Haematological toxicity of Valproic acid compared to Levetiracetam in patients with glioblastoma multiforme undergoing concomitant radio-chemotherapy: a retrospective cohort study.


Abstract
Patients with glioblastoma multiforme (GBM) and symptomatic seizures are in need of a sufficient antiepileptic treatment. Haematological toxicity is a limiting side effect of both, first line radio-chemotherapy with temozolomide (TMZ) and co-medication with antiepileptic drugs. Valproic acid (VPA) and levetiracetam (LEV) are considered favourable agents in brain tumor patients with seizures, but are commonly reported to induce haematological side effects on their own. We hypothesized, that antiepileptic treatment with these agents has no increased impact on haematological side effects during radio-chemotherapy in the first line setting. We included 104 patients from two neuro-oncologic centres with GBM and standard radio-chemotherapy in a retrospective cohort study. Patients were divided according to their antiepileptic treatment with either VPA, LEV or without antiepileptic drug therapy (control group). Declines in haemoglobin levels and absolute blood cell counts for neutrophil granulocytes, lymphocytes and thrombocytes were analyzed twice during concomitant and once during adjuvant phase. A comparison between the examined groups was performed, using a linear mixed model. Neutrophil granulocytes, lymphocytes and thrombocytes significantly decreased over time in all three groups (all p < 0.012), but there was no significant difference between the compared groups. A significant decline in haemoglobin was observed in the LEV treated group (p = 0.044), but did not differ between the compared groups. As a novel finding, this study demonstrates that co-medication either with VPA or LEV in GBM patients undergoing first line radio-chemotherapy with TMZ has no additional impact on medium-term haematological toxicity.