Objective

To report acceptability, feasibility, and preliminary efficacy from a randomized controlled trial of a family-tailored adherence intervention (AI) targeting nonadherence to antiepileptic drugs in pediatric new-onset epilepsy.

Method

30 children with new-onset epilepsy (7.2 ± 3.1 years old, 47% male) and their caregivers participated. At baseline, participants were given adherence electronic monitors. After a 1-month run-in period, participants with good adherence (> 90%) were monitored. Participants with adherence < 90% were randomized to the AI or Treatment-As-Usual (TAU) group. The AI group received four adherence promotion intervention sessions over >2 months. Follow-up adherence data were collected.

Results

8 families were randomized (AI, n = 4; TAU, n = 4). Families perceived AI to be feasible and acceptable. Preliminary results demonstrated that the AI group had improved adherence from baseline to post-test.

Conclusions

A family-tailored AI appears promising and needs to be tested with a larger pediatric epilepsy sample.

Key words

adherence; chronic illness; neurological disorders; randomized controlled trial.

Introduction

Epilepsy, a condition characterized by recurrent unprovoked seizures, affects ~326,000 children younger than 15 years in the United States (Begley et al., 2000). Antiepileptic drugs (AEDs) are the primary treatment modality for the vast majority of patients with epilepsy. Yet, continued seizures continue to be a significant problem for children with epilepsy (30%; Geerts et al., 2010) despite the introduction of several new AEDs in the past 2 decades. Poor seizure control in children can have detrimental effects on the child’s intellectual abilities (Bjornaes, Stabell, Henriksen, & Loyning, 2001; Farwell, Dodrill, & Batzel, 1983; Nolan et al., 2003; Singhi, Bansal, Singh, & Pershad, 1992) and academic functioning (Austin, Huberty, Huster, & Dunn, 1999), along with compromised health-related quality of life (Modi, Ingerski, Rausch, & Glauser, 2011a; Sabaz et al., 2003). Continued seizures in children can also have negative effects on the family, including family conflict and cohesion difficulties (McCusker, Kennedy, Anderson, Hicks, & Hanrahan, 2002; Mims, 1997).

Several factors may contribute to continued seizures in children with epilepsy, including genetics, comedications, seizure/epilepsy type, and adherence to AEDs (Glauser et al., 2006). In fact, a recent study found that 58% of children newly diagnosed with epilepsy have demonstrated nonadherence to the AEDs over the first 6 months of therapy (Modi, Rausch, & Glauser, 2011b). Different patterns of nonadherence were observed, including mild, moderate, severe early, and severe delayed trajectories. Forty-two percent of the sample demonstrated near-perfect adherence over a 6-month period, suggesting that a subset of the population does not require adherence intervention (AI). Although behavioral interventions to improve adherence are needed for a majority of children with epilepsy, they have yet to be developed. Furthermore, the provision of AIs
Improving AED adherence in pediatric epilepsy is important for several reasons. Nonadherence is associated with increased morbidity (e.g., seizures), increased mortality, inaccurate clinical decision making, and high health care expenditures. For example, Bassili, Omar, Zaki, Abdel-Fattah, and Tognoni (2002) found that nonadherent children with epilepsy were 3.5 times more likely to have seizures compared with adherent children (Bassili et al., 2002). Furthermore, the most common triggering factor of status epilepticus in 31 pediatric epilepsy patients was AED nonadherence (Besli, Saltik, Erguven, Bulut, & Abul, 2010). Beyond poor seizure control, research has linked nonadherence to mortality in adults with epilepsy. A recent study involving 33,658 adults with epilepsy found that nonadherent patients had a threefold increased risk of mortality, after controlling for key medical variables (Faught, Weiner, Guerin, Cunnington, & Duh, 2009). Similarly, studies examining sudden unexplained death in persons with epilepsy suggest that patients had suboptimal AED serum levels (i.e., nonadherence) at autopsy (Leestma, Walczak, Hughes, Kalelkar, & Teas, 1989; Neuspiel & Kuller, 1985). Poor adherence also affects health care provider behavior, potentially leading to unnecessary increased dosages, discontinuation of medication believed to be ineffective (DiMatteo, Giordani, Lepper, & Croghen, 2002; Dunbar-Jacob & Mortimer-Stephens, 2001), and/or AED polytherapy. A recent study indicated that ~25% of children with new-onset epilepsy had uninformed AED changes (e.g., dose or AED change) because adherence was not rigorously assessed in clinical practice (Modi, Wu, Guilfoyle, & Glauser, 2012). Finally, nonadherence to AED therapy was associated with a higher incidence of emergency room visits, hospital admissions, motor vehicle injuries, and fractures (Faught et al., 2009), as well as higher inpatient, outpatient, and total health care costs in adults (Ettinger, Manjunath, Candrilli, & Davis, 2009). Overall, addressing nonadherence early in the course of treatment via adherence promotion interventions may prevent the negative consequences associated with AED nonadherence.

