Adherence to Biobehavioral Recommendations in Pediatric Migraine as Measured by Electronic Monitoring: The Adherence in Migraine (AIM) Study

Ashley M. Kroon Van Diest, Cincinnati Children’s Hospital Medical Center
Rachelle Ramsey, Cincinnati Children’s Hospital Medical Center
Brandon Aylward, Emory University
John W. Kroner, Cincinnati Children’s Hospital Medical Center
Stephanie M. Sullivan, Cincinnati Children’s Hospital Medical Center
Katie Nause, Cincinnati Children’s Hospital Medical Center
Janelle R. Allen, Cincinnati Children’s Hospital Medical Center
Leigh A. Chamberlin, Cincinnati Children’s Hospital Medical Center
Shalonda Slater, Cincinnati Children’s Hospital Medical Center
Kevin Hommel, Cincinnati Children’s Hospital Medical Center

Only first 10 authors above; see publication for full author list.

Journal Title: Headache
Volume: Volume 56, Number 7
Publisher: Wiley | 2016-07-01, Pages 1137-1146
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1111/head.12836
Permanent URL: https://pid.emory.edu/ark:/25593/s3r8c

Final published version: http://dx.doi.org/10.1111/head.12836

Copyright information:
Accessed July 27, 2023 1:02 PM EDT
Adherence to Biobehavioral Recommendations in Pediatric Migraine as Measured by Electronic Monitoring: The Adherence in Migraine (AIM) Study

Ashley M. Kroon Van Diest, PhD, Rachelle Ramsey, PhD, Brandon Aylward, PhD, John W. Kroner, MS, Stephanie M. Sullivan, BS, Katie Nause, BS, Janelle R. Allen, MS, Leigh A. Chamberlin, RD, Med, Shalonda Slater, PhD, Kevin Hommel, PhD, Susan L. LeCates, MSN, Marielle A. Kabbouche, MD, FAHS, Hope L. O’Brien, MD, Joanne Kacperski, MD, Andrew D. Hershey, MD, PhD, FAHS, and Scott W. Powers, PhD, ABPP, FAHS

1Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital Medical Center
2Department of Pediatrics, Emory University School of Medicine
3Sibley Heart Center Cardiology, Children’s Healthcare of Atlanta
4Division of Neurology, Cincinnati Children’s Hospital Medical Center
5Headache Center, Cincinnati Children’s Hospital Medical Center
6Department of Pediatrics, University of Cincinnati College of Medicine

Abstract

Objective—The purpose of this investigation was to examine treatment adherence to medication and lifestyle recommendations among pediatric migraine patients using electronic monitoring systems.

Background—Nonadherence to medical treatment is a significant public health concern, and can result in poorer treatment outcomes, decreased cost-effectiveness of medical care, and increased morbidity. No studies have systematically examined adherence to medication and lifestyle recommendations in adolescents with migraine outside of a clinical trial.

Methods—Participants included 56 adolescents ages 11 – 17 who were presenting for clinical care. All were diagnosed with migraine with or without aura or chronic migraine and had at least 4 headache days per month. Medication adherence was objectively measured using electronic monitoring systems (Medication Event Monitoring Systems technology) and daily, prospective self-report via personal electronic devices. Adherence to lifestyle recommendations of regular exercise, eating, and fluid intake were also assessed using daily self-report on personal electronic devices.
Results—Electronic monitoring indicates that adolescents adhere to their medication 75% of the time, which was significantly higher than self-reported rates of medication adherence (64%). Use of electronic monitoring of medication detected rates of adherence that were significantly higher for participants taking once daily medication (85%) versus participants taking twice daily medication (59%). Average reported adherence to lifestyle recommendations of consistent non-caffeinated fluid intake (M = 5 cups per day) was below recommended levels of a minimum of 8 cups per day. Participants on average also reported skipping 1 meal per week despite recommendations of consistently eating three meals per day.

Conclusions—Results suggest that intervention focused on adherence to preventive treatments (such as medication) and lifestyle recommendations may provide more optimal outcomes for children and adolescents with migraine and their families. Once daily dosing of medication may be preferred to twice daily medication for increased medication adherence among children and adolescents.

