorrhagic events during the period. Out-of-range INR was observed in 33% of measurements; under- and over-anticoagulation was observed in 29% and 4%, respectively. The under-anticoagulation group comprised significantly more female patients and those with Fontan physiology compared with the optimal and over-anticoagulation groups (86% vs. 74% vs. 64% and 93% vs. 77% vs. 82%, respectively; both $p <0.003$). In contrast, the over-anticoagulation group showed significantly lower age and lower body weight compared with the optimal and under-anticoagulation groups (5 ± 2 vs. 7 ± 3 vs. 7 ± 3 years and 13 ± 2 vs. 19 ± 8 vs. 20 ± 8 kg, respectively; both $p <0.03$).

Conclusions: Out-of-range INR often occurred in paediatric patients receiving warfarin. Female, Fontan physiology, lower age and lower body weight were the risk factors for out-of-range INR.