A recent Cochrane review of AIs in epilepsy identified six trials (Al-aqeel & Al-sabhan, 2011), with only one focused on children (Shope, 1980). Shope (1980) had a discussion group for mothers of children with epilepsy and compared AED serum levels between those randomized to the group treatment compared with Treatment-As-Usual (TAU). Results indicated better adherence scores based on serum levels in children of mothers from the discussion group. Limitations of this study include biased sampling (e.g., only 14 mothers attended the group), lack of an empirically supported adherence measure, and discussion group content not being well described. Similarly, limitations of the adult trials included lack of (1) randomized controlled clinical trials with attention-control groups, (2) objective adherence measures, and (3) long-term efficacy. While little progress has been made to date regarding interventions to improve adherence in pediatric epilepsy, adherence intervention research in pediatric diabetes, cystic fibrosis, and asthma has burgeoned in the past 10 years (Rapoff, 2010). These successful family-focused adherence interventions (Graves, Roberts, Rapoff, & Boyer, 2010; Kahana, Drotar, & Frazier, 2008) have been multicomponent and disease-specific (LaGreca, 1990; Wysocki et al., 2006) and have often focused on teaching problem-solving skills around barriers to adherence (DeLambo, Ievers-Landis, Drotar, & Quittner, 2004; Wysocki, Greco, Harris, Bubb, & White, 2001; Wysocki et al., 2000, 2006). Similar to other pediatric populations (Hommel & Baldassano, 2010; Modi et al., 2009; Modi & Quittner, 2006), typical adherence barriers in pediatric epilepsy include forgetting, children disliking the taste, oppositional behaviors, pill swallowing difficulties, and competing activities (Modi, Monahan, Daniels, & Glauser, 2010). Notably, few adherence interventions have been conducted with younger children with chronic diseases, for whom caregiver supervision is critical to disease management. By addressing adherence barriers and teaching problem solving around adherence before adolescence, we may be able to reduce the significant decline in adherence during adolescence.

The current RCT had two primary aims. The first aim was to test the feasibility and acceptability of a family-tailored AI focused on improving education and problem solving around adherence barriers for young children (2–12 years old) with epilepsy with demonstrated nonadherence. The second aim was to examine changes in adherence rates from baseline to postintervention for individuals in the AI and TAU groups, with the goal of informing future adherence intervention studies in epilepsy. We hypothesized that participants would report the AI as feasible and acceptable. In addition, it was hypothesized that participants in the AI group would demonstrate improvements in adherence from baseline to postintervention.
Method
Overview of Study Design
The current RCT was developed to pilot test the feasibility, acceptability, and preliminary efficacy of a family-tailored education and problem-solving AI for children with new-onset epilepsy (2–12 years) and their families. Each family was provided a Medication Event Monitoring System (MEMSTM) TrackCap (i.e., electronic monitor) to keep their prescribed AED and to use for the study duration of 4 months. Data from the MEMS TrackCap were downloaded 30 days after baseline (e.g., run-in period) to determine the study arm to which patients belonged. Participants with adherence rates <90% were randomized to one of two groups: (a) TAU or (b) AI. Similar to patients who had adherence rates >90% (Near-Perfect Adherence group), TAU participants were monitored for the study duration. AI participants received a four-session intervention protocol to improve AED adherence over an 8-week period using two primary strategies: epilepsy-specific education and teaching of problem-solving skills (see Table I). Postassessment measures were completed by all participants at the end of the 4-month study. Participants received a small compensation for their time and effort for each study visit, including assessment visits and intervention sessions. The protocol and consent forms were approved by the hospital institutional review board.

