Clinical Relevance of Drug Interactions between Valproate and Oral Anticoagulants

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OBJECTIVE: To assess the risk of clinical relevant interactions between the oral anticoagulant phenprocoumon and valproate. BACKGROUND: Even though valproate and phenprocoumon have a clinical history of forty years, there is no evidence for clinically relevant interactions. Phenprocoumon as the most widely used oral anticoagulant in many European countries shares most of its pharmacological properties with warfarin and acenocoumarol, the main difference being a prolonged half-life. DESIGN/METHODS: Two groups of patients were retrospectively identified during a period of 38 following months: group one received valproate in addition to phenprocoumon, whereas in group two phenprocoumon was started in addition to valproate. For group one, means of International Normalized Ratio (INR) values before valproate were calculated and the last INR correlated to the maximum INR after initiation of valproate. For group two, the average maintenance doses of phenprocoumon were compared to those of a standard population. RESULTS: 18 patients received combined treatment with valproate and phenprocoumon. Three patients met exclusion criteria (phenprocoumon was discontinued early or follow-up data was not available), the remaining were divided into group one (11 patients) and group two (four patients). Means of INR in group one before valproate ranged between 1.6 and 3.2 (SD 0.05–1.22). After initiation of valproate INR values rose significantly (mean +102%, p = 0.0005) with maximum values measured within three days in the majority of patients. In group two, the intended INR values were reached with comparably low loading and maintenance doses of phenprocoumon. CONCLUSIONS/RELEVANCE: There is a clinically relevant interaction between valproate and phenprocoumon. Due to comparable pharmacological properties, this is probably true for other oral anticoagulants including warfarin, too. Patients on valproate need low doses of phenprocoumon for active anticoagulation. In patients receiving valproate with preexisting phenprocoumon a potentially hazardous rise of INR has to be observed.

keywords
valproate, phenprocoumon, interaction, INR

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