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Early View

Research letter

A three-months period of electronic monitoring can provide important information to the healthcare team to assess adherence and improve asthma control

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A three-months period of electronic monitoring can provide important information to the healthcare team to assess adherence and improve asthma control

Anja Jochmann[1,3], Luca Artusio[1], Jakob Usemann[3,4], Angela Jamalzadeh[1], Andrew Bush[1,2], Urs Frey[3], Louise J. Fleming[1,2]

1 Department of Respiratory Paediatrics, Royal Brompton Hospital, London, UK

2 National Heart and Lung Institute, Imperial College London, UK

3 University of Basel, University Children's Hospital (UKBB), Basel, Switzerland

4 Division of Respiratory Medicine, University Children's Hospital Zurich, Zurich, Switzerland; University of Basel, Basel, Switzerland.

Corresponding Author

Dr Louise Fleming

Respiratory Paediatrics

Imperial College, London

Royal Brompton Hospital

Sydney Street

London SW3 6NP

l.fleming@rbht.nhs.uk

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Extract

Electronic monitoring of adherence to inhaled steroids is essential for the identification of severe asthma. During a short monitoring period some children have improved control, likely due to improved adherence; whereas others remain poorly controlled with poor adherence. Adherence does not change significantly after a second period of electronic monitoring; whether or not feedback is given. A single monitoring period is sufficient to determine the patient`s adherence and impact on asthma control and hence, guide future management.

To the Editor

Poor adherence to inhaled corticosteroids (ICS) results in poor asthma control, asthma attacks and increased healthcare costs [1, 2]. Measuring adherence using electronic monitoring devices (EMD) is more accurate than self-report, prescription refill data or canister weight [3-5].

Asthma attacks, hospital admissions and asthma morbidity are reduced in patients with improved adherence after a period of electronic monitoring [6, 7]. However, most children have suboptimal adherence despite being electronically monitored [8]. In our previous observational study we electronically monitored adherence in asthmatic children over three months and checked their asthma control variables before and after monitoring. Those with good adherence (≥80%) during a period of electronic monitoring had improved lung function, inflammatory markers and quality of life after monitoring. We also identified four groups of children defined by asthma control and adherence and described management strategies for each group. For example, those with good adherence and ongoing poor control should be considered for a step up in therapy, such as addition of a biologic [8].

In this proof-of-concept study we compared adherence and asthma control over two monitoring periods in two groups of children: those given feedback on their adherence after the first monitoring period; and those who had two monitoring periods without any intervention. We hypothesized that improvements in asthma control achieved by electronic monitoring would be sustained over a second monitoring period; and that in those whose adherence was poor, adherence would improve between the first and second monitoring period after feedback. This is a small cohort but the largest time series to our knowledge comparing electronically monitored adherence in children with asthma over two monitoring periods.

Sixty children, aged 5–17 years, with asthma diagnosed on conventional criteria as previously described [9] were prospectively recruited from the outpatient department of the Royal Brompton Hospital, London. Thirty-five children had taken part in our previous study [8] and were recruited for

a second period of electronically monitoring adherence. They received feedback on adherence and measures of asthma control following the first period of monitoring. The median time between the two monitoring periods was 3.9 months (IQR: 2.3–5.7).

Twenty-five patients were newly recruited for two consecutive periods of electronic monitoring without any such feedback after the first period. They had no time interval between the first and the second monitoring period. At recruitment, after the first monitoring period (follow-up 1 visit) and after the second monitoring period (follow-up 2 visit) assessments were carried out in both study groups.

Ten patients (17%) were excluded due to technical problems because we were unable to download the Smartinhaler data. Fifteen patients (28%) dropped out during the course of the study (7 lost their Smartinhaler; 7 did not return to clinic and one withdrew). There were no significant differences in age, sex, asthma severity, treatment and comorbidities between the protocol population and those lost to follow-up (data not shown).

Duration of follow-up was variable because research appointments were combined with routine clinic appointments (which, to minimise hospital visits, are scheduled quarterly according to the family's availability).

The study was approved by the Regional Ethical Committee (NRES Committee London-Westminster, registered with clinicaltrial.gov (NCT02252289)). All carers gave written informed consent and the children gave age-appropriate assent.

The following assessments of asthma control were carried out at recruitment, at follow-up 1 and follow-up 2 visit: the Asthma Control Test (ACT) [10] for children aged ≥12 and the Childhood Asthma Control Test (cACT) for children <12 years [11], spirometry, bronchodilator reversibility (BDR) testing, exhaled nitric oxide (FeNO) and the mini Paediatric Asthma Quality of Life Questionnaire (mPAQLQ) [12]. Asthma attacks in the 3 months prior to the baseline visit and during the monitoring period were recorded from interviews and hospital records [8]. If not already known, atopy was assessed at baseline either by skin prick test or specific IgE [8]. Daily adherence was measured for two monitoring periods using an electronic monitoring device (Smartinhaler™ Adherium, New Zealand) that recorded actuation but not inhalation flow. Families were aware that monitoring was taking place. Suboptimal adherence to inhaled corticosteroids was defined as <80% [8, 13].

