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# Incompleteness of Lamotrigine Data

We would like to comment on the review article by Messenheimer et al.[1] on the tolerability of lamotrigine in children. We feel that the review is incomplete as the authors have included only studies conducted by Glaxo Wellcome UK and US, but have not considered other relevant clinical trials.[2] In a multicentre study, Besag et al.[2] used similar methods to quantitatively assess the efficacy and tolerability of lamotrigine in 285 children (<13 years of age) from 37 centres in 11 countries (pooled data from 5 open, add-on studies). In this study,[2] the most common reported adverse events were somnolence (16.8%) and rash (16.5%) which is comparable to the results of the review by Messenheimer et al.[1] Other adverse events were reported comparatively less frequently in the study by Besag et al.[2] including vomiting (12.3%), seizure exacerbations (11.6%), fever (10.9%) and infection (9.8%) than in the review by Messenheimer et al.[1] 12.6% of patients discontinued lamotrigine in the study by Besag et al.[2] compared with a 10.1% discontinuation rate in the add-on studies included in the review.[1]

Messenheimer et al.[1] also made no reference to relevant publications from the Drug Safety Research Unit (DSRU)[3,4] which have provided important real-life data from observational studies. The cohort for the prescription event monitoring (PEM) study of lamotrigine was collected from December 1991 to February 1995 when lamotrigine[3] was indicated for add-on treatment. Of the total cohort of 11 316 patients, 8199 (72.5%) were adults (>16 years of age) and 2189 (19.3%) were children (<16 years age). The age was not specified for 928 (8.2%) patients. Among the children 55% were males and 45% were females. The most frequently reported adverse events in the children were respiratory tract infection (12.6%), convulsions (10.1%) and rash (5.6%). Vomiting (3.1%), somnolence (3.0%), headache (2.1%) and fever (1.6%) were less frequently reported. The lower rates of adverse events observed in the PEM study[3,4] compared with those seen in the review by Messenheimer et al.[1] is to be expected as PEM is an observational study.

With regard to skin rash, the DSRU study[3] demonstrated a higher incidence of skin adverse reactions including serious skin reactions in children compared with adults. The frequency of rash reported in children was 5.6% compared to 4.3% in adults (individuals ≥16 years of age). There were 5 reports[3] (0.23%) of Stevens-Johnsons syndrome in 2189 children compared with 7 reports (0.09%) in 8199 adults giving an unadjusted relative risk ratio of 2.68 [95% confidence interval (CI) 0.85 to 8.42]. Although this is not significant at 95% CI, it is probably a reflection of the low number of reports. Furthermore all 5 children were also taking valproic acid, which corresponds with the risk of serious skin reactions associated with concomitant use of valproic acid that was observed in the review by Messenheimer et al.[1]

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