Keywords
migraine; pediatrics; adherence; electronic monitoring

Introduction
Effective management of migraines requires adherence to treatment recommendations. Nonadherence to treatment recommendations is a significant public health concern, with approximately 50% of children and 65-90% of adolescents being non-adherent. Poor treatment adherence can result in unsatisfactory treatment outcomes, increased healthcare utilization, unnecessary changes to the treatment regimen, reduced cost-effectiveness of medical care, and increased morbidity. For pediatric migraine, biobehavioral treatment regimens are the current standard of care and often request that patients adhere to daily preventive medication, abortive medication at the onset of a headache, and specific, daily behavioral lifestyle recommendations. Lifestyle recommendations for migraine management include consistent intake of food (without skipping meals) and non-caffeinated fluid (on average 8-10 cups per day), physical activity of 30 minutes or more 3-5 times per week, and regular sleep schedules. For adolescents with migraine, treatment non-adherence may result in more frequent or severe migraines, increased migraine-related disability, unnecessary increases or changes in medication, and an increased number of healthcare visits.

No studies have systematically examined adherence to medication and lifestyle recommendations in adolescents with migraine outside of a medical or behavioral treatment clinical trial. Additionally, studies examining adherence within the context of a clinical trial have utilized subjective, self-report measures to assess medication and behavioral adherence. Novel and objective adherence assessment methodologies using technology exist and are critical to understanding the adherence patterns of adolescents with migraine. For example, Medication Event Monitoring System (MEMS®) TrackCaps have been used to provide an objective measure of medication adherence in a variety of pediatric chronic illnesses (e.g., cystic fibrosis, HIV, epilepsy, inflammatory bowel disease, stem cell transplant recipients) by providing information about the number of times a medication
bottle has been opened. In addition, personal electronic devices (PEDs; e.g., cellular telephones, iPod Touch™) have been utilized to capture in vivo assessments of health behaviors in other chronic illness populations. Use of these assessment technologies are very appealing to youth, can provide detailed data on health behaviors experienced in real-time, and allow participants to provide information in their own environment. These assessment technologies limit the potential for recall bias that can be associated with retrospective reports and have the potential to provide more accurate assessment of adherence in pediatric migraine, which in turn, can inform the development of migraine-specific interventions to improve adherence.

The purpose of this study was to utilize novel and increasingly objective data collection techniques to examine treatment adherence to medication and behavioral recommendations in a sample of newly diagnosed adolescents with migraine. Specifically, adolescents were instructed to use a MEMS® TrackCap to monitor their medication adherence and utilize a PED to report daily assessments of medication and lifestyle recommendation adherence. This study fills a critical gap in the pediatric migraine literature in several ways: 1) it uses innovative data collection methods to examine adherence to preventive medication and lifestyle behaviors in adolescents, 2) it establishes an objective report of adherence to preventive medication and a daily, prospective report of lifestyle recommendation in adolescents with migraine, and 3) it provides generalizable information to a clinical population engaged in routine clinical care (which complements recent data on adherence obtained in the context of those families who agree to participate in clinical trials).

**Methods**

**Participants**

Approval was obtained from the Institutional Review Board prior to beginning the study. Adolescents between the ages of 11-17 were recruited from the Headache Center at Cincinnati Children’s Hospital Medical Center (CCHMC). All participants were newly diagnosed with migraine and were recruited at their initial appointment with the Headache Center. Parents of adolescents who agreed to participate provided written informed consent and adolescents provided assent. Inclusion criteria required participants have 1) a primary diagnosis of migraine with or without aura or chronic migraine based on the International Classification of Headache Disorders, 2nd Edition (ICHD-II) criteria, 2) a migraine diagnosis by a headache specialist, 3) headache frequency of ≥4 headache days per month, and 4) be prescribed preventive migraine medication in pill format by a headache specialist. Participants were excluded from the study if they met any of the following criteria: continuous migraine (no pain-free periods for an entire month); developmental delay or impairment; any other diagnoses or conditions that would prevent patients from being suitable candidates (e.g., other chronic pain conditions, abnormal electrocardiogram, severe psychiatric comorbidities such as psychosis, bipolar disorder or major depressive disorder) for the study or would interfere with the medical care needs of the patient.
Materials and Measures

Devices—The iMigraine Application 1.1 was developed by the Divisions of Behavioral Medicine and Clinical Psychology and Bioinformatics at CCHMC. This technology allowed adolescents to wirelessly track daily reports of headaches and adherence to medication and lifestyle recommendations (e.g., dietary and fluid intake and physical activity) on an iPod Touch™ PED device. Adolescents completed a brief training session during their baseline clinic visit, involving the entry of fictional data to ensure user understanding of the iMigraine Application 1.1. Participants were asked to use the alarm function on the iPod Touch™ to set a time based on their schedule to prompt them to provide ratings once per day (ratings could be provided at any time during the day). Each daily assessment took less than 5 minutes to complete. The time stamped data was stored locally on the device and could be synced over wireless internet to a secure CCHMC server.

