

Antiepileptic drug nonadherence in children with epilepsy

Outcomes and potential intervention

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Currently, no cure is available for many children with epilepsy, and the most frequently used treatment for seizures is antiepileptic drug (AED) therapy. Since 20% to 30% of children with epilepsy experience seizures that are not completely controlled with treatment,¹ it is imperative that these children achieve and maintain adherence to prescribed treatment to have the best possible health outcomes. Studies have consistently shown that nonadherence is related to increased health care utilization.² However, adherence rates in children with epilepsy, even within the first month of AED initiation, are not ideal.³ Modi et al.⁴ previously found that 58% of children with newly diagnosed epilepsy exhibited nonadherence over the first 6 months of AED therapy, and they identified 4 nonadherent trajectories: severe early, severe delayed, moderate, and mild, in addition to a near-perfect trajectory.

In this issue of *Neurology*®, Modi et al.⁵ provide a brief report to expand on their 2011 study. A total of 124 children (2 to 12 years of age) with newly diagnosed epilepsy were followed to examine the relationship between adherence trajectories and seizure freedom (absence of seizures for 1 year or more) at 4 years postdiagnosis. Adherence was measured via MEMS TrackCaps, an electronic monitor that records the date and time that a bottle is opened. Children on the near-perfect trajectory were categorized as adherent, and children with severe, moderate, or mild nonadherence within the first 6 months of AED therapy were categorized as nonadherent. MEMS TrackCaps data were downloaded to the electronic medical chart at every visit, starting at 1 month postdiagnosis and every 3 months thereafter. Final medical chart review was conducted at 4 years postdiagnosis. Seizure outcome data were obtained via caregiver report during clinic visits or over the telephone and were complemented by EEG findings. Results revealed that children who were nonadherent with AEDs within the first 6 months of therapy were 3.24 times more likely not to have experienced ≥ 1 year of seizure freedom at the 4-year follow-up compared to children with near-perfect adherence. Thirty-one percent of children who were nonadherent, compared to

12% of children in the near-perfect adherence group, continued to experience seizures.

The Modi et al. study was well-designed and executed. Attrition (20%) was modest for a 4-year longitudinal study. The results make a substantial contribution to the pediatric epilepsy literature and have several implications for clinical practice. However, this study has several inherent limitations. Children with developmental disorders are excluded; therefore, it is not known how adherence rates may differ for these children. Further, exclusion criteria were assessed only at study enrollment, so children may have been diagnosed with a developmental disorder in the 4-year study period and retained in the final analyses. Notably, the authors address this limitation in their discussion. While the use of an electronic monitor provides an unbiased measure of adherence, external validity is compromised due to the high costs of the usage and availability of electronic monitors in clinical practice. Adherence was measured only in the first 6 months, not at the 4-year postdiagnosis timepoint when seizure freedom was abstracted from the medical record. Additional outcome measures, such as health-related quality of life (HRQoL) and epilepsy self-management, would have enhanced the relevance of these study findings. Despite the limitations, this brief report provides valuable information regarding the relationship between early adherence/nonadherence and seizure freedom 4 years post epilepsy diagnosis.

Early adherence intervention could be an important factor in improving long-term seizure control in children with epilepsy. Adherence interventions for children with epilepsy should be designed to address modifiable factors. For example, Modi et al.⁴ previously demonstrated that socioeconomic status (SES), a relatively nonmodifiable factor, was the only demographic predictor of adherence trajectory classification. Epilepsy variables such as seizure frequency, number of AEDs, and number of AED-related adverse events were not predictive of adherence trajectory classification. To date, studies have not investigated potential modifiable psychosocial predictors (e.g., HRQoL, epilepsy self-management)

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for adherence over time. Seizures and AED adverse effects have been linked to HRQoL up to 7 months postdiagnosis.⁶

A recent comprehensive theoretical model integrates self-management behaviors, treatment adherence, and HRQoL, all of which contain modifiable characteristics that may be targeted by psychosocial intervention.⁷ Modi et al.⁸ have developed an intervention to target adherence through education, problem-solving, and goal-setting self-management behaviors, and their pilot study showed improved adherence following intervention. Similarly, self-management behaviors such as coping skills and self-efficacy for seizure management in children with epilepsy have improved following psychosocial intervention.⁹

Moving forward, researchers must design multisite randomized controlled trials to examine further the efficacy of psychosocial interventions that focus on these modifiable factors and whether early intervention targeting such factors will indeed improve adherence as measured by objective evaluation. It will also be important for clinicians to determine systematically which patients are at risk (e.g., low SES, poor HRQoL) and who should be referred for adherence or self-management intervention. Incorporation of standardized assessment of AED side effects,¹⁰ epilepsy medication self-management,¹¹ and HRQoL⁶ at routine epilepsy visits will not only inform potential epilepsy treatment changes but will also assist with referrals for psychosocial intervention. Dissemination of standardized assessment and intervention tools for adherence early in the course of AED therapy will improve access to integrated physical and mental health care¹² and long-term outcomes for children with epilepsy.

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REFERENCES

1. Wirrell EC. Predicting pharmacoresistance in pediatric epilepsy. *Epilepsia* 2013;54:19–22.
2. McGrady M, Hommel K. Medication adherence and health care utilization in pediatric chronic illness: a systematic review. *Pediatrics* 2013;132:730–740.
3. Modi A, Morita D, Glauser T. One-month adherence in children with new-onset epilepsy: white-coat compliance does not occur. *Pediatrics* 2008;121:e961–e966.
4. Modi AC, Rausch JR, Glauser TA. Patterns of non-adherence to antiepileptic drug therapy in children with newly diagnosed epilepsy. *JAMA* 2011;305:1669–1676.
5. Modi AC, Rausch JR, Glauser TA. Early pediatric antiepileptic drug nonadherence is related to lower long-term seizure freedom. *Neurology* 2014;82:671–673.
6. Modi AC, Ingerski LM, Rausch J, Glauser TA. Treatment factors affecting longitudinal quality of life in pediatric new onset epilepsy. *J Pediatr Psychol* 2011;36:466–475.
7. Modi AC, Pai AL, Hommel KA, et al. Pediatric self-management: a framework for research, practice, and policy. *Pediatrics* 2012;129:e473–e486.
8. Modi AC, Guilfoyle SM, Rausch J. Preliminary feasibility, acceptability, and efficacy of an innovative adherence intervention for children with newly diagnosed epilepsy. *J Pediatr Psychol* 2013;38:605–616.
9. Wagner JL, Smith G, Ferguson PL, van Bakergem K, Hrisko S. Pilot study of an integrated cognitive-behavioral and self-management intervention for youth with epilepsy and caregivers: Coping Openly and Personally with Epilepsy (COPE). *Epilepsy Behav* 2010;18:280–285.
10. Morita D, Glauser T, Modi A. Development and validation of the pediatric epilepsy side effects questionnaire. *Neurology* 2012;79:1252–1258.
11. Modi AC, Monahan S, Daniels D, Glauser TA. Development and validation of the pediatric epilepsy medication self-management questionnaire. *Epilepsy Behav* 2010;18:94–99.
12. Wagner JL, Levinsohn P, Onofer C, et al. National center for project access: a framework for implementing recommendations from the Institute of Medicine's report on the epilepsies. *Epilepsy Behav* 2013;29:121–127.