ABSTRACT

Non-adherence with prescribed asthma treatment causes compromised treatment effectiveness, including greater morbidity, mortality, and health care utilization costs. As a result, there is an increasing interest in measuring patient adherence behaviors. Electronic monitoring devices offer a promising method for assessing patient adherence behavior patterns. The reliability of the Doser Clinical Trials (CT) (Meditrack Products, Hudson, MA), an inexpensive, pressure-actuated device that monitors metered-dose inhaler (MDI) usage, was evaluated in a field study of outpatient pediatric asthmatics. Canister weight and various Doser CT measures of patient medication use were compared to determine the reliability and usefulness of the device. Doser CTs were dispensed to 16 research subjects for use on corticosteroid MDIs over a period of several months. One Doser CT per month was dispensed to
each subject. Doser CTs were collected at 30–60 day intervals, with a total of 61 months of Doser CT data obtained across the subjects. MDI canister weights were monitored for a subset of 6 subjects. Usable Doser CT data were summarized and average adherence estimates were computed. Adherence estimates differed from one another and the adherence estimate, as measured by canister weight, was significantly higher than each Doser CT estimate. However, overall, the Doser CT showed adequate reliability as evidenced by high correlations among the Doser CT estimates of adherence and the existing gold standard of canister weight. The Doser CT is likely to be useful for monitoring MDI use in clinical care and research, potentially providing greater accuracy than the standard of canister weight.

Key Words: Asthma treatment adherence; Metered-dose inhaler; Doser CT; Measuring treatment compliance.

INTRODUCTION

Nonadherence with prescribed asthma treatment clearly causes compromised treatment effectiveness including greater morbidity, mortality, and health care utilization costs (1,2). As a result, there is an increasing interest in accurate measurement of patient adherence behaviors in contemporary health care. Traditional approaches for assessing patient adherence include diary cards, questionnaires, canister weights, and pill counts. However, these methods consistently overestimate patient adherence, often by large margins (3–9). Behavioral scientists often conduct treatment adherence studies with electronic devices because of the presumption that they will be objective and accurate (10–13). Electronic monitoring devices offer a promising method for assessing patient adherence behavior patterns given the detailed and objective information they provide. For example, such monitors can provide specifics on time of dosage ingestion and amount of ingestion. As a result, this detailed information allows conceptualizations of patient adherence patterns to develop beyond a simple dichotomy of adherence/nonadherence. Despite the promise of electronic devices for monitoring adherence, there are questions about the reliability of some of these devices, due to their tendency to underreport adherence and experience frequent failures (10,14). There are also concerns about the expense of some of the more elaborate models.

One promising electronic device is the Doser-Clinical Trials version (Doser CT-Meditrack Products, Hudson, MA). The accuracy of this inexpensive, pressure-actuated monitor of metered-dose inhaler usage has been demonstrated in a field study in which 91–96% agreement was obtained between the device and actual use (15). Despite impressive validity obtained in this study, the research design had limitations worthy of note. Most important, the study sample was comprised of clinic personnel who followed a specified protocol for actuating and recording daily usage. Hence, the performance characteristics of the Doser CT were defined under maximal conditions of adherence to a schedule, but not with patients who have asthma.

The current study was designed to assess the Doser CT in a clinical sample of children diagnosed with asthma, with the goal of examining the performance characteristics of the Doser CT in a pediatric outpatient sample. Doing so provides a closer measurement to a ‘‘real world’’ assessment of the device.

METHODS AND PROCEDURE

The participants of this study were 16 children (mean age=11.5 years, range 8–18 years) enrolled in a larger study of treatment adherence. The research protocol was approved by the National Jewish Institutional Review Board. Informed consent was obtained from participating parents and young adults who were 18 years of age. Informed assent was obtained from participating children. All subjects lived within the Denver metropolitan area and had been diagnosed with chronic asthma. Subjects were informed that the Doser CT kept track of medication use and were asked to sign an agreement confirming that they would use only the MDI to which the Doser CT was attached.