In order to assess for presence of headache using the iMigraine Application 1.1 via iPod Touch™ PED, participants were asked to indicate “yes” or “no” to the question of “did you have a headache today?”. For medication adherence, participants were asked to place a check beside the name of the medication(s) that they took today or check a box indicating that they did not take any medication today. Self-reported adherence to medication using the iMigraine 1.1 Application was determined by dividing the number of times participants indicated that they took their preventive medication each day divided by the 45-days to indicate the study duration.

Using the iMigraine Application 1.1, lifestyle recommendations of daily fluid intake, regular dietary intake, and physical activity were assessed by the following questions: “how many cups of non-caffeinated fluid did you drink today?”, “how many meals did you skip today?”, and “did you exercise for at least 30 minutes today?” Average rates of adherence were calculated as follows for the study period to coincide with recommendations given to patients in clinic: average daily fluid intake, average weekly number of meals skipped, average weekly number of times exercising 30 minutes or more.

The Medication Event Monitoring Systems (MEMS6® TrackCap) made by AARDEX Corporation was used to objectively monitor adherence to preventive medication for the current study. The MEMS6® TrackCap uses a micro-electronic circuit to register and store dates and times for over 3518 events (i.e., opening and closing of bottle) for a period of 36 months. Data from the MEMS6® TrackCap are transferrable to a Windows-based computer. Families were instructed on how to use the MEMS6® TrackCap bottle at the visit, and parents were required to transfer the original prescription of preventive migraine medication and any prescription refills to the MEMS6® TrackCap bottle. Families were contacted as a reminder to place the prescription into the MEMS6® TrackCap bottle. MEMS6® TrackCap data was downloaded to a laptop computer and the bottle and cap was collected by the study team at the 45-day follow-up visit. MEMS6® TrackCap is a commonly used device to assess adherence to oral medication, and has been correlated with data on pharmacy refill and serum assays.11-13,20,21 An objective adherence rate was calculated by dividing the number of times the cap was opened provided by the MEMS6® TrackCap by the number of times the patient was prescribed to take their medication. Given that MEMS data will track if
participants open the bottle more than the number of times they should be taking medication based on their prescription, data were capped at 100% to account for any extra openings; however, no extra openings occurred in the current study.

**Demographics**—Parents completed a demographics form including information about the participant’s race, ethnicity, parental education level, and household income level.

**Pediatric Migraine Disability Assessment Scale (PedMIDAS)**—The PedMIDAS is a 6-item instrument that assesses the impact of headaches on functioning in school, home, and social environments over the past three months. The PedMIDAS uses a total score I-IV grading scale of none (I; 0–10), mild (II; 11–30), moderate (III; 31–50) and severe (IV; >50). The measure shows excellent internal consistency and test-retest reliability, and has been shown to be sensitive to intervention effects. The total PedMIDAS score at baseline and post-intervention was used as an indicator of headache-related disability.

**Procedures**

Potential participants were identified during their initial evaluation in the Headache Center at Cincinnati Children’s Hospital Medical Center by a board certified neurology headache specialist based on clinical interview of the patient and family. After determining eligibility and obtaining informed consent and assent, participants completed the PedMIDAS and parents completed demographic information at the baseline study visit. Participants were enrolled in the study for a 45-day period to capture adherence to medication and daily lifestyle recommendations. For the duration of the study, participants were asked to provide one assessment each day about their headaches and adherence to medication and lifestyle recommendations using the provided PED. Participants were also given a MEMS6® TrackCap bottle to record information about their medication use. Instructions were provided to families on how to use the devices during the initial study visit.

Approximately 45 days after their baseline study visit, adolescents returned to the Headache Center at CCHMC for a standard care follow-up appointment and were required to return the PED and the MEMS6® TrackCap bottle at that visit. If participants did not return for a follow-up clinic visit, a separate research visit was scheduled with the family in order to complete the study. Participants were compensated for their time and travel at the baseline and follow-up study visits, and for daily completion of assessment on PED. Compensation for the completion of daily assessments was given to participants once the PED and the MEMS6® TrackCap were returned.

