Monitoring nebulizer use in children: comparison of electronic and asthma diary data

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Background: Measurement of nebulizer medication adherence that relies on self-report of medication use is subject to recall bias and increased patient burden. Electronic monitoring of nebulizer medication use is relatively new technology and provides an objective measure of nebulizer use.

Objective: To examine levels of agreement for nebulizer use between self-report on diary cards and electronic monitor data in young inner-city children with asthma.

Methods: Of 221 enrolled children with persistent asthma, 157 (71%) provided 12 weeks of diary card and nebulizer monitor recordings that were matched by date across days and by patient. Concordance, sensitivity, specificity, and κ coefficients were calculated between self-report and electronic data.

Results: The children were predominantly African American (89%) and male (66%), with a mean age of 4.6 years. Their persistent asthma was categorized as mild (61%) or moderate to severe (35%). Concordance between diary and electronic data was 85%, with overreporting on diary cards noted on 15% of the total days. Sensitivity of the diary data relative to the electronic data ranged from 0.80 to 0.91 during the 12-week study. Diary return rates decreased from 75% during the initial 3 weeks to 44% at 12 weeks.

Conclusions: Electronic monitoring of nebulizer use provides a more precise measure of long-term medication use than does self-report on diary cards, and it is feasible for use in high-risk populations. However, diary cards seem to be a valid alternative for short-term monitoring of nebulizer use, resulting in only a slight overestimation of medication use.


INTRODUCTION

Asthma affects an estimated 4.8 million US children younger than 18 years, with a significant impact on the use of health expenditures.† Dead Despite the availability of advanced pharmacologic therapy, poor adherence to prescribed asthma medicines significantly contributes to increased morbidity in low-income children with asthma.§ Tobacco Measurement of medication adherence often relies on self-report of medication use, yet the validity and reliability of this information varies or is unknown.¶ Frequency of rescue medication use, a common adherence measure for controller medication use, is often based on self-report recorded on diary cards‖; however, overreporting of medication use increased patient burden, ie, having to record in a diary every day, has reduced the reliance on diary data alone for adherence measurement.¶,‖

Electronic monitoring of medication use, ie, objectively providing the date and time of each dosing event, has become the gold standard for validating medication adherence.¶,‖,‖,

The MEDILog (Westmed Inc, Englewood, CO) for metered-dose inhaler use,‡,† a medication event monitoring system (MEMS TrackCap or SmartCap; AARDEX Ltd, Union City, CA) for oral tablet medication use,‖ and the HaloLite Pediatric (Adaptive Aerosol Delivery technology; Profile Therapeutics PLC, Bognor Regis, England) for nebulizer use‖,‖,‖,‖ provide objective measures of medication adherence,‖ but they are not without risk of malfunction.‖,‖,‖,‖

Although electronic monitoring of nebulizer use has been used to compare medication adherence in young children,‖,‖,‖ no studies have validated self-report with electronic monitor data for nebulizer use. The objective of this study was to examine the sensitivity, specificity, and κ coefficients of nebulizer use based on diary records and electronic monitor data in a sample of inner-city children with asthma. We hypothesized that diary data recording would correlate with electronic monitor data of nebulizer use.

METHODS

Study Population

We enrolled 221 children aged 2 to 8 years with persistent asthma and their parents from university-affiliated pediatric practices serving inner-city children in Baltimore, MD, into a randomized clinical trial of an educational nebulizer intervention. The inclusion criteria consisted of (1) physician-diagnosed asthma, (2) asthma severity classified as mild to severe persistent based on national guidelines,‖ (3) use of a nebulizer for administration of at least 1 asthma medication,
(4) consent for electronic monitoring of the child’s nebulizer use, and (5) no other comorbid pulmonary disease. Children and their parents were recruited and followed up between October 1, 2001, and April 30, 2003. The study was approved by the institutional review boards of The Johns Hopkins University Medicine Institutions and the University of Maryland School of Medicine. Informed consent was obtained from all participating parents, and assent was obtained from children 7 years and older.

Study Design
Parents were interviewed at baseline regarding sociodemographic and health characteristics and their child’s nebulizer use. During the prospective study, all the children had an electronic monitor installed on their nebulizer to record nebulizer use for 12 weeks. Their caregivers were given instructions on how to complete asthma diary cards to record daily nebulizer use during the same period. At baseline, nebulized rescue medication use was predominantly albuterol (95%, 211/221) compared with 27% reporting a controller medication. Both medication types were monitored electronically and by diary card recordings. This article describes the validity of self-reported nebulizer use as recorded on diary cards relative to electronic monitoring nebulizer use data in a subset of 157 children with corresponding diary and electronic data during a 12-week study.

