Selective serotonin reuptake inhibitor use is associated with major bleeding during treatment with vitamin K antagonists: results of a cohort study

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Abstract

Aims: To determine whether Selective serotonin reuptake inhibitors (SSRIs) cause major bleeding during vitamin K antagonist (VKA) treatment and investigate the possible mechanisms behind this interaction. Methods: Information on SSRI use and bleeding complications was obtained from patient records at the Anticoagulation Clinics of Leiden and Rotterdam of VKA initiators between 2006 and 2018. Conditional logistic regression and time-dependent Cox regression were used to estimate the effect of SSRIs on a high INR ([?] 5) within 2 months after SSRI initiation and on major bleeding during the entire period of SSRI use, respectively. SSRI use was stratified for (non-)CYP2C9 inhibitors. Results: 58,918 patients were included, of whom 1504 were SSRI users. SSRI initiation versus non-use was associated with a 2.41-fold (95% confidence interval [CI] 2.01-2.89) increased risk for a high INR, which was 3.14-fold (95%CI 1.33-7.43) among CYP2C9 inhibiting SSRIs. SSRI use versus non-use was associated with a 1.22-fold (95%CI 0.99-1.50) increased risk for major bleeding in all SSRI users, which was 1.31-fold (95%CI 0.62-2.72) in CYP2C9 inhibiting SSRIs compared to non-users. Conclusion: SSRIs are associated with an increased risk of high INR and major bleeding. These risks were slightly more elevated for CYP2C9 inhibiting SSRI users, suggesting that this was due to a pharmacokinetic interaction (by CYP2C9 inhibition) as well as a pharmacodynamic effect of SSRIs on platelet activation.

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