

PRESS RELEASE

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Experts call for urgent research into antiepileptic drugs given to children after significant rise in prescribing

Researchers have called for urgent studies into the long-term safety of newer antiepileptic drugs after discovering that the number given to children has increased significantly over recent years, reports the June issue of **British Journal of Clinical Pharmacology**.

When the UK team studied antiepileptic drugs (AEDs) given to nearly 8,000 children over a 13-year period, they discovered that overall prescribing had risen by 19 per cent and there had been a five-fold increase in prescribing of newer AEDs.

The results follow a report by the European Medicines Agency (EMA) which called for greater research into paediatric drugs for epilepsy.

“EMA recommended further research into 21 antiepileptic drugs for children but didn’t indicate which ones should be prioritised” explains Professor Ian Wong from the Centre for Paediatric Pharmacy Research, a collaborative project run by the School of Pharmacy at the University of London, the UCL Institute of Child Health and Great Ormond Street Hospital.

“Our research has narrowed that list down to three drugs that have seen a massive rise in UK prescribing since 1993 – lamotrigine, topiramate and levetiracetam. The uptake of these drugs has been rapid, yet their long-term safety has not been established and further research must now be seen as a priority.”

Worldwide concern has been expressed about the need to reform regulations and develop better research structures for paediatric medicines, says Professor Wong, who is also a member of TEDDY - the Task-force of European Drug Development for the Young.

“The American Food and Drug Administration and the National Institutes of Health have been leading the process for paediatric drug reform over the last ten years. And the European Union has proposed the “Better Medicines for Children” regulation and devised a research strategy to improve paediatric medicines research in the hope of increasing the availability of licensed medicines for children” he says.

Concerns over paediatric AEDs have risen in recent years after prescribing restrictions were issued on vigabatrin in the late 1990s following reports that one-third of users suffered from visual field defects, ranging from asymptomatic to severe and potentially disabling.

In 2004, the National Institute for Health and Clinical Excellence – the UK Government’s advisory body on therapeutic interventions – stated that vigabatrin should only be prescribed in cases of West’s Syndrome (infantile spasms) and then only by an epilepsy specialist, a neurologist or a paediatric neurologist.

Professor Wong and his research colleagues studied 7,721 patients from birth to 18, using data from the UK General Practice Research Database, analysing the results by age and the AED prescribed.

Their findings included:

- More than a quarter of a million prescriptions (257,663) were issued for AEDs during the study period. Of these, 69 per cent were for conventional AEDs and 31 per cent were for newer AEDs.
- The most commonly prescribed newer AED was lamotrigine, which accounted for 20 per cent of all prescriptions and 65 per cent of newer AED prescriptions.
- Valproate was the most commonly prescribed conventional AED, accounting for 36 per cent of all prescriptions and 52 per cent of conventional AED prescriptions.
- 54 per cent of children receiving prescriptions were male and prescribing for new patients was highest in the two to 11 age group (45 per cent) and the 12 to 18 age group (39 per cent). 16 per cent of prescriptions were for children under two years of age.
- 70 per cent of children were receiving just one AED, which is consistent with adult research, which suggests that 60 to 70 per cent of patients have their epilepsy controlled by one AED.

“To our knowledge this is the first large paediatric study to compare newer and conventional AED prescribing in the UK” says Professor Wong, who – as a result of the study - has been awarded a research contract by the Medicine and Healthcare products Regulatory Agency to assess deaths among children and adolescents using antiepileptic drugs.

“Our research found that paediatric prescribing of antiepileptic drugs showed a significant increase over the study period and that newer AEDs are increasingly being prescribed in preference to more tried and tested conventional drugs.

“Newer AEDs have proved popular, mainly because they are less likely to react with other prescribed drugs.

“However, these newer AEDs are subject to fewer licensing restrictions because there is more evidence about their benefits, gathered from controlled trials, than their more traditional counterparts. As new safety data emerges, restrictions in prescribing may be implemented.”

“Many drugs are not tested on children before they are licensed because of the difficulties of including children in clinical trials” adds Dr Jeffrey Aronson, Editor-in-Chief of the Journal and Reader in Clinical Pharmacology at Oxford University.

“This means that clinicians often have to rely on their experience and scale down adult drugs for paediatric use, which is widely regarded as most unsatisfactory.

“The research by Wong and colleagues highlights this important problem, by providing us with an excellent picture of prescribing trends for children with epilepsy. We hope that this important piece of research will help to inform research priorities for the newer AEDs.

“It also raises concerns about the rapid increase in prescribing drugs whose safety has not been established for paediatric use, which is an issue that the Journal has often dealt with and will continue to cover.”

The authors have stressed that it is important that parents continue to give their children medicines that have been prescribed for them, but to make their family doctor or consultant aware of any adverse effects or problems their child experiences.

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Notes to editors

- Prioritizing children’s medicines for research: a pharmacoepidemiological study of antiepileptic drugs. Ackers et al. **British Journal of Clinical Pharmacology**. 63.6, pp 689-697. June 2007.
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