Asthma Diary Card Protocol
Asthma diary cards were developed using a simple checklist format, with 7 days of data on 1 diary card. Each day, the parent recorded on preprinted diary cards the number of times the child used the nebulizer that day. For days with no nebulizer use, the parent was instructed to record a “zero,” indicating no nebulizer use. Participants were instructed to mail in the asthma diary sheets every 2 weeks using the stamped, addressed envelope attached to a diary page in return for food coupons. Retrieving diary cards every 2 weeks limited recall of diary data to 2 weeks for diary responders who completed the diary cards at the end of a 2-week diary period. We excluded diary data from children who recorded fewer than 7 days of data during the 12-week diary period, resulting in a sample of 176 children (80%) with usable diary

![Diagram](image_url)
data for diary completion analysis (Fig 1). All days were categorized into 3-week blocks during the 12-week study. We then examined completion rates by 3-week periods.

Electronic Nebulizer Use Monitor

Electronic nebulizer monitors, developed by Hill-Rom Co Inc, St Paul, MN, recorded the date, time, and total length of each nebulizer use event. The compact monitor connects directly to the nebulizer electrical plug and requires no ongoing maintenance. Trained home visitors installed the monitors on the children’s nebulizers and instructed parents not to unplug the monitor, even when used outside the home. Monitors were retrieved and checked by the home visitor for downloading of electronic data at 3-month intervals. Home visiting nurses checked the air flow rate of every nebulizer for adequate nebulization and ordered replacement nebulizer devices when there were deficient flow rates. The monitors fit all the brands of nebulizer devices used by the families. All electronic monitors were returned to Hill-Rom for downloading of the data, and then they were sent to the investigators for analysis. “Bookmarks,” ie, the actual turning on of the nebulizer for 4 minutes or more, were inserted on every monitor before delivery and on retrieval to ensure accurate start and end dates for the electronic monitor, to verify that the monitor was working, and to affirm our confidence in the actual compliance rates reported.

Nebulizer use ranged from 0 to 8 times per day. An appropriate nebulizer session was defined as greater than 4 minutes to exclude sessions resulting from a child playing with the nebulizer switch. We excluded electronic recordings of 4 minutes or less and recordings of more than 120 minutes based on the monitor manufacturer’s recommendations. Most excluded sessions (86%) were less than 1 minute and were probably due to an electricity surge, per monitor manufacturer. Using the electronic nebulizer data, a “0” recording entry was defined as zero or no nebulizer use. Monitors with no recording for the 12 weeks were considered monitor failures (n = 17) and were excluded from the analysis, resulting in 204 children (92%) having usable electronic data (Fig 1).

Quality Control Measures for Nebulizer Electronic Monitors

A quality control audit of the electronic monitors was conducted on 26 in-house monitors (10% of the total monitors used in the study) by in-office use of the nebulizer. The electronic recordings were compared with written recordings of the date and time that each nebulizer was turned on and off. These monitors were returned to Hill-Rom, Co. for masked downloading. The failure rate of the quality control monitors, defined as a disparity between the electronic and hand-recorded data, was low at 15% (4/26) and is comparable to previous electronic monitor failure rates noted with the Nebulizer Chronolog (4%–19%) but higher than the 2% failure rate with the Doser (both from Meditrack Inc, Hudson, MA).

Statistical Analysis

Initially, diary card completion rates were calculated for all children in 3-week blocks across the 12-week study. Using the diary item “number of nebulizer uses per day,” we compared responses on the diary data (set as a binary outcome of “yes” or “no”) with the electronic monitor recordings for nebulizer use. The electronic monitor nebulizer use data were set as the gold standard. Concordance, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the κ statistic comparing diary records with electronic monitor data for nebulizer use were examined in a subset of children (n = 157) who had corresponding diary and electronic monitoring data across the 12-week study. The κ values of 0.61 to 0.80 were considered a good strength of agreement and of 0.41 to 0.60 as moderate strength of agreement. All analyses were conducted using the SAS statistical software system and STATA version 7.0.

