Quality of life in pediatric epilepsy
A validated questionnaire for side effects of AEDs

Sanjeev V. Kothare, MD
Janelle Wagner, PhD

Correspondence & reprint requests to Dr. Kothare:
Sanjeev.kothare@childrens.harvard.edu

The selection of antiepileptic drugs (AEDs) is based primarily on efficacy; however, in some conditions, efficacy is often equivalent for several AEDs. Hence other factors such as pharmacokinetics, cost, adverse effects (AEs), age, and sex should also be considered when selecting an appropriate AED.1 AEs, which are observed in over one-third of patients with epilepsy on AEDs, affect the ultimate quality of life and dropout rate from AED use, independent of seizure control.1 As a result, AEs are among the most important factors in choosing the appropriate AED for the patient.

The Food and Drug Administration (FDA) has defined an AE as any side effect associated with the use of a drug, whether or not considered related to its mechanism of action, further classified as probable, possible, or definite. The terminology used in the United States to describe patient reports of AEs comes from Coding Symbols for a Thesaurus of Adverse Reaction Terms (CO-STAR) to describe patient events.2 Other sources for listing AEs include WHO Adverse Reaction Terminology (WHO-ART). To improve the terminology used to describe AEs, the FDA plans to replace CO-STAR with Medical Dictionary for Regulatory Activities (Med-DRA).2 AEs can be collected by many different methods, such as reports from patients or checklists. However, establishing a cause-effect relationship for a particular AE in persons with epilepsy is fraught with difficulties related to seizure activity, mental health comorbidities, and concurrent medications, and therefore a standardized questionnaire to assess AED AEs could provide a beneficial tool for clinicians and researchers.

In this issue of Neurology®, Morita et al.3 report on the development of a questionnaire (Pediatric Epilepsy Side Effects Questionnaire [PESQ]) to screen for AEs of AEDs in children with epilepsy. The PESQ can be used by providers in their clinical practice to screen effectively for and to follow AEs during subsequent visits. Forty-four items were selected from a pediatric AED side effect questionnaire, with additional input from 12 expert pediatric epileptologists and 21 caregivers of children with epilepsy. These initial 44 items were administered to caregivers of 495 children with epilepsy. After exploratory factor analysis, 19 items were finally selected, with 5 subscales (cognitive, motor, behavioral, general neurological, and weight) accounting for 99% of the variance. Appropriate reliability and validity estimates were strong.

The Morita et al. study was well-designed and conducted to provide appropriate psychometrics for the PESQ, a measure of AED AEs, which was not otherwise available. For example, construct validity was demonstrated by increased PESQ values with increased number of AEDs used. Large sample size and feasibility of caregiver completion in the epilepsy clinic are also clear strengths. Morita and colleagues as well as the authors of this editorial conclude that the PESQ is a reliable and valid measure of AED side effects in children across the epilepsy spectrum and can be used in both clinical and research settings.

Similar to other scale development studies, the current study has its limitations. Rare side effects will be not be assessed by this questionnaire, but would need to be included separately in the medical record by the provider. The literacy of the family or patient was not assessed in this study. It is unclear how the 20 questions were chosen from the Hague scale, or how the expert panel or the other caregivers communicated with the authors on developing the other 24 questions. The rationale for the 4-week time frame for assessment of the side effects after initiation of AED is unclear. Lack of an adolescent self-assessment for side effects is an additional limitation, which needs to be addressed in future modifications to the questionnaire. The PESQ does not address the issue of separating out side effects based on etiology, whether related to AEDs, epilepsy syndrome, seizure frequency and duration, or other unrelated medical conditions. In addition, when multiple AEDs are used, whether the AE is related to a particular AED will be difficult to sort out using this questionnaire.

See page 1252
Use of the PESQ fills a current clinical practice and research gap. Historically, information on AEs of AEDs has been gathered via a clinician’s personal style and perceived relevance, and in a random fashion. Indeed, the National Institute for Neurological Disorders and Stroke has assembled “epilepsy-specific common data elements (CDE).”4 CDEs inform research design and subsequent practice by providing standardized and generalizable data to develop evidence-based guidelines and recommendations for the treatment of seizures and epilepsy, which can influence all areas of quality of life and functioning (e.g., learning, behavior, social).5,6 Development and utility of the PESQ fits well within the framework of epilepsy-specific CDEs. Morita and colleagues posit, in their discussion, that clinicians could use the PESQ as a template to assess side effects beyond what spontaneous or open-ended questioning would produce. Further, as part of a clinical research protocol, the PESQ could standardize the monitoring of side effects over time. In either case, Morita et al. offer that the PESQ provides a “guide” for clinicians to assess and discuss side effects, potentially informing dosage or medication changes. If AED side effects are intolerable for children with epilepsy, they may affect adherence to AED use.7 Routine use of the PESQ thus provides an opportunity for this discussion, which may contribute to improved adherence, quality of life, and health outcomes for children with epilepsy.8

The PESQ thus provides a valuable standardized questionnaire to assess AED AEs in youth with epilepsy, which did not previously exist. Use of the PESQ in new-onset or established epilepsy and also in well-controlled as well as refractory seizures may provide a “common data element” for AEs associated with AED use that can inform future clinical decisions and provide data to formulate recommendations for AED use, ultimately improving adherence and quality of life in youth with epilepsy.

DISCLOSURE
The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES