The Reliability of Reports of Medical Adherence From Children With HIV and Their Adult Caregivers

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Objective  To compare children’s reports of their medication adherence to those of their adult caregivers.  Method  Several indicators of medication adherence were assessed for 48 adult-child dyads. Kappa statistics were calculated as measures of agreement.

Results  Adherence problems were common, although the level of agreement between the child and the adult was quite low (kappas for adherence variables ranged from .05 to .32). Compared to adult-child dyads that agreed, dyads that disagreed tended to include older children who had more responsibility for managing their own medications.

Conclusions  Both researchers and clinicians would benefit from acquiring information on children’s adherence from multiple sources.

Key words  HIV; medication adherence; pediatric AIDS; adherence reliability.

The introduction of antiretroviral therapy has resulted in a significant decrease in morbidity and mortality in the pediatric AIDS population (Abrams et al., 2001; de Martino et al., 2000; Gortmaker et al., 2001). However, initial optimism about the efficacy of antiretroviral therapy has been tempered by an increasing understanding of the high level of adherence necessary for effective treatment and the difficulties involved in attaining such levels of adherence. While 80% adherence may be sufficient for most illnesses, a higher level of adherence may be crucial for HIV/AIDS management (Carpenter et al., 2000; Patterson et al., 2000). Even brief episodes of missed medication doses can permanently undermine HIV treatment, leading to reduced efficacy of and increased resistance to medications (Bangsberg et al., 2000; Chesney, Morin, & Sherr, 2000; Macilwain, 1997).

Many factors make attaining high levels of adherence a challenge: multiple medications, high pill burden, poor palatability, side effects, long-term toxicities, issues of disclosure, and simple forgetfulness. Across other chronic medical conditions, 40%–50% of adults and children typically do not use medications as prescribed (Ley, 1988; Matsui, 2000; Quittner, Espelage, levers-Landis, & Drotar, 2000). Although the literature is limited, the few studies of HIV-infected children’s adherence to antiretroviral medication indicate that nonadherence is a problem (Albano, Spagnuolo, Canani, & Guarino, 1999; Falkenberg, 1999; Martinez et al., 2000; Van Dyke et al., 2002; Weidle et al., 1998). Furthermore, the majority of children born with HIV disease are living in chronic poverty with limited resources and are affected by discrimination, family disruption and substance abuse, and inner-city stressors (Havens, Mellins, & Hunter, 2002), all of which can impair the families’ ability to manage the children’s illness, including the proper administration of medications.

One major barrier to measuring and ultimately improving adherence is the lack of any gold standard for measuring this behavior. A number of measurement strategies exist, including pill counts, electronic monitors, diaries, and interviewer-administered or self-report questionnaires (Chesney, Ickovicks, et al., 2000; Drotar, 2000; Matsui, 2000). Each of these methods has limitations and can provide different estimates of adherence (La Greca & Schuman, 1995; Rapoff, 1999; Steele et al., 2001).

The limitations of these strategies can be even more pronounced with children. For example, regarding pill counts, many children have difficulties swallowing pills and require liquid medication (if available). Electronic
monitors, or MEMS caps (Medication Event Monitoring Systems; also known as eDEM caps: electronic Drug Exposure Monitors), which record each time a pill bottle has been opened, are not currently practical with liquid medications. Furthermore, they overestimate adherence problems when patients prefill pill boxes. As a result, self-reports are commonly used in most research studies and clinical work. However, accurate measurement of adherence remains a challenge. Younger children are typically given their medications by a parent or other family member and may not even know their medication regimen or even their illness diagnosis (Mellins, Brackis-Cott, Dolezal, & Abrams, 2002). As children get older, they may assume more responsibility for taking their own medications and, in the transition, the role of the adult caregiver changes.

Rather than administering all of the medications, the adult might simply remind the child to take her or his medicine, check medications to determine whether the child has taken them, or continue to administer some, but not all, of the medications. Other people may be involved in the process: other family members, babysitters, home health aids, school nurses. In these situations several people may have different information, and it is not clear who, if anyone, is the most accurate reporter.

