Brief Report: Assessing Adherence to Pediatric Antiretroviral Regimens Using the 24-Hour Recall Interview

Stephanie L. Marhefka,1 PHD, Vicki J. Tepper,2 PHD, John J. Farley,2 MD, MPH, John W. Sleasman,3 MD, and Claude Ann Mellins,1 PHD
1HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute and Columbia University of the City of New York, 2Department of Pediatrics, University of Maryland School of Medicine, and 3Department of Pediatrics, University of South Florida College of Medicine

Objective Examine the 24-hr Recall Interview (24RI) for assessing children’s antiretroviral medication adherence.

Methods Caregivers of 54 children with HIV (aged 2–12 years) completed a clinical adherence interview and the 24RI by telephone. Children’s viral load and 3-month pharmacy records were obtained.

Results Thirty-seven percent of children missed ≥1 dose of medicine over 3 days. In 22% of the samples, adherence varied across medications. The 24RI adherence scores (Frequency, Interval, and Dietary Adherence) were moderately reliable across the three interviews. Pharmacy refill rates were significantly related to viral load, and 24RI barriers were marginally significantly related to viral load.

Conclusions The 24RI, with its systematic, cued recall, and decreased focus on adherence, may reduce socially desirable responding compared to other self-report methods, and reporting adherence barriers may indicate adherence difficulty. However, the validity of the 24RI must be improved to make it a useful measure to include in an adherence assessment battery.

Key words antiretroviral therapy; HIV; patient adherence; patient compliance.

Antiretroviral medication (ART) has dramatically increased the life span of US children who were perinatally infected with HIV, such that many are living into adolescence and young adulthood (Brown, Lescano, & Lourie, 2001). The benefits of ART are only realized with high levels of adherence, which in turn prevent the development of opportunistic infections (San-Andres et al., 2003) and drug resistance (Mullen et al., 2002). Healthcare teams assess children’s ART adherence to determine when a regimen change or behavioral intervention is needed. Unfortunately, the commonly used 3-day recall of missed doses is highly subject to social desirability and does not consistently relate to viral load, a biomarker of disease progression (Farley, Hines, Musk, Ferrus, & Tepper, 2003). Electronic tracking caps may be more accurate but are expensive, cumbersome, and unrealistic for many families (Quittner, Espelage, Levers-Landis, & Drotar, 2000). Thus, the field is lacking inexpensive, cost-effective, reliable, and valid measures for routinely assessing ART adherence.

Borrowing from the diabetes literature, researchers adapted a diary recall method, the 24-hr Recall Interview (24RI; Johnson et al., 1992), to assess ART adherence among children and adolescents (Naar-King, Frey, Harris, & Arfken, 2005; Wiener, Riekart, Ryder, & Wood, 2004). In these studies, 24RI adherence was not related to ART adherence based on caregiver-report surveys (Wiener et al., 2004) or physician reports (Naar-King et al., 2005), yet 24RI adherence was significantly related to viral load, a biomarker of disease progression. The present study furthers that research by testing the hypotheses that (a) 24RI scores will be moderately reliable across the 3 days, (b) 24RI scores will moderately relate to viral load and pharmacy refill rates, and...
(c) 24RI barriers to adherence will relate to barriers to adherence reported during a clinical interview.

Method
Participants
Participants were caregivers whose children attended three pediatric HIV specialty clinics based in university teaching hospitals located in Florida and Maryland. We limited the limited participating caregivers to those whose children ranged in age from 2 to 12 years, due to developmental differences in medication management needs among infants and adolescents. Children of eligible caregivers were those (a) perinatally HIV infected, (b) prescribed the same ART regimen for ≥3 months, and (c) living with the caregiver for ≥1 month with plans to continue living with the caregiver for ≥3 months. Eligible caregiver–child dyads were asked to (a) participate in a study to help researchers and clinicians “understand what it is like for families with children who take medications,” (b) provide written informed consent in accordance with local Institutional Review Board approval, (c) grant written permission for accessing pharmacy refill information, and (d) complete a clinical interview. A clinic provider extracted from the medical record the most recent viral load before enrollment. Two weeks following the clinic visit, caregivers were contacted for 24RI interviews. Trained undergraduate and graduate students conducted all study interviews. Three months subsequent to enrollment, pharmacies provided 3-month refill histories.

