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Usefulness of parental response to questions about adherence to prescribed inhaled corticosteroids in young children

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ABSTRACT

Background Adherence to prescribed inhaled medication is often low in young children. Poor adherence to medication may contribute to lack of symptom control. Doctors are not good at predicting the adherence rates of their patients, and parental report of adherence does not correlate with objective measures of adherence. The objective of this study was to investigate whether parental admission of non-adherence and reasons given for non-adherence correlated with objectively measured adherence.

Methods Adherence to prescribed inhaled corticosteroid treatment was monitored electronically in 132 children aged 2–6 years who were participating in a randomised controlled trial comparing different inhaler devices. Follow-up was carried out every 3 months for a year. Parental answers to simple questions about adherence were compared to electronically measured adherence.

Results Mean adherence ranged from zero to 100%. Intra-participant adherence varied throughout the year-long study period (mean variance for individual children between quarterly periods was 28.5%). Parents who reported missed doses, generally missed at least half of the prescribed doses. Parents who reported that not a single prescribed dose was missed, still missed 20% of doses on average. Adherence was particularly low when parents cited initiating their own trial off medication as a reason for missing doses.

Conclusions By examining parental response to questions enquiring whether any doses were missed, healthcare providers can gain a modest degree of insight into their patients' true adherence to prescribed medication. Adherence to prescribed asthma medication is extremely variable in young children.

Trial registration number Data from this study were derived from a randomised controlled trial (ACTRN12608000294358).

What is already known on this topic

- Adherence to prescribed inhaled medication is often low in young children.
- Poor adherence to medication may contribute to lack of symptom control.
- Doctors are not good at predicting the adherence rates of their patients.

What this study adds

- This study confirms that adherence to prescribed inhaled medication is extremely variable in young children.
- By asking simple questions about adherence, a healthcare provider can gain a modest degree of insight into actual levels of adherence.

INTRODUCTION

Preschool asthma and wheeze phenotypes are notoriously challenging to treat. Doctors are often confronted with patients with poor symptom control. Inhaled corticosteroids are widely prescribed for asthma and wheeze in the preschool age group, but are at best only moderately effective in preventing symptoms, irrespective of wheeze phenotype.[1–5] For inhaled corticosteroids to be effective, adherence to prescribed treatment is essential. Poor adherence to prescribed medication is known to be a cause of medication non-efficacy.[6–8]

Young children are unique in that they are dependent on their parents for medication administration and are known to, at times, display oppositional behaviour when their medication is being delivered, adversely affecting parents' willingness to administer inhaled asthma preventers.[9 10]

Parental report of adherence is not accurate,[11 12] and clinicians are not good at predicting the adherence rates of their patients.[13] For the clinician, the ability to differentiate between non-adherence and medication non-efficacy could potentially be of great value when planning management options.

The aim of this study was to investigate whether parental admission of non-adherence, and reasons given for non-adherence, correlate with objectively measured adherence.

METHODS

Adherence to prescribed inhaled corticosteroid treatment was monitored electronically in 132 children who were participating in a randomised controlled trial (ACTRN12608000294358) where two valved holding chambers were compared for clinical efficacy.[14] Children and their parents were followed up every 3 months over a 1-year period. Adherence data specifically related to the clinical trial but less relevant to the aim of this study are supplied in the online supplemental document.

Participants

Children aged 2–6 years with 'doctor diagnosed asthma', who were being prescribed inhaled corticosteroids, were included in the study. More details

of all participants[14] and of participants who only completed the clinical trial[15] are provided elsewhere. Parents gave written informed consent and children gave verbal assent. Ethics approval was obtained from Princess Margaret Hospital for Children Research and Ethics Committee (933/EP).

Study design

Background information was obtained by standardised questionnaire about asthma symptoms, and personal and family history of atopy and asthma.