Statistical analyses were performed using Stata® (Stata Statistical Software: release 15. STATA Cooperation; College Station, TX). Data were tested for normality using visual inspection, histograms and Kolmogorov-Smirnov testing. Mann–Whitney U, Fisher's Exact, Wilcoxon signed rank, ANOVA or Kruskal Wallis were used with $p<0.05$ indicating statistical significance.

Thirty-five patients (21 male) mean age of 11.9 years (SD: ±3 years), completed the two monitoring periods. 8 (23%) were severe therapy resistant asthmatics (STRA), 16 (46%) difficult asthmatics and 11 (31%) mild to moderate asthmatics. The majority (91%) were atopic. The median inhaled corticosteroid (ICS) dose was 800 (range 200–2400) mcg/day of budesonide or equivalent. Median duration of the first monitoring period was 84 days (IQR 63, 98), and the second monitoring period was 105 days (IQR 70, 161).

The median adherence level of the whole study population was not significantly different over the two monitoring periods (Table 1). Most participants (30/35 = 86%) retained their adherence classification (good/suboptimal) at the end of each monitoring period, 5 participants had improved adherence in the second period and changed classification from suboptimal to good (3 who received feedback and 2 who did not).

After the first monitoring period there were significant improvements in lung function, bronchodilator reversibility testing, inflammatory parameters and exacerbations which were sustained over the second monitoring period. There were further improvements in ACT, mPAQLQ and exacerbation rate (Table 1). It is acknowledged that there were five missing data points for FeNO at follow-up 2, which may have influenced our results. However, although there was a large decrease in FeNO from baseline to follow-up 1, FeNO then remained stable until follow-up 2, which means the missing data likely had no major impact on our conclusions. Irrespective of whether feedback was given or not, both groups showed significant improvements in all shown asthma control parameters.

This study has demonstrated that a single period of monitoring of 2–3 months can help to classify a participant`s adherence to inhaled corticosteroids. This is important when deciding on appropriate management, particularly when a biological is being considered. However as noted elsewhere, even non-adherent children may merit treatment with a biologic to prevent an asthma death [14]. For those with poor adherence despite monitoring, an additional adherence intervention is needed [15]. Since adherence is a trait that can vary over time, if management becomes difficult—even in patients with previously documented good adherence—monitoring should be repeated.

The clinical benefits of improved adherence seen after one period of electronic monitoring are maintained in the medium term over a second monitoring period of three months.

The number of dropouts in this study and those without usable data is noteworthy and reflects the reality of monitoring adherence in patients with difficult asthma. It is likely that many of these had suboptimal adherence that they did not want to disclose to the healthcare team or their caregivers and therefore decided to not return their Smartinhaler.

Future studies looking at a larger population are needed to evaluate whether adherence monitoring can improve the outcome of asthma patients in the long-term. This is particularly important since Smartinhalers are expensive and not available in many centres. The data on asthma control and adherence obtained during a period of monitoring could also be used to tailor adherence interventions.

This study demonstrates that three months of electronic monitoring can give the healthcare team important information about a patient`s adherence to help guide further management.

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Table 1: Change in asthma control parameters between baseline, follow-up 1 and follow-up 2

	Baseline (n=35)	**Follow up 1 (n=35)**	**Follow up 2 (n=35)**	**p-value: comparison baseline vs. FU1**	**p-value: comparison FU1 vs. FU2**
FEV1, mean % pred ± SD	82.2 ± 21.8	92.5 ± 16.1	95.8 ± 16.2	**<0.001**	0.087
BDR, %	20.3 ± 22.8*	8.7 ± 10.4*	7.2 ± 9.3+	**<0.001**	0.445
FeNO, ppb	55 (26–87)+	21 (13–61)+	22.5 (11–40)§	**0.002**	0.724
mPAQLQ	3.5 (3–4.7)	5.5 (4.3–6.4)	5.9 (4.3–6.8+	**0.001**	**0.006**
Exacerbations, n	2 (0–8)	1 (0–4)*	0 (0–4)	**0.033**	**0.001**
Adherence	Not assessed	78 (54–92)	83 (56–93)		0.302
ACT	12.6 ± 6.1*	16.2 ± 6.1*	19.1 ± 5.8+	0.001	**0.005**

* *Missing data for one child. + Missing data for 2 children. § Missing data for 5 children. Data are presented as median (interquartile) or mean ± standard deviation unless stated otherwise. According to the data distribution, Wilcoxon signed rank or paired t-test were used. FU1: follow up 1, FU2: follow up 2. BDR: bronchodilator reversibility, %, FeNO: fractional exhaled nitric oxide, mPAQLQ: median paediatric quality of life questionnaire score, FEV1: forced expiratory volume in 1s, ACT: asthma control test*