**Statistical Analyses**

All statistical analyses were completed using SPSS version 23.0. Use of technology data including malfunctions with the MEMS6® TrackCap, iPod Touch™, and the iMigraine 1.1 Application were examined. Descriptive analyses, including means, standard deviations, and ranges were conducted for each of the following: demographic information, headache disability via PedMIDAS, objective medication adherence using MEMS6® TrackCap, self-reported medication adherence and adherence to daily lifestyle recommendations (i.e., regular fluid and dietary intake and physical activity) using iMigraine 1.1 Application.
correlation was calculated between self-report of medication adherence using the iMigraine 1.1 Application and the MEMS6® TrackCap objective measure of medication adherence, and a t-test was conducted to determine if the mean of the two measures of medication adherence differed significantly. Additional t-tests were conducted to determine if there were significant differences in means of adherence between participants taking once-a-day or twice-a-day medications. A significance level of \( p > .05 \) was used in all analyses.

**Results**

**Participants**

The sample included 56 adolescents between the ages of 11 and 17 years (\( M = 14.6, \ SD = 2.0 \)). No attrition occurred for these 56 participants who enrolled in the study at their initial headache center visit. The majority of participants were female (71%; \( n = 40 \)) and White (80%; \( n = 45 \)). The majority of participants were taking amitriptyline once daily as their headache preventive medication (\( N = 34, 60.7\% \)), followed by topiramate twice daily (\( N = 20, 35.7\% \)), and divalproate twice daily (\( N = 2, 3.6\% \)). More detailed demographic information is provided in Table 1.

**Headache Characteristics**

Participants in the sample reported their average headache disability as 61.1 (\( SD = 41.4 \)) on the PedMIDAS at baseline, indicating severe disability related to migraine. Average headache disability from PedMIDAS scores at follow-up was 31.5 (\( SD = 23.2 \)), which was significantly lower than average baseline headache disability scores (\( p < .001 \)). The average number of headache days reported using the iMigraine 1.1 Application across the 45 day study period was 14.5 (\( SD = 12.2 \)).

**Use of Technology**

**MEMS6® TrackCap**—The majority of MEMS6® TrackCap bottles functioned as expected with no technological difficulties. One MEMS6® TrackCap malfunctioned during the study, resulting in unreadable data. One participant did not return their MEMS6® TrackCap; thus, no data are available for that participant given that data cannot be downloaded remotely for MEMS6® TrackCap.

**iMigraine 1.1 Application via iPod Touch™**—Two iPod Touch™ devices malfunctioned, resulting in unavailable data for two participants. All iPod Touch™ devices were returned at the end of the study. No reports of the iMigraine 1.1 Application malfunctioning were reported. On average, participants completed the entire iMigraine 1.1 Application log 31.5 days (\( SD = 12.36 \)) out of the 45 day study period (70% usage). The medication portion of the iMigraine 1.1 Application log was completed an average of 31.2 days (\( SD = 12.56 \)) for the 45 day period (69% completion of medication portion of the log).

**Adherence to Medication**

**MEMS6® TrackCap**—Average adherence to medication using MEMS6® TrackCap was 75% (\( SD = 25\% \), range 1 – 100%). Average adherence to medication via MEMS6® TrackCap for participants taking once daily medication (\( N = 34 \)) was 85% (\( SD = 20\% \), range...
= 33 - 100%), and 59% (SD = 24%, range = 1 - 81%) for participants taking twice daily medication (N = 22). The difference in medication adherence between these groups was significant, \( t(51) = 4.28, p < .001 \), with participants prescribed once daily medication having higher adherence than those who were prescribed twice daily medication.

**iMigraine 1.1 Application via iPod Touch™**—Average self-reported adherence to medication was 64% (SD = 31%, range = 7 - 100%). It is important to note that for the iMigraine 1.1 Application, participants were only asked to indicate if they took their preventive medication and were not specifically asked to indicate if they took both doses (for participants using a twice daily medication). Self-reported adherence to medication using iMigraine 1.1 Application for participants taking once daily medication (N = 34) was 74% (SD = 26%, range = 7 – 100%), and 66% (SD = 28%, range = 18 – 100%) for participants taking twice daily medication (N = 22). The difference between these groups on self-reported adherence using iMigraine 1.1 Application was not significantly different (\( t(51) = 1.04; p = .30 \)).

