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Antidepressants and risk of epilepsy and seizures

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Introduction

There is conflicting evidence for an association between antidepressant use and the risk of epilepsy and/or seizures. This study aims to clarify the picture by using a large representative cohort from a primary care database.

Methods

- QResearch primary care database.
- 687 different UK practices.
- Cohort of patients aged between 20 and 65 with a first recorded diagnosis of depression between 1/1/2000 and 31/7/2011.
- Patients diagnosed with schizophrenia, bipolar or other psychosis were excluded.
- Patients prescribed antidepressant medication more than 36 months before the date of their depression diagnosis, before the age of 20, or before study entry date were also excluded.
- Information extracted on demographic data, potential confounders and all prescriptions for antidepressant drugs.
- Cox regression used to estimate hazard ratios for the association between antidepressant treatment and epilepsy/seizures during the follow-up period.

Results (1) – Study cohort

The study cohort comprised 238,963 patients, 88% of whom received at least one prescription for an antidepressant during follow-up. The most common class of antidepressant prescribed was selective serotonin reuptake inhibitors (SSRI) comprising 71% of prescriptions, with tricyclic and related antidepressants (TCA) second (14%) and other antidepressants third (12%). Monoamine oxidase inhibitors (MAOI) and combined prescriptions accounted for less than 3% of antidepressant prescriptions.

In the first five years of follow-up there were 878 patients with a first diagnosis of epilepsy/seizures. We found a statistically significant association between all antidepressant drug classes and the risk of epilepsy/seizures. All dosages, apart from low dose SSRI and low doses of other types of antidepressant were significantly associated with an increase in the risk of epilepsy/seizures.

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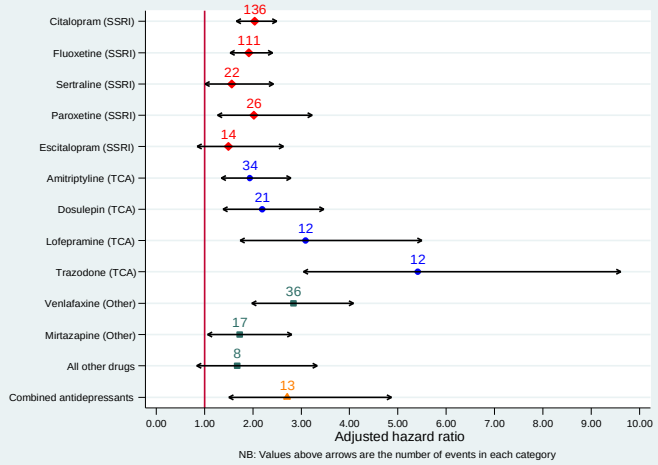
Results (2) – Hazard ratios for the first five years of follow-up

There were significantly increased hazard ratios for 8 of the 11 most commonly prescribed drugs compared to no treatment, with the highest risks associated with trazodone (adjusted HR=5.41, 95% CI 3.05 to 9.61), lofepramine (adjusted HR=3.09, 95% CI 1.73 to 5.50), and venlafaxine (adjusted HR=2.84, 95% CI 1.97 to 4.08). Sertraline, mirtazapine, and escitalopram were not associated with a significant increase in the risk of epilepsy/seizures (at P<0.01).

Adjusted hazard ratios for epilepsy/seizures



NB: Values above arrows are the number of events in each category

Results (3) – Numbers needed to harm (NNH)

The table below shows the NNH for those 5-year hazard ratios that were significant (P<0.01). The drug class with the highest NNH is the SSRIs, 312 patients would have to be treated over five years for there to be an extra case of epilepsy/seizures. For combined prescriptions only 166 patients would have to be treated for five years for there to be one extra case. For individual drugs the lowest NNH is for trazodone: only 65 patients would have to be treated for five years for one extra case.

Drug class	NNH	95% CI
SSRI	312	229 to 453
TCA	217	143 to 363
Other	215	137 to 378
Combined	166	74 to 551

Antidepressant	NNH	95% CI
Citalopram	278	193 to 434
Fluoxetine	313	204 to 546
Paroxetine	280	129 to 1072
Amitriptyline	306	161 to 819
Dosulepin	241	117 to 748
Lofepramine	138	64 to 392
Trazodone	65	34 to 140
Venlafaxine	156	93 to 294

Conclusion

This study highlights the risk of epilepsy/seizures for different classes, doses, and individual antidepressants. All antidepressant drug classes had a significantly increased risk of epilepsy/seizures compared to no treatment. Of the individual antidepressants, trazodone, lofepramine and venlafaxine had the highest risk. Further confirmation is needed via additional studies.

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