Participants
Children newly diagnosed with epilepsy, along with a primary caregiver, were approached for study participation from a new-onset seizure clinic at a pediatric children's hospital in the Midwest. Participants were between 2 and 12 years of age, diagnosed with epilepsy within the past 7 months, and prescribed one AED. To complete questionnaires and assent/consent forms, families had to read/speak English. Exclusion criteria included diagnosis of a nonepilepsy medical disorder requiring daily medication, a significant developmental disorder (e.g., autism), or the family living >90 miles away from the hospital.

Procedure
Recruitment
In collaboration with the epilepsy team, potential participants and their caregivers meeting eligibility criteria were identified by a trained research assistant with significant experience recruiting families with children with new-onset epilepsy. Recruitment occurred during routine clinic visits. The trained research assistant approached families, provided a thorough overview of the study, including study procedures, benefits, and risks, along with answering any questions. Caregiver/guardian participants provided written informed consent, and verbal assent was obtained from older children. Once consent/assent was obtained, caregivers completed baseline assessment questionnaires, and all families were provided a MEMS TrackCap to monitor adherence and were instructed to keep their prescribed AED in the bottle. Caregivers also completed several questionnaires, which were used during the AI (e.g., epilepsy knowledge, social problem-solving skills, epilepsy medication management), to measure feasibility and acceptability, and psychosocial outcomes (e.g., quality of life). With the exception of treatment acceptability and feasibility, these questionnaires were not analyzed for purposes of the current study.

Run-in Period
For the first 30 days of the study after baseline assessment, participants kept their AED in the MEMS TrackCap. Research assistants met families at their home or a convenient location after this period to download MEMS TrackCap data. Participants demonstrating a ≥90% adherence rate via the MEMS TrackCaps were placed into the Near-Perfect Adherence group, which was based on previously published adherence trajectories ( Modi et al., 2011 b) suggesting stable high adherence rates. This Near-Perfect Adherence group was monitored for the remainder of the study. Participants with adherence rates <90% were randomly assigned to one of two groups using a permuted block randomization with block size 2: TAU or AI. Stratification occurred based on baseline adherence data (e.g., stratification occurred based on baseline adherence data (e.g., stratification occurred based on baseline adherence data (e.g., baseline adherence for 1 month ≥80% [48 doses of 60] or <80%) to eliminate imbalance of participants across groups.

Near-Perfect Adherence and TAU Groups
Participants in the Near-Perfect Adherence and TAU groups were monitored for the remaining 3 months. Approximately 3–4 months after study enrollment, participants returned to clinic for clinical care. At this time, the MEMS TrackCaps were collected and downloaded. The only contact made with Near-Perfect and TAU groups was a reminder postcard to bring the MEMS TrackCaps to their next clinic visit (e.g., final study visit). The Near-Perfect Adherence and TAU groups served two purposes in the current study, although procedurally they were followed in a similar manner. The primary reason for monitoring the Near-Perfect Adherence group (≥90% adherence) was to confirm that adherence rates remained stable over time and the group did not require adherence promotion interventions. The TAU group (participants
with adherence <90%) served as a comparison group with the AI group to aid in determining AI preliminary efficacy.