RESULTS

Study Population

Of the 221 eligible children enrolled in the ongoing randomized trial, most were African American (89%) and male (66%); they had a mean ± SD age of 4.6 ± 2.04 years and reported Medical Assistance health insurance (80%). Most parents (76%) reported having a high school or college education, and 58% were employed. Most children were categorized as having mild (61%) or moderate to severe (35%) persistent asthma at baseline. At the time of enrollment, most children reported the use of a controller medication (80%), including nonnebulizer medications such as inhaled corticosteroids, mast cell stabilizers, leukotriene modifiers, long-acting β2-agonists, or xanthine derivatives. Only 38% of parents reported having an asthma action plan in the home. We compared diary completers with noncompleters for differences in the baseline characteristics of age, sex, race, asthma severity, and reported controller medication use. None of the differences between groups were statistically significant.

Description of Diary Data

For the 176 children who returned usable diary cards, the number of complete diary days per child ranged from 1 to 84 (mean ± SD, 63.2 ± 22.0 days). A total of 17,209 diary days were analyzed. Overall, the return rates for the diary data measuring nebulizer use decreased over time by study period: first period, 75%; second period, 62%; third period, 57%; and fourth period, 44%. Most diary card recording was for “no” nebulizer use (28%–47%). Recording of “yes” to nebulizer use decreased from 23% in the first period to 14% in the last period. Missing nebulizer use was low at 1% to 5% of days across the 12-week study.

Pattern of Nebulizer Use Based on Electronic Monitor Data

For the 204 children (92%) with usable electronic nebulizer monitor data, the nebulizer was primarily used for the deliv-
ery of rescue medications (95%, n = 194), with only 27% of children (n = 55) reporting nebulizer use for controller medications, ie, budesonide or cromolyn. The mean ± SD duration of a nebulizer session was 12.93 ± 8.5 minutes (range, 5–96 minutes). Overall, most nebulizer sessions (57%) lasted 10 to 30 minutes. On days with multiple nebulizer use, the mean ± SD duration between nebulizer sessions was 6.86 ± 5.1 hours. Most electronic monitor days indicated “no” use of the nebulizer (66%), followed by 1 and 2 times a day (12.3% and 12.5% of days, respectively). Monitor failure occurred in 17 monitors.

Concordance of Diary and Electronic Monitor Use

Overall, the concordance on diary and electronic monitor use of the nebulizer was high at 84.7% agreement for use and nonuse of the nebulizer (n = 157) (Table 1). The κ coefficient for diary and electronic monitor data was 0.61 (95% confidence interval, 0.59–0.63; z = 56.9; P < .001). Over-reporting of nebulizer use occurred in 15% (1,007/6,962) of the total days. Mean sensitivity, specificity, PPV, and NPV, using the electronic data as the gold standard, are given in Table 2. When missing electronic data were excluded, the range of sensitivity, specificity, and NPVs for the self-report diary nebulizer use data was high (0.80–0.97), and PPV had a lower range (0.53–0.64). Only the mean sensitivity for diary self-report of nebulizer use slightly decreased when missing nebulizer diary entries were set to zero use rather than excluding the missing electronic data (Table 2). Sensitivity for diary data increased and specificity decreased across the study periods. The PPVs remained constant during the first 3 study periods but decreased in the fourth period. In contrast, the NPVs showed little variation during the study.

**DISCUSSION**

Our results indicate that electronic monitoring of nebulizer medication administration is superior to self-report on diary cards for an extended period of 12 weeks. Self-report data showed reasonable concordance with electronic data in the initial 3 weeks and good sensitivity and specificity during the entire 12 weeks. However, increasing rates of missing data by 12 weeks limited its usefulness in nonreturned diaries. This study is unique in that it is one of the first studies to demonstrate the feasibility of using electronic monitors for nebulizer use in an underrepresented, high-risk population, ie, inner-city children with asthma. Overreporting of nebulizer use on diary cards was infrequent, but this may reflect the fact that the diary data were limited to a binary measurement of nebulizer use (ie, use or nonuse) and did not include the number of times the nebulizer was used each day for comparison with the electronic data.