**Comparing MEMS6® TrackCap and iMigraine 1.1 Application**—Overall self-reported medication adherence via iMigraine 1.1 Application was significantly correlated with objective medication adherence from MEMS6® TrackCap (\( r = .429, p = .002 \)). Mean self-report of medication adherence via iMigraine 1.1 was lower than the mean medication adherence via MEMS6® TrackCap.

Comparisons of medication adherence between MEMS6® TrackCap and iMigraine 1.1 Application were also explored separately for participants that took medication once a day (amitriptyline) versus twice a day (topiramate and divalproate combined). Rates of medication adherence between MEMS6® TrackCap and iMigraine 1.1 Application were significantly related for participants taking a once daily medication (\( r = .68, p < .001 \)). The correlation between MEMS6® TrackCap and iMigraine 1.1 Application for participants taking twice daily medication was not significant (\( r = .25, p = .33 \)).

Given that the iMigraine Application did not ask participants if they took all of their doses of medication per day, medication adherence was also explored based on indications from MEMS6® TrackCap that medication was taken at least once per day for participants on a twice daily medication. The mean number of times medication was taken at least once per day for twice daily medication participants was 36 (out of 45 possible days). This mean was compared to the mean number of times twice daily medication participants indicated that they took medication each day via iMigraine Application (M = 32, SD = 12.01), and this correlation was not significant (\( r = .21, p = .41 \)). A t-test indicated that this difference was not significant (\( t(17) = -1.36, p = .19 \)).

**Adherence to Daily Lifestyle Recommendations**

Adherence to lifestyle recommendations of consistent fluid and dietary intake, and physical activity for migraine management were self-reported daily by participants using the iMigraine 1.1 Application. Based on data from the application, participants reported exercising 30 minutes or more 3.4 (SD = 2.03, range = .16 - 7) days each week. Participants
also indicated that they skipped 1.45 (SD = 1.22, range = 0 – 5.91) meals per week and drank 5.01 (SD = 2.97, range = 0 – 10.11) cups of non-caffeinated fluid per day.

**Discussion**

The current study is the first, to our knowledge, to objectively measure adherence to preventive medication and lifestyle behaviors for pediatric migraine treatment. Using electronic monitoring systems (MEMS6® TrackCap) to record date and time stamped records of medication use, average adherence to preventive migraine medication was 75%. Given that this is the first study to use electronic monitoring of medication in pediatric migraine patients, no comparisons can be made in terms of rates of medication adherence. However, previous studies using MEMS6® TrackCap to explore medication adherence among pediatric patients with other health conditions reported mean rates of nonadherence to medication between 50-90%,\textsuperscript{1,11,23} suggesting that rates of adherence to preventive migraine medication among adolescents in the current study may be similar to rates of adherence to medication in other pediatric populations.

When exploring rates of adherence to medication in participants taking a once a day medication versus a twice a day medication, participants taking once a day medication (85%) had significantly higher rates of adherence to medication than participants taking twice a day medication (59%). It should be noted that daily dosing was dependent on the medication prescribed with amitriptyline being prescribed once daily and topiramate and divalproate being prescribed twice daily. Although side effects of these medications are somewhat different, they are not significantly greater for one medication over the other;\textsuperscript{24,25} thus, it was not expected that side effects of any drug would influence rates of adherence. This difference suggests that it may be preferential to prescribe a once a day medication to adolescents for migraine prevention in order to increase adherence to medication.

In addition to the objective measure of medication adherence, participants provided a daily report of adherence to their preventive migraine medication, allowing for a direct comparison of objective electronic monitoring of medication adherence against a more subjective daily self-report of medication adherence. Electronic monitoring of adherence to medication reflected higher rates of adherence when compared with self-reported adherence to medication for the total sample, as well as for patients taking once a day medication only. This finding is inconsistent with previous research comparing MEMS6® TrackCap to self-reported measures of medication adherence in other pediatric health conditions, as previous studies have found that electronic monitoring of medication use typically reflects lower rates of adherence in comparison to self-reported use of medication, estimates by physicians, and refill records from pharmacies.\textsuperscript{26,27} Only patients taking twice a day medications self-reported higher rates of medication adherence via iMigraine 1.1 Application when compared to the objective MEMS6® TrackCap measure of medication adherence.

