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LETTER

Impact of carbamazepine and lacosamide on serum lipid levels

To the Editors:

We read with interest the recent article titled "Effects of lacosamide and carbamazepine on lipids in a randomized trial" by Mintzer et al.[1] The authors have shown that carbamazepine (CBZ) elevates serum lipids, whereas lacosamide (LCM) does not affect lipids levels. We wish to add certain points.

The authors have used analysis of covariance to determine whether the difference between the two groups in terms of elevation of serum lipids was significantly different. However, in the results, they have not mentioned the variance explained by the independent variable (i.e., between-group variance) and unexplained variance (ie, within-group variance).[2] It could have revealed how much of the difference in change of lipid profile parameters between the LCM and CBZ groups was truly due to the effect of antiseizure medications (ASMs) and how much was due to covariates such as age, sex, body mass index, and baseline lipid level. The *p*-value as mentioned by the authors only signifies that the two groups are different with respect to the distribution of serum lipid levels. Second, the authors could have included a few more clinically relevant covariates such as dietary habit/daily caloric intake, daily physical activity, presence of diabetes, smoking, and alcohol use, which are important determinants of serum lipid levels.

Moreover, the authors have compared the change in individual serum lipid levels between the two groups. However, they have not compared whether the changes in these individual serum lipid levels are corelated with each other in the same group, and few individuals are at risk for the elevation of multiple serum lipid level parameters. The patients with derangement in more than one serum lipid parameter are at higher risk of acute coronary ischemic events and other atherosclerotic complications than those with derangement in a single parameter.

This subgroup analysis is clinically more relevant to medical professionals, as Phase II studies in lacosamide have previously shown no significant dyslipidemic adverse effects and carbamazepine has been shown to cause dyslipidemia in multiple previous studies.[3,4] The authors have mentioned that CBZ elevates serum lipid by activation of CYP5A1 and also causes elevation of lipoprotein (a) and C-reactive protein (CRP). Thus, it would have been more informative if the authors would have explored some subgroups in this post hoc analysis, such as whether those with elevated liver transaminases, those receiving higher doses, and those having higher serum CBZ levels, as mentioned in the original study results, had more significant dyslipidemia. Patients receiving enzyme-inducing ASMs with certain CYP450 polymorphisms are more likely to have more hepatic dysfunction and dyslipidemia.[5] As the authors have not performed any analysis for cytochrome P polymorphism, CRP, lipoprotein (a), and other markers of atherosclerosis in the original study protocol, they could have explored the subgroup with drug-induced transaminitis as a potentially high-risk group for having more dyslipidemia.[6] Similarly, the authors should also have screened for whether the cases with well-controlled epilepsy and uncontrolled epilepsy had any significant difference in change in serum lipid levels.

The authors have mentioned that only 271 of 886 patients randomized were included in this post hoc analysis, so the study is more likely a subgroup analysis rather than a true randomized controlled comparison as mentioned by the authors. They have also mentioned that the included sample size in both arms in this post hoc analysis is sufficient to detect any level of change in lipid parameters. They should have corroborated this opinion by calculating the post hoc power analysis for this study. Lastly, in such cases, number needed to harm provides a more comprehensive overview of the increased risk of dyslipidemia incurred by administration of CBZ instead of LCM.[7]

CONFLICT OF INTEREST

Neither of the authors has any conflict of interest to disclose.

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