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CORRESPONDENCE

The 'number needed to treat' with Levetiracetam (LEV): comparison with the other new antiepileptic drugs (AEDs)

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To the Editor,

Levetiracetam (LEV, Keppra) is a new antiepileptic drug for the add-on treatment of partial onset seizures. Pivotal studies have shown a significant efficacy for all tested doses (pooled data: 28% of responders with 1000 mg per day, 32% of responders with 2000 mg per day and 41% of responders with 3000 mg per day). Its safety profile is also quite encouraging: in pivotal studies, adverse events were mostly central nervous system related and manifested as somnolence, asthenia and dizziness; often being mild to moderate in severity. No life-threatening adverse events related to the study drug were described. Furthermore, LEV has a very straightforward pharmacokinetic profile: no protein binding, no potential or significant drug interactions, no hepatic metabolization, as well as displaying linear kinetics and no active metabolites.

Because neurologists have received numerous new therapeutic possibilities over the last few years, it is important to compare this new antiepileptic drug (AED) to the others in terms of efficacy and potential new advantages.

A first attempt to compare AEDs for efficacy and/or safety was made by Marson *et al.*[1] using the odds ratios from meta-analysis of double-blind placebo-controlled studies. This analysis did not show significant differences between the new AEDs. This could be due to the fact that the odds ratio does not take into account the placebo response and the variability of the therapeutic answer between the different studies. Other comparative methods used include the Star Rating system of Brodie[2] and the improvement rates at recommended doses suggested by Cramer *et al.*[3]. The first method is partially subjective while the second one could give some interpretations about the notion of 'recommended' doses. The number needed to treat (NNT) to obtain one additional (to placebo) responder is an objective datum, based on pivotal studies and takes into account the absolute benefit between the active drug and the placebo groups. This analysis showed some differences between the newer AEDs (Elferink and Van Zwieten-Boot[4]). Furthermore, it immediately gives quick information in clinical practice, even if the value of such an analysis remains a controversial point between clinicians and statisticians (Lesaffre *et al.*[5]). We used the method described by

Table 1: Comparative number needed to treat to obtain one addition (to placebo) responder.

AEDs	Data		NNT	
	Active	Placebo	Number	Range
Gabapentin	93/459	27/291	9.10	6.27–16.61
Lamotrigine	68/330	25/268	8.87	5.93–17.56
Tiagabine	104/493	17/276	6.7	5.12–9.66
Zonisamide	12/269	25/230	6.29	4.44–10.81
Oxcarbazepine	260/659	50/302	4.37	3.51–5.79
Levetiracetam	206/592	29/312	3.92	3.28–4.88
Vigabatrin	118/292	28/203	3.76	2.94–5.19
Topiramate	146/360	17/174	3.25	2.67–4.16

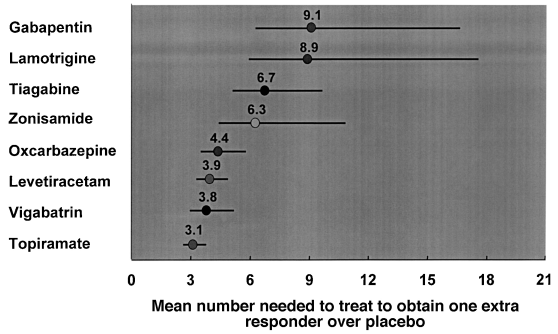

Fig. 1: Number needed to treat.

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Cook and Sacket[6] with SAS software and analysed data by studies and pooled data from the three pivotal studies (904 patients: 592 LEV and 312 placebo) and compared our results with the NNT data kindly provided by E. Elferink for the other AEDs (Table 1, Fig. 1). Results for ZNS and OCBZ were calculated from data provided in the Cochrane Library.

CONCLUSIONS

LEV is an efficacious and well tolerated AED. NNTT analysis shows that LEV belongs to the group of most effective AEDs. This, in combination with its good tolerability and its straightforward pharmacokinetic profile, gives a new therapeutic option for refractory epilepsy patients.

CONFLICT OF INTEREST

No conflict of interest.

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