After a 1-month run-in period for the clinical trial, children were followed up every 3 months for a year. Adherence to prescribed fluticasone pressurised metered dose inhaler (pMDI) use was monitored by Smartinhaler (Nexus 6, Auckland, New Zealand) electronic devices.[16] The Smartinhaler devices recorded the time and date of inhaled corticosteroid pMDI actuations, and data were uploaded at each study visit. Smartinhaler devices were replaced at each study visit when they were damaged, destroyed or lost by participants.

While investigators only had access to adherence information after study visits, participants were not blinded to the fact that their adherence was being monitored. At 3-monthly study visits, children's parents were asked the following question about adherence: 'Did you miss any doses?' If parents replied 'Yes', they were then asked: 'What were the reasons for you missing doses? Did you forget, were you too busy, did your child refuse to take the medication, or where there other reasons?' If the parents cited other reasons they were asked to describe those reasons. Parental report of adherence, and reasons cited for non-adherence, were compared to electronically measured adherence.

Medication

Before recruitment into the study, all children with the exception of one were being prescribed inhaled fluticasone pMDIs in the community. The single child, who was not being prescribed a fluticasone pMDI, was changed over to a fluticasone pMDI. All children who were using a valved holding chamber with a mask were successfully trained during the run-in period to use a holding chamber without a mask. Preventer medication was prescribed as a bi-daily regimen. Children who were being prescribed additional salmeterol before commencement of the trial were prescribed salmeterol during the trial. Medication was weaned during follow-up visits if patients had minimal symptoms and the parents agreed.

Technical aspects of adherence measurement

Adherence was calculated as the number of times that doses were administered as a percentage of doses prescribed. Doses administered before 12 noon were seen as morning doses. Doses administered after 12 noon were seen as evening doses. A participant (or the parent responsible for administering the medication) was seen as being adherent to a prescribed morning or evening dose if the pMDI was actuated the prescribed number of times or more during the particular morning or evening. If the pMDI was actuated fewer times than prescribed (eg, one actuation where two actuations were prescribed), then the participant/parent was assessed to be non-adherent to that particular prescribed dose. If the pMDI was actuated more than eight times during a 1 min period, the participant was assessed to be 'dumping' doses and was considered to be non-adherent to the particular prescribed dose.

Statistical analysis

Paired samples were compared using the Wilcoxon signed rank sum test, and unpaired samples were compared using the Mann–Whitney U test. Where the data were normally distributed, unpaired samples were compared using the Student t test. Linear regression was used to correlate data. The χ^2 statistic was used to investigate whether distributions of categorical variables differed from one another. When basic statistics indicated that more detailed analysis might be of benefit to clarify results, the data of the four study visits were pooled together and stepwise regression was utilised. To adjust for inherent correlations within individuals, generalised estimating equations (GEE) were used.

RESULTS

Demographics and medication

A total of 132 children were included in the study and 111 (84%) completed the study. The male:female ratio of children included in the study was 8 : 5. A large proportion of children were atopic, with 55% reporting doctor diagnosed eczema, and 88% reporting a first degree relative with atopy (asthma, eczema or hay fever).

A number of children were weaned off inhaled corticosteroids during the course of the study, with 78 children still being prescribed inhaled corticosteroids at the final study visit.

Adherence

Electronic adherence data were recovered for 80% of children during the first 3 months of the study. Recovery of adherence data decreased to 65% (of the initial group of children recruited) for the final 3 months of the study. Reasons cited by parents for not bringing back the electronic adherence monitoring devices (or bringing back damaged devices) were: lost device, forgot to bring device to study visit, did not know the device was not waterproof, and device was stolen. A small number of devices (±10%) failed during the study period. A number of parents admitted that they at times failed to insert new pMDI canisters into the Smartinhaler monitoring device when the old pMDI canisters needed replacement.

