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Nitroso-urea-cisplatin-based chemotherapy associated with valproate: increase of haematologic toxicity.

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Abstract

BACKGROUND: The incidence of haematologic toxicity of valproate (VPA) ranges from 1% to 32% and consists mainly of asymptomatic, dose-dependent thrombopenia. We describe a potentiation of haematologic side-effects of nitroso-urea (NU) when prescribed in association with VPA.

PATIENTS AND METHODS: We followed a cohort of 70 patients (58 men, 22 women, mean age: 56 years, range 20-75 years). Patients with high-grade gliomas were treated with up-front chemotherapy regimen consisting of fotemustine (d3: 100 mg/m²), cisplatin (d1-3: 33 mg/m²) and etoposide (d1-3: 75 mg/m²) followed by whole brain radiotherapy at progression. Sixty patients required anti-epileptic drugs (AED) for either a single, well-documented epileptic seizure, or immediatly initiated after neurosurgical procedures. AED included VPA (35 of 60), phenobarbital (PB) (17 of 60), carbamazepine (CBZ) (2 of 60) and phenytoin (PHT) (3 of 60). Two patients had both PB and CBZ and one PB and PHT.

RESULTS: Haematologic toxicity (grade 3-4 thrombopenia, neutropenia or both) was observed in 37 of 70 (52.85%) patients. Among them 24 (65%) had VPA. Group C were patients treated with fotemustine alone with or without VPA (23 patients).

CONCLUSION: When prescribed in association with a fotemustine-cisplatin regimen, VPA treatment results in a three-fold higher incidence of reversible thrombopenia, neutropenia or both. Haematologic side-effects decrease after AED modification during the continued chemotherapy. This adverse event should be managed with caution.

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