**AI Group**

Families randomly assigned to the AI group received four intervention sessions over a 2-month period (see Table I). The first component of the intervention (Session 1) provided education on epilepsy treatment, AED adherence, and information on the family’s specific epilepsy treatment regimen (i.e., dosing schedule). Intervention targets included correcting misunderstandings about the epilepsy regimen and improving knowledge about the disease and reasons for treatment. Both caregiver responses on the Epilepsy Knowledge Questionnaire and the participant’s prescribed treatment regimen (based on medical chart information) were reviewed. Feedback on the participant’s adherence over the past month (e.g., run-in period) via the MEMS TrackCaps was also provided. This intervention session was designed to encourage active collaboration, build rapport with the family, and introduce the building blocks for the problem-solving sessions.

The second component of the intervention (Sessions 2–4) aimed to teach families a problem-solving approach for their identified AED adherence barriers. Both caregivers and their children actively participated in the problem-solving sessions. These sessions also empowered families by (1) giving them the skills necessary to identify specific problem behaviors, (2) identify realistic goals, and (3) develop an action plan to improve adherence. Families identified a specific adherence barrier, and then a problem-solving exercise was conducted. Families generated potential solutions to overcome the barrier, and then each family member participating in the session rated each solution. A final solution was agreed on by the family. The written action plan provided a detailed solution with specifics regarding when, where, and how the new solution should be implemented. A behavioral contract outlining the action plan was signed by all participants of the problem-solving session. The family was instructed to use the plan between intervention sessions. During this period, the interventionist contacted the family in between Sessions 2 and 3 via phone/e-mail to provide continued guidance and support as the family implemented the action plan. This provided families the opportunity to fine-tune the solution or renegotiate a new solution if the solution identified in Sessions 2 or 3 was not working well. A similar problem-solving format was used for Sessions 3 and 4, with a follow-up phone contact in between visits.

<table>
<thead>
<tr>
<th>Sessions</th>
<th>Session components</th>
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</table>
| Session 1 | - Education of epilepsy treatment and AED adherence  
- Review of patient’s prescribed treatment regimen  
- Review of Epilepsy Knowledge Questionnaire  
- Medication adherence feedback |
| Session 2 | - Medication adherence feedback  
- Identify one specific barrier/problem behavior to target for change  
- Introduction to problem-solving skills  
1. Problem definition: family identified an important adherence barrier  
2. Generating alternative solutions: family taught to generate several creative solutions  
3. Family decision making: family writes down solutions and systematically evaluate  
4. Implementation of new solution: family selects one solution to implement (action plan)  
5. Evaluation and renegotiation: follow-up phone call between visit |
| Session 3 | - Follow-up phone call 1 week later  
- Medication adherence feedback  
- Identify one specific barrier/problem behavior to target for change  
- Problem-solving exercise and detailed action plan  
- Follow-up phone call 1 week later |
| Session 4 | - Medication adherence feedback  
- Identify one specific barrier/problem behavior to target for change  
- Problem-solving exercise and detailed action plan |

Note. AED = antiepileptic drug.
Postintervention Assessment
Participants in the Near-Perfect Adherence and TAU groups completed postassessment measures ~3–4 months after study initiation. This typically occurred during their routine clinic appointment. If they did not return to clinic at this time, questionnaires were completed and sent back or picked up from the families’ homes. Adherence data were collected for the entire 4-month study period. Postassessment questionnaire completion for the AI group occurred at the last intervention session, and adherence data were monitored and downloaded 1-month after the end of intervention. AI was offered to all Near-Perfect Adherence and TAU group participants at the end of study completion.

Interventionist Training
The intervention was developed by two pediatric psychologists specializing in epilepsy. Master’s-level graduate students in clinical/counseling psychology programs at a local university and postdoctoral psychology fellows served as interventionists. Before providing the intervention, they participated in a rigorous training conducted by the intervention developers. The training included shadowing in our medical clinic, comprehensive didactics that reviewed intervention materials, role-playing exercises to practice intervention sessions, and live feedback to optimize intervention delivery. Each of the interventionists first shadowed one of the intervention developers before taking the primary lead as an interventionist. Interventionists also participated in weekly supervision regarding the cases, as well as ensuring treatment fidelity through review of the session.