Inter-participant variability in adherence to prescribed medication was marked throughout the study. Adherence to prescribed medication ranged from 1% to 99% (figure 1). The median adherence dropped significantly ($p<0.01$) over the

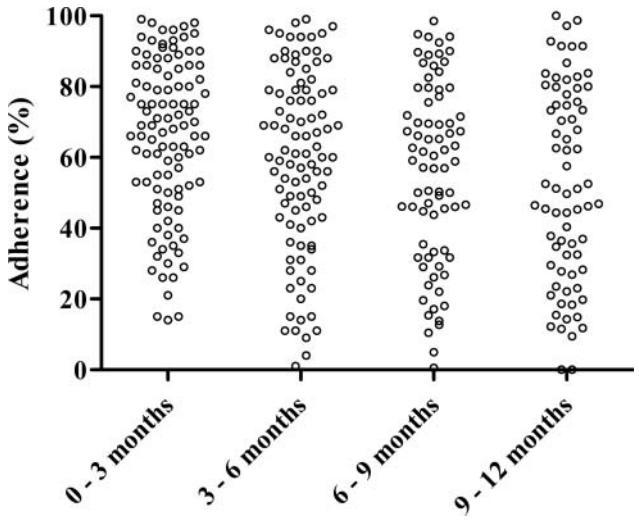

Figure 1 Scatter plot illustrating mean adherence to prescribed medication, for each participant, over the year-long study period.

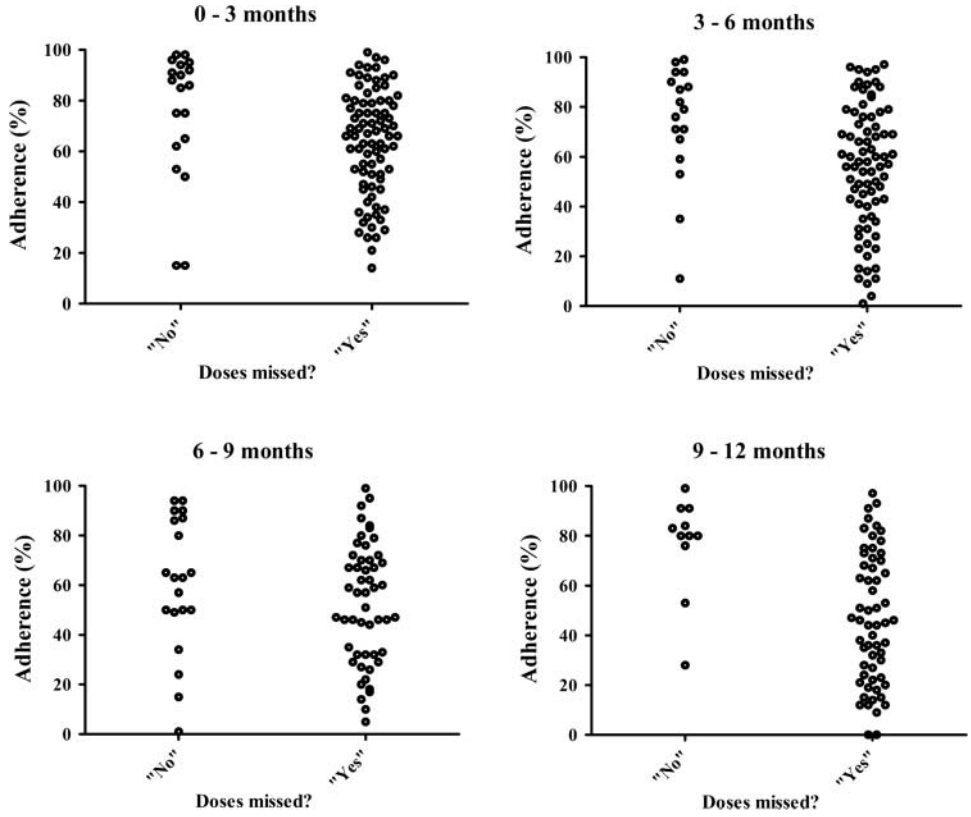

Figure 2 Mean adherence for participants grouped according to the parent's response at the end of each 3-month period to the question 'Did you miss any doses?'.

course of the study. Median (range) adherence was 68.5% (14.0–99.0%), 60.6% (1.0–99.0%), 60.0% (0.5–99.5%) and 50.4% (0–100%) for each respective 3-month period.