The current study is the first to report longitudinal, self-report of adherence to daily lifestyle recommendations in pediatric migraine treatment. Generally, lifestyle recommendations for migraine management include consistent dietary intake and intake of non-caffeinated fluid (on average 8-10 cups per day), at least 30 minutes of regular physical activity 3-5 times per
week, and regular sleep schedules.\textsuperscript{7} Based on self-reported data collected daily by the application, on average, adolescents in the current study meet the recommended amount of physical activity per week, but do not drink enough non-caffeinated fluids each day and continue to skip approximately one meal per week. These data suggest that pediatric migraine treatment could place more emphasis on adherence to lifestyle recommendations to potentially provide greater reductions in frequency and intensity of migraine. Sleep should be included in future studies to determine if adolescents with pediatric migraine are adherent to recommendations of regular sleep schedules.

A potential barrier to obtaining complete data sets in adherence studies is the malfunctioning of technological devices used to monitor adherence to treatment. Although rates of malfunction-related issues reported for devices was low (one MEMS6\textsuperscript{®} TrackCap, and two PEDs), they did result in lost data for those participants. This is comparable to previous data on malfunctioning MEMS6\textsuperscript{®} TrackCap which has reported rates of error resulting in missing data ranging from 0 to 24\%.\textsuperscript{20,27} Previous data are not available for malfunctions and loss of data from PEDs in the pediatric adherence literature. Future studies could also combine use of electronic monitoring systems with collecting serum levels to compare levels of active medications with objective measure of medication adherence.

The iMigraine 1.1 Application did not ask participants to report if they took all of the doses of their medication daily. This could limit accuracy of daily self-report of medication adherence for patients taking twice daily medication, who may indicate that they took their medication if they only took one dose rather than both doses as prescribed. Additionally, medication compliance using iMigraine 1.1 Application data was conducted using the 45 day trial period, assuming that participants did not take their medication on days that they did not complete the medication portion of the daily electronic log. However, the MEMS6\textsuperscript{®} TrackCap did allow for specific assessments of adherence between once daily and twice daily dosing. Future studies should re-evaluate measures of medication adherence in patients taking twice daily medications by asking participants to self-report taking all, half, or none of their doses of medication daily in longitudinal designs.

While the current study suggests that once a day medications may result in greater adherence to medication among pediatric migraine patients, it is important to note that while neither medication has significantly greater side-effects over the other, factors such as the type of side effects, size, and taste of the pills themselves may differ which could result in different rates of adherence. For example, amitriptyline has a smaller tablet size than topiramate or divalproate, making it easier to swallow and perhaps contributing to higher rates of adherence to amitriptyline. Additionally, while all medications are known to have potential side effects of increased symptoms of sad feelings, other side effects differ from one medication to another. Specifically, amitriptyline and divalproate may cause dry mouth and eyes, while topiramate may cause weight loss or decreased appetite and tingling in the fingers. Factors specific to each medication (other than dosing information) were not assessed within this study. Future studies could assess additional factors related to the medications (e.g., taste of pills, size of tablets, side-effects specific to each drug) as potential correlates of medication adherence in addition to dosing and number of times medication is taken each day.
Future studies on medication adherence among pediatric migraine patients could also include a comparison group that uses only self-report of medication adherence to compare with other patients who use only electronic monitoring via MEMS6® TrackCap, as well as a third group of participants who utilize both self-report and electronic monitoring. Such a study would help to further clarify differences in rates of medication adherence between self-report and electronic monitoring. Further, participants were not systematically asked to provide information on the ease of use of the iMigraine 1.1 Application within the current study. During the development of this app, this type of information was obtained and used to refine the technology. In future studies, it will be important to gather systematic information directly from participants using the application to determine ways to improve this form of self-reported monitoring of medication adherence, and potentially expand upon the application to allow it to be used to set specific goals and track progress towards goals for behavioral recommendations and medication adherence.

Another limitation of the current study is the size of the clinical sample used. Future studies utilizing larger sample sizes may be able to detect significant relationships between adherence to treatment and treatment outcomes such as headache days and disability.