Given the complicated nature of the issue, collecting information on adherence from multiple sources has been recommended (Matsui, 2000), at a minimum, from the child and from his or her primary adult caregiver. However, the mixed responsibility for administering the medications, limited child knowledge of the regimen or even HIV diagnosis, the changing developmental stage of the child, and the issue of social desirability (some adults and children may feel social pressure and be reluctant to admit to nonadherence) may result in poor concordance between children and adults in their reports of adherence. To understand more about the quality of self-reported adherence in children infected with HIV disease, we devised this study to examine medication adherence in children with HIV and to assess the level of agreement between reports of adherence from the children and their adult caregivers. In light of the multiple challenges, we hypothesized that concordance would be difficult to establish and that agreement between the adults' and the children's reports would be low.

Method

Research Participants

Participants included families recruited from two pediatric HIV programs in northern Manhattan in 2000. Families were eligible if (1) the child had a confirmed diagnosis of HIV infection; (2) the primary caregiver was a birth parent, relative, or adoptive caregiver; (3) the child and his or her primary caregiver spoke English or Spanish; and (4) the child was between the ages of 3 and 13 years. Overall, we were able to interview 90% (77/86) of eligible families who were approached (96 children were eligible from both clinics; 10 were not approached because we had achieved our target sample size). Among the nine approached families who did not participate, six guardians refused and three guardians were too ill at the time. As a result, 77 families participated in the study. Interviews were conducted with all primary caregivers (n = 77) and children who were 7 years of age or older (n = 50).

For these analyses, we included participants for whom there were both child and caregiver reports of adherence to antiretroviral medications (n = 48). There were 27 families who were excluded because the child was too young (i.e., too young). Among the 50 children who were interviewed, 2 were not taking antiretroviral medications; thus, adherence data were not available. As a result, data are available on a total of 48 caregiver-child dyads. These 48 families did not differ from the other dyads in demographic characteristics, other than child age. Children did not need to know their HIV diagnosis to participate. Informed consent was obtained from each adult, and each child gave assent. The study received local institutional review board approval.

Measures

Demographics and Medical Data. Demographic variables included child and caregiver gender, age, and ethnicity; caregiver relationship to the child (biological or adoptive parent, other relative); and caregiver HIV status. Also available from the child’s medical charts were CD4+ cell count and percent, HIV RNA viral load, and CDC AIDS diagnosis. The determination of whether the child knew her or his HIV status was based on the caregiver’s report.

Child’s Adherence to Antiretroviral Medication. First, were medications missed, off schedule, or only partially administered in the past 2 days? For the caregiver interview, we modified a self-report procedure used by the Adult AIDS Clinical Trials Group (AACTG) (Chesney, Ickovics, et al., 2000) and more recently by the Pediatric AIDS Clinical Trials Group (PACT-G; Van Dyke et al., 2002). This instrument is based on previous research on adherence to medication regimens in clinical trials (Besch, 1955; Urguhart, 1991), and significant correlations between self-reported medication use on the AACTG measure and participant viral load have been found (Mannerheimer, Friedland, Matts, Child, & Chesney, 2000; Mellins et al., in press). Participants were asked to describe their child’s antiretroviral medication regimen (e.g., the names/colors/descriptions of all antiretroviral medications, pre-
scribed doses per day, prescribed number of pills/teaspoons/etc. per dose). They were then asked for each medication to report on the number of missed, partial, or off-schedule (late by 1 hour or more) doses for each medication per day, during the past 2 days. We selected two days to maximize accurate recall. A dichotomous variable was calculated that indicated whether the adult reported any missed, partial, or off-schedule medication in the past 2 days.

The child interview was structured differently based on cognitive/developmental differences and the fact that many children did not know the names of their medications or their HIV status. Adherence questions referred to all of their medications as a group. We asked them to report on whether they had taken all, some, or none of the medications that were supposed to take at different time points during the previous day: morning, afternoon, evening, and night. We also asked them the same questions about the day before yesterday. As with the adults, a dichotomous variable was calculated indicating whether there were any adherence problems in the previous 2 days.