Two children in the sample were African-American, two children were Hispanic, and twelve children were Caucasian. On the Hollinghead 4-factor score of socioeconomic status (16), the sample was primarily middle class (Level I: 0%, II: 47%, III: 40%, IV: 13%, and V: 0%). The majority resided in a suburban setting (suburban: 74%, urban: 13%, rural: 13%). The average mother, father, and stepfather education was some college (14.5 years, SD=1.81, range=12–18 years;
13.6 years, SD=2.03, range=11–17 years; 14.5 years, SD=2.12, range=13–16 years, respectively). Two of the children were from families that were separated or divorced.

In order not to influence participant adherence behavior, Doser CTs were set in the blinded test mode to disable the display and auditory alerts. Doser CTs were collected at 30–60 day intervals, with a total of 61 months of Doser CT data obtained across all subjects. One Doser CT per month was dispensed to each subject, either through the mail or at a followup visit to the clinical research center. Subjects who received Doser CTs in the mail were asked to return used Doser CTs in an enclosed envelope on a monthly basis. Subjects who received Doser CTs during followup visits were asked to return Doser CTs every two months, at the end of their next followup appointment.

MDI canister weights were monitored for a subset of 6 subjects (a total of 31 canisters) in order to compare canister weight with medication actuations as assessed by the Doser CT. These 6 subjects were provided with canisters as part of the larger study. However, the remaining subjects in this sample received medication from their physicians as part of the larger study, and, therefore, those MDI canisters could not be weighed before they were dispensed.

Canister Weights were recorded before medication was dispensed to subjects and upon the return of the canisters to the laboratory. The conversion factors to transform Canister Weight changes to number of puffs were determined as follows. At least 5 (and up to 10) new MDIs of each medication type were weighed before and after being vigorously shaken for ≥5 seconds and discharged 10 times in succession with 5 sets of measurements taken on each MDI. The high and low weights for each individual MDI were discarded and the remaining 3 averaged. This is a standard weighting technique in analytic chemistry designed to arrive at the “true weight.” Canister weight variation obtained by the laboratory procedure is believed to be similar to the variation of canister weight due to MDI actuation by subjects.

The mean of weight changes for all individual MDIs within each MDI type divided by 10 provided the weight/puff conversion factors used. The resulting conversion factors in mcg/puff were: Aerobid, 69.0; Azmacort, 70.2; Beclovent, 90.2; Flovent 44, 85.7; Flovent 110, 87.4; Flovent 220, 81.6; Intal, 71.8; Tilade, 150.6; and Vanceril DS, 91.1.

Adherence was assessed by five different methods in order to 1) compare the accuracy of the various adherence measures, and to 2) determine the most reliable measure for assessing adherence.

Canister Weights were recorded before and after patient use. The change in weight was used to estimate the number of puffs of medication taken over the last 45 days, as described above. Canister weights were used as a benchmark against which to measure the other adherence measurements. Total Doser Count was calculated by summing the number of puffs of medication used over the last 45 days and dividing by the total number of puffs of medication prescribed. Raw Doser History Count was determined by summing the number of puffs of medication used during days that participants reportedly had Doser CTs in their possession and dividing by total number of puffs of medication prescribed. Adjusted Doser History Count was determined by truncating values, or limiting values of puffs of medication, to the prescribed doses per day, in an effort to exclude spurious recordings of Doser CT data. The Adjusted Doser History Counts were then calculated by dividing the truncated value, or shortened value, of the total inhalations of medication by the number of inhalations prescribed. Finally, No Use Days were calculated by summing the number of zero puff days and dividing by the number of days that medication use was recorded.

RESULTS

Eight percent of the Doser CTs failed for mechanical reasons, and one of them had recoverable data. Doser CT failures included a blank display screen, an unreadable display screen, an unreturned Doser CT battery failure, an error message stating that Doser CT should be replaced, or a display that recorded only a few days of use. The remaining usable Doser CT data were summarized for each subject and average adherence estimates were computed for various measures.