**Conclusion**

This is the first study to provide objective measures of medication adherence, comparisons between self-reported and electronically monitored indices of medication adherence, and self-reported adherence to daily lifestyle recommendations among pediatric migraine patients using time-stamped electronic diary technology. Results indicate that adolescents adhere to their medication 75% of the time based on electronic monitoring. Surprisingly, rates of objectively monitored adherence were higher than self-reported rates of medication adherence. Adolescents taking once a day preventive migraine medication had higher objective levels of adherence than adolescents taking twice a day medications, suggesting that once a day medications may be preferred to twice a day medications in order to increase medication adherence. Moreover, for once a day dosing, MEMS6® TrackCap data and self-report were significantly correlated (but not for twice a day dosing). Adolescents also reported adhering to the lifestyle recommendation of regular physical activity, but reported lower than recommended levels of daily non-caffeinated fluid intake, and skipping meals rather than consistently eating three regular meals daily throughout the week. Results suggest that some adolescents have difficulty adhering to the medication and behavioral treatment recommendations made by healthcare providers. Future research should be conducted that will allow for self-reported medication adherence at the time in which the medications is taken and if necessary at multiple time points throughout the day. In addition, the development of technologies with the ability to transmit objective medication adherence data to health care providers in real time could be beneficial. Finally, interventions specifically focused on maximizing adherence to preventive treatments – be they medications, nutraceuticals, and/or cognitive behavioral therapy, as well as lifestyle recommendations, are needed to improve outcomes for children and adolescents with migraine and their families.
Acknowledgements
Cincinnati Children’s Hospital Data Core Center, Cincinnati Children’s Hospital Headache Center


Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCHMC</td>
<td>Cincinnati Children’s Hospital Medical Center</td>
</tr>
<tr>
<td>ICHD-II</td>
<td>International Classification of Headache Disorders, 2nd Edition</td>
</tr>
<tr>
<td>MEMS</td>
<td>Medication Event Monitoring System</td>
</tr>
<tr>
<td>PED</td>
<td>Personal Electronic Device</td>
</tr>
</tbody>
</table>

References

1. Rapoff, MA. Adherence to pediatric medical regimens. 2 ed. Springer; 2010.


Table 1
Baseline demographics and migraine-related disability

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (29)</td>
</tr>
<tr>
<td>Female</td>
<td>40 (71)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>45 (80)</td>
</tr>
<tr>
<td>Black/African-American</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Biracial or multiracial</td>
<td>4 (7)</td>
</tr>
<tr>
<td><strong>Preventive Medication</strong></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>34 (60)</td>
</tr>
<tr>
<td>Topiramate</td>
<td>20 (36)</td>
</tr>
<tr>
<td>Divalproate</td>
<td>2 (4)</td>
</tr>
<tr>
<td><strong>Parent Education</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Mother</strong></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>1 (2)</td>
</tr>
<tr>
<td>High school diploma</td>
<td>9 (16)</td>
</tr>
<tr>
<td>Some college/tech</td>
<td>22 (39)</td>
</tr>
<tr>
<td>College grad</td>
<td>13 (23)</td>
</tr>
<tr>
<td>Graduate degree</td>
<td>11 (20)</td>
</tr>
<tr>
<td><strong>Father</strong></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>1 (2)</td>
</tr>
<tr>
<td>High school diploma</td>
<td>12 (21)</td>
</tr>
<tr>
<td>Some college/tech</td>
<td>20 (36)</td>
</tr>
<tr>
<td>College grad</td>
<td>15 (27)</td>
</tr>
<tr>
<td>Graduate degree</td>
<td>7 (13)</td>
</tr>
<tr>
<td><strong>Household Yearly Income</strong></td>
<td></td>
</tr>
<tr>
<td>Under $20,000</td>
<td>4 (7)</td>
</tr>
<tr>
<td>$20,000 – 34,999</td>
<td>7 (13)</td>
</tr>
<tr>
<td>$35,000 – 49,999</td>
<td>7 (13)</td>
</tr>
<tr>
<td>$50,000 – 74,999</td>
<td>7 (13)</td>
</tr>
<tr>
<td>$75,000 – 99,999</td>
<td>7 (13)</td>
</tr>
<tr>
<td>$100,000 – 149,999</td>
<td>13 (23)</td>
</tr>
<tr>
<td>$150,000 or more</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (7)</td>
</tr>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>14.6 (2.0)</td>
</tr>
<tr>
<td>Variable</td>
<td>Total (N = 56)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td></td>
<td>N (%)</td>
</tr>
</tbody>
</table>

**Score for Migraine-related Disability**

| Headache Disability at Baseline $^d$ | 61.1 (41.4)    |
| Headache Disability at Follow-up $^d$ | 31.5 (23.2)    |

$^d$ Per Pediatric Migraine Disability Score (PedMIDAS)$^{22}$

*Headache: Author manuscript; available in PMC 2017 July 01.*