Second, were medications missed in the past 2 days because the child refused to take them or the child “threw it up”? Both the adult and the child were asked how many times this had happened, and two dichotomous variables were calculated to indicate whether any medications were missed because of refusal or vomiting.

Third, were medications missed on the previous weekend? We asked both adult and child in a simple yes/no format.

Fourth, were medications missed in the previous week? Both child and adult were asked when was the last time the child’s medications were missed and responded using a 5-point response scale that ranged from never to within the past week. From these responses, we calculated a dichotomous variable to indicate whether the children had missed any medications in the past week.

Fifth, does the child have some responsibility for taking his or her own medications? The adults were asked whether the children was totally dependent on their adult caregivers for taking their medications or whether the children had minimal, some, or primary responsibility themselves. The children were asked about who was responsible for giving them their medications. For both the adult and the child, a dichotomous variable indicated whether the child had any responsibility.

**Data Analysis**

Kappa was calculated as a measure of agreement between the children and their caregivers for all six of the variables. This statistic measures the extent of agreement between two raters, adjusting for the amount of agreement expected by chance (Cohen, 1960). Landis and Koch (1977) have provided guidelines for interpreting the kappa statistic and consider kappas of .20 and below “slight” agreement; kappas of .21 to .40 “fair”; and kappas of .41 to .60 “moderate.” Additional analyses compare child-adult dyads with discordant adherence reports to dyads with discordant reports. T tests were used to compare the two groups on continuous variables; chi-square tests were used for dichotomous variables. McNemar tests were used to determine whether the children or their adult caregivers were more likely to report adherence problems.

**Results**

Table I describes the 48 dyads. Mellins et al. (2002) contains demographics on the total sample of 77 families (i.e., including those dyads that did not contribute to the analyses in this manuscript). Five children had CD4 counts below 200 and 8 had CD4 percents below 15, indicators of severe immunosuppression. The goal of antiretroviral therapy is to achieve undetectable viral load, which was the case for 25% of the children.

The six dichotomous adherence-related variables available from both the adult and the child were compared (see Table II). In 46% of the child-adult dyads, at least one of the pair reported adherence problems in the last 2 days, and 44% reported missing doses in the past week (the past week question does not consider partial or off-schedule doses, as the 2-day questions do). Child refusal and medication-related sickness were rare in the previous 2 days.

In general, the level of agreement was quite low. When considering missed, partial, or off-schedule medications in the last 2 days, we found that 38% of the adult-child pairs were in disagreement. Of the five variables that assess adherence problems, the highest level of agreement was for missed medications during the past week (κ = .32), although there was disagreement in 29% of the cases. Agreement was somewhat better, although still moderate, regarding whether the children had some responsibility for taking their own medications (κ = .42).

McNemar tests were conducted to examine whether children or adults reported nonadherence more often. Two variables approached statistical significance, with children being more likely to report nonadherence: whether medications were missed during the previous week and whether medications were missed on the previous weekend.

We compared adult-child dyads who disagreed regarding missed doses in the past 2 days, past weekend, and past week to dyads that agreed. They were compared on the child’s gender, age, responsibility for taking med-
indications, and knowledge of HIV status. Disagreement was more common when the child was a boy. For example, 41% of the boys disagreed with the adult regarding missed medications in the past week, compared to 19% of the girls. However, none of the gender differences was statistically significant.

Children who disagreed with the adult on these three adherence variables were older than those who agreed. This age difference was statistically significant for missed medications on the previous weekend, \( t(46) = 2.2, p = .03 \); there was a 1.3-year age difference between the two groups (\( M = 10.6, SD = 2.0 \) vs. \( M = 9.4, SD = 1.7 \)). There was also a marginally significant age difference for missed medications in the past week. Neither the adults’ rating of whether the child had some responsibility for taking his or her medications nor whether the child knew if he or she was HIV+ was related to adult-child disagreement on any of the three adherence variables. However, the child’s rating of responsibility for taking his or her medications was related to disagreement regarding adherence for the previous weekend and the past week. The children reported having some responsibility for taking their medications in 100% of the cases where there was disagreement regarding the past weekend, compared to 57% of those cases where there was agreement (\( \chi^2 p = .01 \)). Similar differences were found regarding the past week (\( \chi^2 p = .04 \)). These findings, combined with the age effects, suggest that, as the children get older and take on more responsibility for their medications, the adult is less aware of the child’s actual adherence, and, therefore, there is more likely to be adult-child disagreement on reports of the child’s adherence.