Measures
MEMS 6 Track Cap (Aardex Group, Sion, Switzerland)
The MEMS TrackCap is an electronic monitoring system that measures the time and date a pill bottle and cap were opened. The MEMS TrackCap stores times and dates for a period of 36 months, and the data were transferred to a Windows-based computer. Daily adherence data from the MEMS TrackCap were downloaded at each study visit and obtained for the 4-month study period but not shared with the medical team. Parents were also asked whether there were any situations or times that the cap was not used to account for vacations, etc., and these periods were excluded from analyses.

Feasibility–Acceptability Questionnaire
Caregivers who participated in the AI were asked to complete a study-specific questionnaire assessing feasibility and acceptability of the AI. Similar questionnaires have been used by adherence researchers and provide critical information on ways to improve on the AI (Hommel, Herzer, Ingerski, Hente, & Denson, 2011). Content includes items related to the caregiver’s preferences in format, content, length, convenience of sessions, and caregiver use of skills and perceived impact of the intervention on outcomes. The questionnaire used several different 7-point Likert scales, including 1 = strongly disagree to 7 = strongly agree and 1 = too short to 7 = too long.

Medical Chart Review
Chart reviews were conducted to collect information regarding the treatment regimen, seizure type, and clinic appointments.

Background Information Form
The Background Information Form is a demographic questionnaire completed by caregivers that provides general information about the child’s age, caregiver work history, socioeconomic status, family history of seizures, history of seizures (e.g., type, who witnessed, when they occurred), and comorbid illnesses (e.g., learning disorders). Occupational data were used to calculate the Revised Duncan score (Stevens & Featherman, 1981) for each family, an occupation-based measure of socioeconomic status (Hauser, 1994). Duncan scores range from 15 to 97, with higher scores representing greater occupational attainment. For two-caregiver households, the higher Duncan score was used.

Statistical Analyses
Means, standard deviations, and frequencies were calculated for demographic, medical, and adherence variables. Although daily adherence data were used during AI sessions, adherence rates were calculated for the 30-day run-in period and the month after intervention (30-day post-AI) to examine pre–post differences in adherence for all individuals, as well as by group. The same time frame was used to calculate adherence rates for the TAU and Near-Perfect Adherence groups to ensure comparability. Adherence rates were calculated by taking the number of doses taken divided by the number of doses prescribed and then multiplying by 100. Adherence was capped at 100% to account for extra openings due to prescription refills. IBM SPSS Statistics version 20 was used to perform the proposed analyses.

Results
Participants
Of the 40 participants approached for study participation, 30 families agreed to participate and enrolled in the
current study. Four families were randomized to the AI, four were randomized to TAU, 19 exhibited near-perfect adherence during the run-in period, and three withdrew or did not return to the clinic for care (see Figure 1 for CONSORT diagram). Withdrawals occurred due to busy schedules or changes in the caregiver’s schedule and occurred before the randomization and/or run-in period. Demographic characteristics by group are presented in Table II. Statistical comparisons on demographic, medical, and baseline adherence data were not conducted owing to small sample sizes; however, group means for baseline adherence were arguably different from a clinical perspective (Figure 2d).

**Aim 1—Feasibility and Acceptability of the AI Treatment**

Of the four families who completed the AI, two included only the mother and child, one included the mother, father, and child, and one included the mother, child, and sibling. Ratings were high across the FAQ items for all AI families (see Table III). Regarding the session timing, location, and content, three of four families thought that just the right amount of information was covered in the right amount of time (e.g., 60 min); however, one family reported wanting additional time, wanting additional sessions, and feeling that the sessions were slightly inconvenient based on time/location. Families also indicated a preference for having sessions in Behavioral Medicine and Clinical Psychology instead of Neurology (M = 6.25 of 7, with 1 = strongly disagree and 7 = strongly agree). Comments from families on the FAQ included the following: “I thought the program was great the way it was,” “I learned ways and came up with plans from this program to help my daughter with her med,” “I will recommend the [AI] to any family dealing with medication taking or family members that deal with seizures,” and “We enjoyed the one-on-one attention and the way the whole family felt involved. Our son seemed to blossom from being included.” Finally, all four AI families completed all intervention sessions and assessments (100% retention), and children from all AI families actively participated in the intervention. Although TAU and Near-Perfect Adherence
families were offered the intervention, none of these families opted to accept the intervention after the study.