Effect of Collection Method on Adherence

A preliminary analysis was conducted to determine whether there were group differences in adherence rates for the two methods of obtaining Doser CTs (the group who mailed Doser CTs back to the lab versus the group who returned Doser CTs during clinic visits). There were no group differences in adherence rates when adherence was assessed by mean Total Doser Counts (F=.061, p=n.s.), Raw History Counts (F=.045, p=n.s.), Adjusted Doser History Counts (F=.086, p=n.s.), or No-Use Days (F=.842, p=n.s.). Furthermore, there were no group differences in the rates of
failed Doser CTs (chi square=1.98, p=n.s.). Hence, both groups’ data were pooled for subsequent analyses.

Comparison of Adherence Measures

Adherence estimates (Mean%±SD) were as follows: Canister Weight (72%±34), Total Doser Count (68%±33), Raw History Count (58%±31), Adjusted Doser History Count (54%±29), and No-Use Days (26%±29).

Rates of adherence varied depending on the method of assessment. Canister Weights resulted in the highest estimate of adherence with each Doser CT method reporting lower adherence rates compared with Canister Weights. In order to gain a greater understanding of the discrepancies among the various measures of adherence

![Figure 1](image)

**Figure 1.** Adherence estimates based on canister weight and total Doser CT count.

<table>
<thead>
<tr>
<th>N</th>
<th>Paired t-test</th>
<th>Spearman correlation</th>
<th>Intraclass correlation</th>
<th>95% confidence interval</th>
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<td>5.23*</td>
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<td>No-use days</td>
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</table>

*p<.01; **p<.001; ***p<.0001.
Figure 2. Doser CT time series data for “adherent” subject.

Figure 3. Doser CT time series data for “poorly adherent” subject.
and to illustrate those discrepancies, individual mean scores were plotted for both Canister Weights and Total Doser CT Count. Six subjects were selected to most clearly represent those differences. As shown in Fig. 1, the mean Canister Weights were consistently higher than mean Doser Counts for each subject. Thus, the Canister Weights consistently report greater MDI use in this sample of children.

Paired t-tests were performed to evaluate the difference in mean levels between canister weight and the various Doser CT estimates. All of the t-tests were significant with the exception of canister weight and Total Doser Count (Table 1). Additionally, correlations among adherence estimates based on Canister Weights, Total Doser Count, Raw History Count, Adjusted History Count, and No-Use Days were calculated using both Spearman’s Rho and intraclass correlations. Rank order correlations were selected due to the small sample size. Spearman’s correlations among the measures of adherence ranged from .94 to 1.0, interclass correlations among the measures ranged from .87 to .99, and correlations between measures of adherence and No-Use Days ranged from -.83 to -.97. These correlations indicate that all measures of adherence consistently rank order subjects’ level of adherence.

Extremes of Adherence Behaviors

Two individual Doser CT records were graphed to illustrate extreme examples of adherence behavior. In Fig. 2, it appears that in all but three of thirty days, the Doser CT recorded MDI use within one puff of this child’s prescribed dose. On three other days of the month, the child was at or within one puff of half of the prescribed dose. The pattern of recording MDI use within one puff of the prescribed dose or within one puff of half of the prescribed dose may be indicative of sources of error (discussed below) which occur when using the Doser CT to assess adherence.

Fig. 3 provides another example of a Doser CT record, illustrating the case of a child who demonstrates poor adherence with medication use. There are many No-Use Days, including an eight-day chain of zero use. These No-Use Days and the chains of zero days suggest that the child may have 1) not adhered to the prescribed dose, 2) used the study MDI without the Doser CT attached, or 3) used another MDI previously prescribed despite explicitly agreeing not to do so. In any event, the child was nonadherent with the study protocol. The few days of recorded medication use indicate that, most often, the Doser CT recorded medication use of one puff less than the prescribed dose. Thus, the child either took one puff less than the prescribed dose on a rather regular basis or, more likely, that the Doser CT underrecorded the child’s MDI use.