**Discussion**

Adherence problems were quite common in this population. In nearly half of the sample, either the adult or the child reported having medication problems in the past 2 days or having missed medications within the past week. This level of adherence is typical of pediatric populations with other chronic illnesses (La Greca & Schuman, 1995; Rapoff, 1999), and, thus, does not appear to be disease-specific. There was a general lack of concordance for adherence ratings between the children and their caregivers, which is also not specific to HIV (Matsui, 2000); 38% of the caregiver/child dyads disagreed about adherence problems in the past 2 days, and 29% disagreed about missing medications in the past week. Discrepancies may be due to insufficient knowledge of the regimen by one or both members of the dyad. Younger children may not know all of the details about their regimen and simply take whatever their caregiver gives them. Older children may have taken on more responsibility for their medications, so their caregivers may not monitor their behavior closely and therefore are unaware of medication problems. Also, child or adult participants may have wanted to give socially acceptable responses.

There are clinical and research implications of these findings. As noted in other pediatric conditions (Bender, Milgrom, Wamboldt, & Rand, 2000), it is not sufficient to
assess adherence levels based only on the child or the caregiver, and adherence problems may more likely be identified if both are interviewed. In a clinical setting, asking about adherence problems from both the child and the caregiver raises awareness for both about the proper medication regimen and potential barriers to adherence that they are experiencing. It also provides an opportunity to encourage the adult to monitor the child’s adherence even in situations where the child has primary responsibility for taking his own medications.

In research regarding adherence to HIV medications, these findings also illustrate the importance of multiple informants. Sometimes the child is aware of problems that the adult is not aware of and vice versa. One approach to resolving discrepancies in a research setting may be to have a joint interview with caregivers and children, following the individual ones, to discuss any discrepancies. First, if the discrepancies are resolved, the researcher obtains a more accurate assessment of actual adherence. Second, if qualitative data are collected regarding the discrepancies, something could be learned about the sources of inaccurate reporting. We speculate that discrepancies are sometimes due to lack of child or adult knowledge regarding adherence, as well as issues of social desirability. A joint qualitative interview would provide data to see how often this is the case or whether other factors are more relevant.

There are several limitations to this study. The relatively small sample may not be representative of all children who perinatally contract HIV. However, the sample was demographically similar to the general population of perinatally HIV-infected children in New York City, in which 91% are black or Hispanic and living in inner-city impoverished neighborhoods (NYC DOH Surveillance, 2002). In addition, we did not have an objective measure of actual adherence (electronic monitoring pill bottles, blood tests, etc.), and so were unable to determine which participant, the child or the adult, was providing the more accurate information. We cannot therefore determine who is the better source of adherence data if only one member of the dyad is to be assessed. However, until more objective measures of adherence are developed and commercially available for pediatric HIV studies (e.g., therapeutic blood monitoring, electronic monitoring devices for liquids, etc.), self-report will continue to be the primary mode of collecting adherence to antiretroviral data. Thus, a better understanding of the validity of such data is important. Another limitation is that, when assessing problems in the past 2 days, we asked the child and the adult somewhat different adherence questions due to developmental/cognitive considerations. The goal in research should be to get the most accurate data possible, and that will often require questions in a different form for the adults and the children. Unfortunately, this presents serious limitations for assessing interrater reliability.

In conclusion, studies on medication adherence in children should consider multiple sources of information regarding adherence. The children’s information is important but should be supplemented by data from their caregiver. Research is needed that attempts to identify the reasons for discrepancies between reports so that reliable assessments of adherence can be collected. Objective measures of adherence should also be developed, such as electronic monitoring devices more appropriate for the medications commonly administered to children. Finally, biological markers of medication in the body would be useful to validate various methods of assessing adherence among children.

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