Measures
Clinical Interview
During this interview, caregivers were asked the following: “What kinds of things make it hard for your child to get (medication name) like the doctor recommended?” and “What other things keep your child from getting (medication name) when and how the doctor suggested?” (Marhefka et al., 2004).

24-Hour Recall Interview
Modeled after the 24RI used to assess adherence to diabetes regimens (Johnson et al., 1992), this procedure includes three telephone interviews (two weekdays and one weekend) within a 2-week period. Interviewers enquire about details of the child’s previous day. Also, for this study, at the end of each interview, informants were asked to list “the things that made it difficult to follow the physician’s medical recommendations during the previous day” and “the things that kept them from following the recommendations exactly during the previous day.” Adherence scores derived from the 24RI are the following: (a) Frequency Adherence, the percentage of prescribed doses that were taken; (b) Diet Adherence, the percentage of received doses taken consistent with dietary specifications; and (c) Interval Adherence, the concordance between the reported number of hours between doses and prescribed number of hours between doses. Scores were computed for each interview and then averaged across the 3 interview days.

Pharmacy Refill History
Pharmacies were given pharmacy record release forms, and 3-month refill histories were obtained. Beginning with the first date medication was dispensed following enrollment, the intended number of days to the next refill (typically 30 days) was divided by the actual number of days to the next refill. Values >1 were scored as 100% adherent. If medication was dispensed only once within the 3-month period, the score was 33% adherent. If no medication was dispensed within the period, the score was 0% adherent.

Data Analyses
Wilcoxin-signed ranks tests examined differences in the number of barriers reported during the 24RI versus the
clinical interview. Reliability of Frequency, Interval, and Dietary Adherence scores across the 3 days of the 24RI was assessed with intraclass correlations. Kappa statistics, sensitivity, and specificity were calculated to assess the agreement of 24RI scores and clinical interview barriers with pharmacy refill rates and viral load of >400 copies/mL.

Results
Children (aged 2–12 years, M = 8) were primarily male (62%) and African-American (80%), had been prescribed ART for 6 years (SD = 3) and had a median viral load of 447 copies/mL. Caregivers (aged 22–73 years, M = 46) were mostly female (90%) and African-American (64%), with a median monthly income of $1,300. Caregivers were biological (58%), or adoptive parents (28%), or other relatives (14%).

24RI Descriptives
Mean 24RI Frequency Adherence was 93% (SD = 13) and did not differ between weekends and weekdays. Of those with 24RI data, 20 (37%) missed ≥1 dose of medication over the 3 days of the 24RI procedure. Of those with missed doses, 60% had inconsistencies across medications (e.g., in a given day, they received all doses of one medication but missed doses of another medication). For 18 children, adherence varied across 24RI days (e.g., both doses of medication were taken on one day, and another day, only one was taken). When taken, 13% of doses prescribed for two times per day and 19% of doses prescribed for three times per day were >2 hr early or late. Most children with medication-specific dietary instructions (93%) did not adhere to them. Reliability was moderate across the 3 days, with intraclass correlation coefficients (ICCs) as follows: Frequency ICC = .55; Interval ICC = .71; Dietary ICC = .68.

Twenty-eight caregivers (52%) reported barriers during the 24RI or clinical interview. There was a statistical trend for caregivers to report more barriers during the 24RI (n = 29) than during the clinical interview (n = 15; p = .075). Eighteen caregivers reported barriers during the 24RI, thirteen reported barriers during clinical interview, and only three reported barriers during both procedures. Qualitatively, barriers were similar except that only 24RI barriers included specific medication attributes (e.g., poor taste, pills are too big, and too many pills). Some caregivers reported that their child refused or resisted medications. Multiple caregivers reported that they or their child forgot; reasons for forgetting included being away from home and either not having the medication or forgetting to administer/take it, and departing from typical daily routines. Finally, caregivers reported that medication taking was not compatible with daily life, and children missed doses because they or their caregivers were sleeping or were distracted by other activities.