**Aim 2—Preliminary Efficacy of the AI on Adherence**

Adherence data were complete for all participants in the TAU and AI groups, with the exception of one TAU participant who was missing daily adherence data from day 78 to 120. Because sample sizes were small, we examined individual changes in adherence over time (Figure 2a–c). Descriptive data suggest two of the four AI families had large improvements in adherence but had low baseline adherence rates (i.e., 2 and 33%). One family had a baseline adherence rate of 83% but demonstrated improvements during the treatment period, which declined 1 month post-treatment. The other family had a baseline adherence rate of 89%, and adherence rates were variable throughout the treatment period, with further decline during the 1 month post-treatment. The mean percentage change in adherence from baseline to postintervention was 31.5 ± 32.9 for the AI group (Figure 2d).

In contrast, the TAU families had baseline adherence rates of 68, 80, and 83%, with two families demonstrating small improvements (2–7%) and one family exhibiting a 19% increase. The fourth TAU family, who exhibited 67% adherence during the run-in period, was excluded owing to missing post-treatment data. The mean percentage change in adherence from baseline to postintervention was 9.3 ± 8.7 for the TAU (Figure 2d).

The Near-Perfect Adherence families had baseline adherence rates >90%, based on our study design; however, 12 families demonstrated declining adherence, and 5 exhibited no change or minimal improvement in adherence. Five families fell <90% adherence by the post-treatment period.

**Conclusions**

The current study is the first pilot RCT using a multicomponent education and problem-solving adherence

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<table>
<thead>
<tr>
<th>Table II. Participant and Epilepsy-Specific Descriptive Statistics</th>
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<tbody>
<tr>
<td><strong>Characteristics</strong></td>
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</tr>
<tr>
<td>Child age (mean ± SD)</td>
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<tr>
<td>Child male (%)</td>
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<tr>
<td>Child race (%)</td>
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<tr>
<td>Caucasian: non-Hispanic</td>
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<tr>
<td>African American</td>
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<tr>
<td>Biracial: non-Hispanic</td>
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<tr>
<td>Biracial: Hispanic</td>
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<tr>
<td>Caregiver relation to child (%)</td>
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<tr>
<td>Mothers</td>
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<tr>
<td>Fathers</td>
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<tr>
<td>Other (e.g., female legal guardian)</td>
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<tr>
<td>Caregiver marital status (%)</td>
</tr>
<tr>
<td>Married</td>
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<tr>
<td>Single</td>
</tr>
<tr>
<td>Divorced</td>
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<tr>
<td>Socioeconomic status (mean ± SD)</td>
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<tr>
<td>Months since diagnosis (mean ± SD)</td>
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<tr>
<td>Epilepsy diagnosis (%)</td>
</tr>
<tr>
<td>Idiopathic localization related</td>
</tr>
<tr>
<td>Idiopathic generalized</td>
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<tr>
<td>Idiopathic unclassified</td>
</tr>
<tr>
<td>Cryptogenic localization related</td>
</tr>
<tr>
<td>Initial prescribed antiepileptic drug (%)</td>
</tr>
<tr>
<td>Carbamazepine</td>
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<tr>
<td>Levetiracetam</td>
</tr>
<tr>
<td>Ethosuximide</td>
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<tr>
<td>Valproic acid</td>
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<tr>
<td>Oxcarbazepine</td>
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<tr>
<td>Topiramate</td>
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Note. AI = Adherence Intervention; TAU = Treatment-As-Usual; SD = standard deviation.
promotion intervention for young children with newly diagnosed epilepsy and their families. Innovative aspects of the AI included targeting young children with newly diagnosed epilepsy and involving them in the family-based intervention with a primary focus on problem solving. All children actively engaged in the AI. For example, older children actively identified barriers and solutions to adherence, whereas young children contributed by modifying solutions (e.g., choosing rewards for a behavioral plan). In addition, our innovative study design focused on providing intervention to families who demonstrated nonadherence early in the treatment process. This is in contrast to a majority of published pediatric adherence intervention trials (Graves et al., 2010; Kahana et al., 2008), which offer intervention to all families without considering whether families actually need intervention. Finally, the use of objective electronic monitors to provide consistent feedback to AI families to identify real-time adherence barriers was novel and critical in developing targeted solutions that families could implement relatively quickly.

