BJPsych | The British Journal of Psychiatry (2019) 214, 305–307.

Correspondence

Edited by Kiriakos Xenitidis and Colin Campbell

Contents

Response to the article entitled 'Mood stabilisers and risk of stroke in bipolar disorder'

We read with great interest the article 'Mood stabilisers and risk of stroke in bipolar disorder' by Chen *et al*, published in this esteemed journal.[1] The authors have assessed the association between mood stabilisers and risk of stroke in patients with bipolar disorder. They have addressed multiple potential confounders such as age, gender, physical illness and concomitant medication. However, we would like to discuss some important factors that could have influenced the study findings.

First, the study did not consider the role of psychiatric comorbidity. Only admission for bipolar disorder was taken into account. Certain psychiatric illnesses are common in patients with bipolar disorder and are noted to be risk factors for stroke as well. For example, the lifetime prevalence of anxiety disorder in bipolar disorder has been found to be 42.7%.[2] Further, anxiety disorders have been associated with a 24% increased risk of stroke compared with the general population.[3]

Second, the role of psychosocial factors in stroke is not addressed. It is important to note that bipolar disorder is associated with several psychosocial factors and a recent meta-analysis mentions that the risk of stroke is increased by psychological, vocational and interpersonal factors by almost 39%, 35% and 16%, respectively.[4]

Third, bipolar disorder is associated with high rates of non-adherence to medication. As the study focuses on the association between mood stabiliser and bipolar disorder, the adherence to mood stabilisers is an important variable to be considered. This point is worth highlighting as the mean prevalence of non-adherence to medication has been found to range from 41.5% to 43%.[5]

Fourth, the role of oral contraceptive pills has not been discussed. The increased risk of stroke with oral contraceptives is well-known. About 42.7% of participants are women. Oral contraceptives are used commonly by women for contraception as well as prescribed for polycystic ovarian syndrome, which is not uncommonly seen with use of valproate.

Fifth the comorbidity of seizure disorder has not been considered. This is important to address mainly for two reasons. Both valproate and carbamazepine are prescribed in patients with seizure disorder or epilepsy as well as in patients with bipolar disorder. Further, literature exists that late-onset epilepsy has been associated with increased risk of stroke.[6] This is a point to be noted as almost 61% of the participants were recruited when more than 45 years old.

Finally, the term 'any mood stabiliser' is not clearly defined. For example, the number of patients on any mood stabiliser during the case period is 212. However, the sum of patients as per numbers given separately for carbamazepine (35), valproic acid (118), lithium (62) and lamotrigine (18) is 233.

References

1 Chen PH, Tsai SY, Pan CH, Chang CK, Su SS, Chen CC, et al. Mood stabilisers and risk of stroke in bipolar disorder. *Br J Psychiatry* 2019; **214**: 305.

2 Nabavi B, Mitchell AJ, Nutt D. A lifetime prevalence of comorbidity between bipolar affective disorder and anxiety disorders: a meta-analysis of 52 interview-based studies of psychiatric population. *EBioMedicine* 2015; **2**:1405–19.

3 Perez-Pinar M, Ayerbe L, González E, Mathur R, Foguet-Boreu Q, Ayis S. Anxiety disorders and risk of stroke: a systematic review and meta-analysis. *Euro Psychiatry* 2017; **41**: 102–8.

4 Lightbody CE, Clegg A, Patel K, Lucas JC, Storey H, Hackett ML, et al. Systematic review and meta-analysis of psychosocial risk factors for stroke. *Semin Neurol* 2017; **37**: 294–306.

5 Chakrabarti S. Medication non-adherence in bipolar disorder: review of rates, demographic and clinical predictors. *World J Metaanal* 2017; **5**: 103–23.

6 Ben-Menachem E. Epilepsy as a warning sign for stroke. *Epilepsy Curr* 2005; **5**: 42–3.

Pooja Patnaik Kuppili, Senior Resident, All India Institute of Medical Sciences, India; **Kartik Singhai**, Junior Resident, All India Institute of Medical Sciences, India; **Naresh Nebhinani**, Associate Professor, All India Institute of Medical Sciences, India. Email: poojapatnaik.aiims@gmail.com.

doi:10.1192/bjp.2019.63

Author's reply

We thank Kuppili, Singhai and Nebhinani for their recent comments on our article 'Mood stabilisers and risk of stroke with bipolar disorder'.[1] Their comments drew attention to several confounding factors that could have influenced our study findings.

The association between anxiety disorders and risk of stroke has recently received increased attention because of its high prevalence in bipolar disorder.[2] In addition, this association might be observed between seizure disorders and risk of stroke because evidence suggests a link between bipolar disorder and epilepsy.[3] With these considerations, we examined the association between these two types of comorbidities and risk of stroke in our patients with bipolar disorder; however, results were not significant. The crude risk ratios of anxiety disorder and seizure disorders for the risk of stroke were 1.21 (95% CI 0.74–1.96, $P = 0.446$) and 2.18 (95% CI 0.35–13.49, $P = 0.403$), respectively, based on the case–crossover study.[1] These findings suggested that the association between acute exposure to mood stabilisers and risk of stroke in patients with bipolar disorder may not be confounded by anxiety and seizure comorbidities.

We agree with the comment that the role of psychosocial factors in stroke should be addressed in patients with bipolar disorder. Information on these variables was unavailable in the National Health Insurance Research Database (NHIRD) of Taiwan; this is one of the limitations of this study. However, the design of a case–crossover study has the advantage that study participants serve as their own controls and therefore this may minimise the effects of such unmeasured variables.

We would also like to address the limitation issues indicated by Kuppili and colleagues. In Taiwan, the prescription of oral contraceptive pills is not covered by national health insurance. Therefore, the effect of oral contraceptives on the association between valproic acid use and risk of stroke cannot be excluded.

https://doi.org/10.1192/bjp.2019.63 Published online by Cambridge University Press