This study had a low equipment failure rate (8%, 17/221). Quality control procedures, including our bench quality control study and bookmarking every electronic device, make us confident that the concordance rates reported are accurate and not due to equipment failure. Diary card return rates decreased significantly, from 75% during the first 3 weeks to less than half of study days by 12 weeks, consistent with peak flow meter manual recordings in inner-city children with asthma, which also decreased markedly by 3 weeks.11 Our results suggest that the optimal length of a health diary is 3 weeks when used with high-risk populations. More extensive use of self-reporting may be of limited validity in chronically ill patient populations32 unless concurrent electronic monitoring is conducted. We cannot determine whether the low diary

### Table 1. Comparison of Corresponding Days of Diary (Self-report) and Electronic Monitor Use of the Nebulizer

<table>
<thead>
<tr>
<th>Nebulizer use</th>
<th>Diary data response, d</th>
<th>Electronic monitor response, d</th>
<th>Agreement, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2,548</td>
<td>1,793</td>
<td>1,541</td>
</tr>
<tr>
<td>No</td>
<td>5,673</td>
<td>6,428</td>
<td>5,421</td>
</tr>
<tr>
<td>Total</td>
<td>8,221</td>
<td>8,221</td>
<td>6,962</td>
</tr>
</tbody>
</table>

### Table 2. Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) for Diary Data by 3 Week Periods

<table>
<thead>
<tr>
<th></th>
<th>Weighted mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Period 1 (n = 133)</td>
</tr>
<tr>
<td></td>
<td>(weeks 1–3)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>0.89 (0.87–0.91)</td>
</tr>
<tr>
<td></td>
<td>0.86 (0.84–0.89)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>0.84 (0.83–0.86)</td>
</tr>
<tr>
<td></td>
<td>0.86 (0.84–0.87)</td>
</tr>
<tr>
<td>PPV</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>0.64 (0.62–0.66)</td>
</tr>
<tr>
<td></td>
<td>0.64 (0.62–0.66)</td>
</tr>
<tr>
<td>NPV</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>0.96 (0.96–0.97)</td>
</tr>
<tr>
<td></td>
<td>0.95 (0.95–0.96)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
return rate at 12 weeks was due to diary fatigue or decreased nebulizer use across time owing to improvement in the child’s asthma. Our respondents achieved consistently high sensitivity across all study periods, suggesting that parents were accurately recording nebulizer use across all study periods. The sensitivity of diary reports was the highest during the last study quarter, suggesting that the validity of self-reported nebulizer use on the diary was highest when reported by the most compliant diary respondents. The relatively low PPV suggests that some parents may have overestimated their child’s nebulizer use on the diary, consistent with our 15% overreporting rate.

The mean length of nebulizer use in our study (12.9 minutes) was comparable to previous nebulizer electronically recorded treatment times (mean, 7.5 minutes; range, 2.5–21.8 minutes). Nebulization delivery or performance is affected by diluent volume, aerosol flow, nebulizer brand, and nebulizer type. Malfunctioning nebulizers may put children at risk for inadequate delivery of asthma medication. This suggests that home nebulizer function, including flow rate and technique, should be evaluated, in either the clinic or the home, so that clinicians can be assured that the prescribed dose of aerosolized medication is available to the patient.

This study has several limitations. We cannot verify concurrent metered-dose inhaler delivery of medication or confirm the type of medication delivered by the nebulizer. Parent self-report indicated that most nebulizer use was for β-agonist medications. Comparisons between the electronic and self-report nebulizer use data were limited to binary outcomes, ie, the use or nonuse of the nebulizer. Because time of use was not recorded in the diary, we cannot examine concordance for dosing intervals of nebulizer use, a more absolute reflection of the level of agreement between electronic and self-report data. Concordance would most likely decrease if the dosing interval were recorded in the diary and compared with electronic data. Nevertheless, we believe that comparing any use to nonuse provides an overall snapshot of the validity of self-report on diary cards. We also cannot determine the timing of diary recording to examine for backfilling, which may threaten the validity of the diary data. We attempted to control for backfilling by collecting the diary records every 2 weeks; however, more frequent retrieval may further decrease the chance of backfilling in high-risk populations. Last, the electronic monitoring of adherence in this study was unmasked, and the families were aware of the function of the monitoring devices. This known monitoring may have had an initial effect on the accuracy of self-report; however, studies of electronic monitoring suggest that the influence of unmasked electronic monitoring on behavior is small and transitory.

In conclusion, electronic monitoring of nebulizer use provides a more precise measure of long-term medication use than does self-report on diary cards, and it is feasible for use in high-risk populations. However, diary cards seem to be a valid alternative for short-term monitoring of nebulizer use, resulting in only a slight overestimation of medication use.

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