Study findings indicated that AI was feasible and acceptable for families of children with newly diagnosed epilepsy demonstrating nonadherence. Our 75% recruitment rate and 100% retention of AI families highlight that the study design (i.e., run-in period and 8 weeks of intervention) was viable to implement. The study design also capitalized on reducing burden for families by meeting them at their preferred date, time, and location for assessment and intervention. Regarding acceptability, families in the AI reported that they enjoyed the intervention, felt they received good information, and learned skills that improved both adherence and outcomes. Interestingly, when considering the perceived impact of AI on outcomes, all families reported a significant benefit to their child’s quality of life. This may be due to the individualized attention families received related to improving their adherence
behaviors and teaching generalizable problem-solving skills. In addition, the location, content, format, and timing of the intervention were perceived to be ideal by most families. No modifications to the intervention were suggested by the families, indicating that the next iteration of the trial continue with the same intervention content.

Results of the current study also indicated that the AI is promising but needs further design refinement and testing. Specifically, preliminary results indicate AI participants had a positive change in adherence rates from baseline to postintervention. This is likely driven by the two AI participants with low baseline adherence rates. Although these data are pilot in nature, results are consistent with other multicomponent adherence interventions in children with chronic pediatric conditions (Graves et al., 2010; Kahana et al., 2008). Benefits of AI compared with TAU likely included (1) reviewing family-specific knowledge about epilepsy and treatment, (2) ensuring families were aware of their individual prescribed treatment regimen, (3) providing adherence feedback via the MEMS TrackCaps, (4) providing education about AED adherence and its potential impact on the child’s seizures and quality of life, (5) identifying family-specific barriers to adherence, and (6) teaching problem-solving skills that includes all family members involved in the intervention that can then be generalized to future adherence barriers. Combined, these components of AI appeared to improve adherence for the families who participated in the intervention. Notably, adherence rates declined after the active intervention component, suggesting a potential need for booster sessions. Additionally, although we used stratification with baseline adherence rates of greater and less than 80% in the randomization procedure, the baseline adherence values appeared lower for the AI group. As a result, we may need to reduce this baseline adherence stratification rate to ensure equality in groups for future trials.

Although the study suggests good preliminary feasibility, acceptability, and efficacy, several limitations are noteworthy and will impact the next iteration of adherence promotion intervention in young children with newly diagnosed epilepsy. First, although 30 families were recruited for the study, surprisingly, only 8 families were randomized to TAU or AI. One reason for this is that the run-in period may yield higher rates of adherence due to reactivity (i.e., adherence behaviors may have been influenced by the monitoring itself), or initial high adherence rates that are typical when patients are newly diagnosed and initiating new therapies (de Klerk et al., 2003). Our previous longitudinal adherence data suggested that 42% of families would demonstrate near-perfect adherence within the first 6 months of AED therapy, not 1 month of data. The previous study also indicated that adherence declined over time for several families, which would not have been captured by the 1-month run-in period. In fact, our current pilot RCT data for the Near-Perfect Adherence group do suggest that adherence rates were declining over time. Post hoc analyses revealed that an additional 5 of 19 Near-Perfect Adherence families would have been eligible for