Agreement with Criterion Variables
Based on previous findings that show a relationship between various cut-points of adherence and virologic suppression (Farley et al., 2003; Van Dyke et al., 2002; Wiener et al., 2004), and given that data non-normality was not correctable with transformations, Adherence was categorized based on three different cut-points (≥80, ≥90, and =100%) for the following variables: 24RI Frequency, 24RI Dietary, and Pharmacy Refill. Results were similar across the three categorizations, except that only when the 100% cut-off was used did Pharmacy Refill agree significantly with viral load (κ = -.26, p < .01). Results based on an Adherence cut-off of 100% are presented here to be comparable with those of a previous study that examined 24RI adherence (Wiener et al., 2004). Interval Adherence was defined as receiving doses, on average, within 2 hr of the expected interval. Dietary Adherence was not included in agreement analyses because of extremely low rates (e.g., only three children were Adherent).

Most measures had good specificity (i.e., those Adherent based on the criterion were also deemed Adherent based on the indicator, Table I) and poor sensitivity (i.e., those non-Adherent based on the criterion

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<tr>
<th>Table I. Agreement Between Adherence Scores and Indicators</th>
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<tr>
<td>Pharmacy refill rate (100%)</td>
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<tr>
<td>Pharmacy refill rate (100%)</td>
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<tr>
<td>24RI frequency (100%)</td>
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<tr>
<td>24RI interval deviance (&gt;2 hr)</td>
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<tr>
<td>24RI barriers (Yes)</td>
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<tr>
<td>Clinical interview barriers (Yes)</td>
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<tr>
<td>Viral load (&gt;400)</td>
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<sup>a</sup>Kappa (p < .01).
<sup>b</sup>Kappa (p < .10).
were often deemed Adherent based on the indicator). Both 24RI barriers (κ = .21, p = .08) and clinical interview barriers (κ = .20, p = .08) tended to agree with viral load. Neither 24RI Frequency nor Interval Adherence scores agreed with viral load or Pharmacy Refill.

Discussion

This multisite study employed the 24RI to assess children’s ART adherence and barriers to adherence and compared findings with viral load, pharmacy refill rates, and barriers reported during a clinical interview. The 24RI procedure involved three telephone interviews within 2 weeks and resulted in three scores: Frequency, Interval, and Dietary Adherence, which were moderately reliable across the 3 days of the procedure. No differences were found between weekdays and weekends. Only pharmacy refill rates were significantly related to viral load, although clinical interview and 24RI barriers were marginally associated with viral suppression.

The 24RI revealed a high rate of nonadherence. Many children (37%) missed ≥1 dose of medication over 3 days, consistent with rates derived from electronic monitoring and pharmacy records (Farley et al., 2003; Watson & Farley, 1999). The number of children with missed doses is greater than that some studies have reported when using the PACTG procedure (Farley et al., 2003; Giacomet et al., 2003), which suggests that the 24RI may be more successful at measuring when doses are missed. However, 24RI Adherence was not significantly related to pharmacy refill or viral load. It may be inappropriate to compare measures that cover vastly different time periods—24RI covers 3 days over a 2-week period, pharmacy refill covers a 3-month period, and viral load is an aggregate measure reflecting multiple variables over a yet unknown time period. Variations in the patterns of adherence over time (Hill, Kendall, & Fernandez, 2003) may make such comparisons difficult. Also, problems such as excess medications stored at home may add error to pharmacy refill rates. Furthermore, the cohort was heavily ART experienced, and it is not clear whether full viral suppression was a reasonable goal of therapy because of previously acquired drug resistance (Hoffmann et al., 2002). Although in studies with even smaller sample sizes, Naar-King et al. (2005) and Wiener et al. (2004) found that concurrent viral load was associated with 24RI adherence, Naar-King et al. (2005) found that 24RI adherence was not associated with average viral load over 12 months, and Wiener et al. (2004) found that 24RI adherence was associated with viral load for one class of medications only. Together, these findings suggest that the relationship between 24RI adherence and viral load is tenuous, which is consistent with failure to establish concordance between the 24RI for diabetes and diabetes control (Johnson et al., 1992).

