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Letter to the editor

Crossreactivity in antiepileptic drug monitoring: Reply to: Real-life experience with brivaracetam in 101 patients with difficult-to-treat epilepsy-a monocenter survey

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Dear editor

We have read with great interest the article 'Real-life experience with brivaracetam in 101 patients with difficult-to-treat epilepsy–A monocenter survey' (Steinhoff et al.; 2017 May; 48:11–14) [1]. However, we wish to complement this article's use of laboratory testing for brivaracetam and levetiracetam analysis.

In their article, Steinhoff et al. investigated the efficacy of brivaracetam and levetiracetam. They also demonstrated therapy switching from levetiracetam to brivaracetam and vice-versa, as well as the concomitant administration of these drugs. In specific situations, one must question whether routine laboratory tests can reliably differentiate the level measurements of each therapeutic drug individually. In that context, it is notable that brivaracetam and levetiracetam share many similarities, such as starting from the same mechanism of action (blocking of the SV2A-receptor) and having similar pharmacokinetical and pharmacodynamical characteristics. Importantly, both drugs exhibit similar chemical-structural characteristics, which could complicate the level measurement discrimination of each antiepileptic drug, depending on the laboratory method used [2].

Major advances in therapeutic drug monitoring, particularly laboratory analysis, have been achieved in the last decades. We wish to emphasise that analytical methods based on mass spectrometric techniques were once an exclusive research approach but are now routine, which has led to new opportunities in antiepileptic drug monitoring. There is extensive evidence that mass spectrometric techniques offer greater sensitivity and specificity, lower imprecision and, above all, lower potential interference and laboratory crossreactivity compared to immunological assays. In contrast, level measurement with immunological assays requires less time to reach a result (in our institution, ~45 min versus 3 h) [3].

Along with this comparison, we want to note our observations regarding routine work associated with brivaracetam and levetiracetam analysis: in accordance with the aforementioned potential weakness of immunological methods, we found strong crossreactivity of brivaracetam in our immunological levetiracetam level measurement of four blood samples. Therefore, we used a spectrometric method to analyze samples of patients under reported brivaracetam therapy who had not received levetiracetam for more than a month. All samples that yielded the expected positive results for brivaracetam and negative results for levetiracetam by mass spectrometric technique were then analyzed for potential levetiracetam levels using the immunological method. Surprisingly, after executing that workflow, we measured the relevant levetiracetam levels in all samples using immunoassay, which indicated significant crossreactivity of brivaracetam.

So which is the superior method in antiepileptic drug monitoring? We could not answer this question disjunctively because we believe both methods have merit depending on the clinical situation and clinical question. Therefore, we recommend laboratory analysis with mass spectrometric methods in cases of therapy switching or concomitant use of structurally similar antiepileptic drugs.

Antiepileptic drug monitoring with immunoassays remains an acceptable method primarily when an antiepileptic monotherapy is established because it offers quicker results. However, in cases of uncertainty, a confirmatory mass spectrometric analysis should be performed. Finally, the most important factor is effective interdisciplinary cooperation between neurologists and specialists in laboratory medicine to overcome these challenges.

Declaration of Competing Interest

None.

References

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