<table>
<thead>
<tr>
<th>Title items</th>
<th>N in the ideal range</th>
<th>Mean rating (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I liked the individualized format&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4</td>
<td>7.00 (0)</td>
</tr>
<tr>
<td>2. Amount of information&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4</td>
<td>4.25 (0.3)</td>
</tr>
<tr>
<td>3. Treatment session length (i.e., 60 min)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4</td>
<td>4.25 (0.3)</td>
</tr>
<tr>
<td>4. Number of sessions&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3</td>
<td>3.50 (1.7)</td>
</tr>
<tr>
<td>5. Total time commitment for treatment (i.e., 4 weeks)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3</td>
<td>3.50 (1.7)</td>
</tr>
<tr>
<td>6. I thought attending sessions was convenient&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>6.00 (2.0)</td>
</tr>
<tr>
<td>7. I used the education information I learned&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4</td>
<td>6.75 (0.5)</td>
</tr>
<tr>
<td>8. I used the problem-solving skills I learned&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4</td>
<td>6.50 (1.0)</td>
</tr>
<tr>
<td>9. Family’s ability to work together to solve problems improved&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4</td>
<td>6.75 (0.5)</td>
</tr>
<tr>
<td>10. Valued feedback from the MEMS TrackCaps&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4</td>
<td>7.00 (0)</td>
</tr>
<tr>
<td>11. I thought handouts were helpful&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4</td>
<td>7.00 (0)</td>
</tr>
<tr>
<td>12. Treatment helped improve my child’s adherence&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>6.25 (1.3)</td>
</tr>
<tr>
<td>13. Treatment helped improve my child’s seizures&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>5.00 (2.2)</td>
</tr>
<tr>
<td>14. Treatment helped improve my child’s quality of life</td>
<td>4</td>
<td>6.75 (0.6)</td>
</tr>
<tr>
<td>15. Treatment helped reduce my stress about managing epilepsy</td>
<td>3</td>
<td>6.25 (1.3)</td>
</tr>
<tr>
<td>16. Our family’s involvement in treatment was beneficial</td>
<td>4</td>
<td>7.00 (0)</td>
</tr>
</tbody>
</table>

Note: Ideal range is based on assumption that ratings in this range represent a high degree of acceptability for respondents.

<sup>a</sup>Ideal range = 5–7 on 7-point Likert scale.
<sup>b</sup>Ideal range = 3–5 on 7-point Likert scale.
randomization (adherence ≤90%) within the 3 months after the run-in period. These data suggest that in a future trial, it may be beneficial to have multiple opportunities for randomization or a longer run-in period for patients who demonstrate nonadherence later in the course of therapy.

Additional limitations include the small sample size, recruitment at a single site, potential group differences in demographic/medical variables at baseline, and lack of short- and long-term follow-up data. While several questionnaires were completed by families, due to the small sample size for those randomized, we were unable to examine group differences regarding potential mechanisms of action, including epilepsy knowledge, barriers to adherence, and social problem-solving skills. Furthermore, important psychosocial and seizure outcomes were not analyzed. Future research should focus on a larger multisite study design with longer follow-up periods to better understand mechanisms of change, the long-term efficacy of AI, and its impact on patient-reported and health outcomes. Finally, the control condition for the current trial was a TAU arm. In future studies, testing the AI with a more rigorous control group (i.e., attention control group) is likely warranted.

The current pilot study demonstrates that AI is feasible, is acceptable to families, and shows promising improvements in adherence for children with newly diagnosed epilepsy and their families. Developing an AI, such as our family-tailored education and problem-solving intervention, is an important first step in the field of pediatric epilepsy adherence, given the high rates of nonadherence to AED therapy early in the treatment process; the impact of nonadherence on seizure control, clinical decision making, and psychosocial outcomes; and the lack of empirically supported AIs for youth with epilepsy. The innovative study design (i.e., enrichment design, use of electronic monitors for assessment and treatment) requires further testing, and future AI studies can build from the current trial.

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References