It is noteworthy that the 24RI procedure used in this study included three telephone calls over a 2-week period, although Naar-King et al. (2005) conducted only one interview, in person, and Wiener et al. (2004) scheduled dates and times for telephone interviews on 3 consecutive days. Without comparing electronic monitoring data for the same data collection periods, it is difficult to determine the validity of 24RI scores. Future studies should consider evaluating ways to improve the validity of the 24RI (e.g., caregivers complete six interviews instead of three) using electronic monitors for comparison and increasing the sample size.

Despite limitations, these results have implications for research and practice of adherence measurement. Twenty-eight caregivers reported barriers to adherence during either the 24RI or clinical interview, although only two did so during both procedures. Such variations in barrier reporting suggest that all barrier assessments are not equally effective and more research on barrier assessments may be informative. Also, variation in adherence across medication suggests that monitoring one medication only during electronic assessment (Farley et al., 2003) or asking global questions about adherence to all medications may provide deceiving results. Additionally, assessment of dietary adherence may be important for medication prescribers—especially as most children (93%) with regimen-related dietary instructions had difficulty adhering to them. Self-report measures often neglect these aspects of adherence, yet ignoring them may have negative health consequences. The primary concern is and should be that the medication is taken at all, yet it is also important that the medications are taken within certain parameters.

In conclusion, the 24RI procedure appears to be a moderately reliable measure of children’s ART adherence, and reported barriers to adherence may indicate adherence problems, although the validity of this method had not been well established. The systematic, cued recall of the child’s previous day, with decreased focus on adherence, potentially reduces response bias because of social desirability. Unique among available measures, the 24RI assesses adherence to diet and dosing intervals as well as to the prescribed number of doses. Although not explored in this study, the 24RI also offers an opportunity to learn about families’ daily activities, including those that facilitate or hinder adherence.
Administering the 24RI via telephone over 3 or more days would be ideal, yet clinicians might more realistically consider administering a single 24RI in person during routine visits. By relying on the recall of a single day, a clinician might obtain critical information about discrepancies between the prescribed regimen and actual regimen behavior; however, such an approach could result in a grossly inaccurate snapshot of adherence (or nonadherence) and thus should be undertaken with caution. More efforts are needed to improve and examine the validity and clinical utility of the 24RI as well as of other less-expensive and practical measures. To increase our understanding of adherence to pediatric HIV regimens, we must persist in improving our methods of assessment.

Acknowledgments

This research was conducted as the first author’s dissertation while she was at the University of Florida and was supported by a grant from the Children’s Miracle Network at the University of Florida and Shands Hospital. During the production of this manuscript, Dr Marhefka was supported by the Center Grant P30 MH43520 from the National Institute of Mental Health to the HIV Center for Clinical and Behavioral Studies, Anke A. Ehrhardt, PhD, Program Director. The first author gratefully acknowledges her dissertation committee (James R. Rodrigue, PhD, Samuel F. Sears, PhD, Alexandra L. Quittner, PhD, and Fonda D. Eyler, PhD) and her research assistants for their hard work on this project. Many thanks to Susie Hoffman, DPh, and to the participants of the HIV Center manuscript writing workshop for their helpful comments. Finally, we thank the study participants and the leadership and staff of the pediatric HIV clinics where the families were recruited.

Received May 31, 2005; revision received November 18, 2005 and January 31, 2006; accepted February 9, 2006

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