A more ethical way to compare epilepsy treatments

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For the first time, a new research methodology recently approved by the Food and Drug Administration has been used to demonstrate that converting patients from one anti-epileptic drug to another - in this case, lamotrigine extended-release (LTG XR) - is well-tolerated, effective and safe. The work by Jacqueline French and her team, from New York University in the US, illustrates how the new methodology addresses ethical issues inherent in more traditional study designs. It is published online in Springer's journal, *Neurotherapeutics*.

The use of traditional control groups in experimental designs can raise some ethical concerns, such as using inferior treatments for the control group in the study of an illness with significant morbidity and mortality, such as epilepsy. What French and team have done is compare their intervention group - the one where they are moving patients from one drug to another - with a so-called 'historical control group' obtained from a dataset of eight previously published studies, rather than recruit a new control group and give them a potentially less effective drug.

In their study, a total of 226 patients aged 13 years or older undergoing treatment for epilepsy across seven countries were randomly allocated to one of two groups: the first group received LTG XR 250mg; the second received 300mg once daily. During the conversion phase (11-12 weeks), the LTG XR dose was increased progressively as the previous drug was withdrawn gradually. The subjects then had a 12-week maintenance phase with LTG XR as monotherapy. Throughout the study period, the researchers monitored both the type and frequency of seizures and

compared them to pre-intervention assessments.

The results demonstrate that LTG XR is effective as monotherapy. Approximately half of the study participants experienced at least a 50 percent reduction in seizure frequency compared to the number recorded before the study. More than half the group reported minor adverse events, including headache and dizziness predominantly.

The authors conclude: "A conversion-to-monotherapy study like ours, which incorporates a historical control, provides important information to clinicians, who often wish to convert their patients from one anti-epileptic drug to another. Without putting a group of patients at undue risk of seizure worsening, we demonstrated that it is possible to convert patients from another drug to LTG XR and that this conversion is well tolerated."

More information: French J et al (2011). Lamotrigine XR conversion to monotherapy: first study using a historical control group. *Neurotherapeutics*. DOI 10.1007/s13311-011-0088-3

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