Abstract: P2548

Lithium use and risk of out-of-hospital cardiac arrest in patients with bipolar disorder: A nationwide nested case-control study

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Background: Lithium is a mood stabilizer widely used in the treatment of bipolar disorder. Lithium has been linked to malignant proarrhythmic electrocardiographic changes such as QT-prolongation, atrioventricular and sinoatrial block. However, evidence regarding the risk of cardiac arrest with lithium use is lacking.

Purpose: We investigated the risk of out-of-hospital cardiac arrest associated with lithium use among patients with bipolar disorder.

Methods: All out-of-hospital cardiac arrest cases from 2001 through 2014 of presumed cardiac cause with a history of bipolar disorder were identified from the nationwide Danish Cardiac Arrest Registry. We conducted a nested case-control study by matching all cardiac arrest cases with bipolar disorder on age, sex and time since first diagnosis of bipolar disorder with four controls from the general population who also had a history of bipolar disorder. Conditional logistic regression adjusted for comorbidities and concomitant pharmacotherapy was used to determine the association between lithium monotherapy and risk of out-of-hospital cardiac arrest compared to mood stabilizing monotherapy with valproate, lamotrigine and quetiapine, respectively. Exposure was defined as redeemed prescriptions for only one of either lithium, valproate, lamotrigine or quetiapine up to two months before index.

Results: The study population consisted of 1,410 patients with bipolar disorder, comprising 282 out-of-hospital cardiac arrest cases each matched with 4 controls. The median age was 69 years, 47.2% were male and the median time from first diagnosis of bipolar disorder was 7.25 years. Among cases, 59 (20.9%) were in lithium monotherapy and among controls the number was 299 (26.5%). For monotherapy with other mood stabilizers we observed the following distributions: quetiapine 18 (6.4%) cases and 51 (4.5%) controls, valproate 12 (4.3%) cases and 51 (4.5%) controls, and lamotrigine 15 (5.3%) cases and 64 (5.7%) controls. Lithium was not associated with an increased risk of OHCA compared to other mood stabilizing drugs: Hazard ratio (HR) 0.64 [95% confidence interval (CI) 0.31-1.33] (reference quetiapine), HR 0.56 [95% CI 0.25-1.24] (reference valproate) and HR 0.53 [95% CI 0.25-1.10] (reference lamotrigine).

Conclusion: Among patients with bipolar disorder, lithium was not associated with an increased risk of cardiac arrest compared to other mood stabilizing drugs. Further studies focusing on the cardiovascular safety of mood stabilizing drugs are warranted.
Lithium versus: | HR (95% CI)
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Reference | 1.00 (1.00-1.00)
Quetiapine | 0.64 (0.33-1.33)
Valproate | 0.56 (0.25-1.24)
Lamotrigine | 0.53 (0.25-1.10)