DISCUSSION

The Doser CT demonstrated adequate reliability as evidenced by the high correlations among Doser CT estimates of adherence and the gold standard of canister weights. Nonetheless, there were various sources of error inherent in Doser CT reports of medication use. Mean scores for each Doser CT measure (Total Doser Counts, Raw History Counts, and Adjusted History Counts) were consistently lower than mean scores for canister weights. Although these discrepancies may, at times, be caused by subjects using MDIs without the Doser CT attached, an examination of individual Doser CT records suggest that this is an infrequent occurrence. The more consistent finding that the Doser CT recorded one puff less than a prescribed dose or one puff less than half of the prescribed dose, may be related to the finding that the Doser CT does not always record an actuation when the medication is dispensed. Most likely, children with small fingers may have difficulty discharging the Doser CT properly. By pressing the Doser CT from the sides of the device without a finger on the recording diaphragm, one can dispense medication without the actuation being recorded. Furthermore, when children take two puffs of medication in quick succession, the Doser CT is able to record the second puff of medication only when at least one second lapses between the puffs. Hence, “double-puffing” may be another important source of underreporting error.

An additional source of error for the Doser CT relates to over recording of medication use, as there were times when the Doser CT recorded an actuation when medication was not being discharged by the subject. The majority of these errors occurred before the Doser CT was in the possession of the research subjects, most often as the Doser CT was prepared for distribution to a participant or as the Doser CT was mailed to individual subjects. Accordingly, we recommend that the time series of Doser CT data be limited only to days when the Doser CT is known to be in the possession of the research subject since errors clearly can arise in setting up and distributing data, despite careful handling.

Despite limiting data to the days in which the Doser CTs were in the possession of research participants, there remained occasions in this study when the device was in the subjects’ possession, yet still recorded actuations when the medication was not actually dispensed. These
scenarios may include 1) a participant who actuated the Doser CT when it was not attached to the canister, for example, when the Doser CT was transferred from one canister to another or when the Doser CT fell off and needed to be reattached; or 2) actuations when medication was dispensed but not taken, for example, when the device was actuated while it was transported in a pocket or backpack.

Additionally, finding an overuse of MDIs by the Doser CT may relate to subject adherence behaviors. A relatively frequent finding in Doser CT records were occasions when participants consistently took one puff over the prescribed dose. Many of these participants later told us that they had been instructed to discharge test puffs prior to inhaling their medication. As a result, Doser CT records would show one puff over the prescribed dose, or potentially one puff over half the prescribed doses, if only one dose of a BID dose was taken.

Another possible cause of the Doser CT overrecording MDI use may be related to a subject’s physician increasing a daily dose, without the knowledge of research personnel. As a result, the participant would be adherent in taking the prescribed dose, but the change in the prescription would not be taken into account when calculating adherence for that participant. Furthermore, participants may have increased their dose in response to becoming ill. In this manner, the Doser CT would show MDI use greater than expected, as expected usage was based on the doses provided by each subject’s physician at the start of the study.

Finally, Rand and colleagues (17) have identified a phenomenon of canister “dumping” in subjects from clinical trials. This phenomenon is defined as canister actuation of medication more than 100 times in a three hour period just prior to a scheduled return visit, when a research subject knows canisters will be weighed as a measure of medication adherence. Although it is possible that dumping could account for the Doser CT overrecording MDI use in this study, no records of increased MDI use coincided with followup visits, and there were no maximal daily history recordings (e.g., a daily recording of 99 puffs, the maximum “daily dose” that can be recorded in the two-place Doser history record) in the day prior to a scheduled visit. Although there were subjects who had medication discharges over and above their usual dosage just before a clinic visit, none approached 99; hence, it appears unlikely that dumping was an important source of Doser CT overuse error.

Despite these observed errors, the Doser CT is a useful and economical electronic monitoring device for evaluating adherence in field research and clinical care settings. Thus, the construct of adherence can move beyond a dichotomy of adherence/non-adherence as compared with using more traditional approaches. The device displays data about daily use of medication, number of “No-Use Days,” and amount of usage pre/post asthma exacerbations. The Doser CT can provide more thorough information about how and when individuals take the medication, how frequently individuals do not take medication, what type of individual patterns of nonusage may emerge, and how extended underuse of medication may precede asthma exacerbations. In this regard, the Doser CT provides data that moves clinicians and researchers toward more fully understanding the richness and variability of individual medication adherence behaviors.

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REFERENCES