Intra-participant adherence also varied throughout the year-long study period (mean variance for individual children between quarterly periods was 28.5%). In order to further evaluate intra-participant adherence, participants were categorised by adherence into three groups: 0–50%, 51–80% and 81–100%. Electronic adherence data for both the first 3 months of the study and the final 3 months of the study were available for 59 participants. Between the first and the last study visit, only one (1.7%) participant changed from a lower to a higher adherence category. Twenty-three (39.0%) of the participants changed to a lower category, and 35 (59.3%) of the participants did not change category.

Reasons for non-adherence and relationship to measured adherence

Frequent reasons cited by parents for non-adherence were: forgot, child refused and too busy. Other reasons for non-adherence commonly cited by parents were:

- Parents refrained from giving medication as part of their own 'therapeutic trial', that is, they thought the child may not need the medication.
- Another carer who periodically is responsible for the child's care may not be administering the medication, that is, parental separation.
- Evening doses missed when the child falls asleep before parents have administered medication.

Parents who reported that they missed doses, generally had missed at least half of the prescribed doses. Parents who reported that not a single prescribed dose was missed, still missed an average of 20% of prescribed doses (figure 2). The agreement between parents admitting that they missed doses, and electronically measured adherence was weak, with kappa values of less than 0.2 at all study visits.

When the adherence data of the four study periods were pooled together, stepwise regression indicated that three reasons given for non-adherence were significantly associated with decreased adherence to prescribed medication (table 1), namely 'forgot to administer medication' ($p=0.03$), 'child refused medication' ($p=0.05$) and 'parent initiated trial off medication' ($p=0.003$). Adherence was particularly low (around 35% during the second half of the study) when parents admitted to initiating their own trial off medication (see table 1). When GEE were used to adjust for inherent correlations within individuals, only the reason 'parent initiated trial off medication' was a significant contributing factor for decreased adherence rates ($p=0.001$), whereas parental report of forgetting to administer medication, and child refusal to be administered medication were not significantly associated with decreased adherence rates ($p=0.08$ and $p=0.34$, respectively). Parents' 'trials off medication' were at times successful: of the seven parents to trial their children off medication before the 9-month study visit, three recommenced the medication due to the return of symptoms.

DISCUSSION

Adherence to inhaled medication ranged from zero to 100%. When asked if any doses were missed, parents who denied any non-adherence administered approximately 80% of prescribed doses, whereas parents who admitted to missing doses generally missed at least half of the prescribed doses. Adherence was particularly low (around 35% during the second half of the

Table 1 Reasons cited by parents for non-adherence, with associated actual median adherence (doses administered as % of doses prescribed)

	Months 0–3				Months 3–6				Months 6–9				Months 9–12			
		n	Adherence	p Value		n	Adherence	p Value		n	Adherence	p Value		n	Adherence	p Value
Forgot*	Cited	77	64.4	0.27	Cited	68	56.2	0.11	Cited	54	56.1	0.76	Cited	53	45.8	0.07
	Not cited		67.8		Not cited		63.8		Not cited		55.1		Not cited		60.8	
Child refused*	Cited	12	62.3	0.44	Cited	9	42.0	0.05	Cited	2	46.6	0.74	Cited	5	21.6	0.05
	Not cited		66.1		Not cited		60.5		Not cited		55.8		Not cited		53.8	
Parent initiated trial off medication	Cited	1			Cited	4	54.6	0.76	Cited	7	35.9	0.05	Cited	5	37.2	0.65
	Not cited				Not cited		58.9		Not cited		57.4		Not cited		52.7	
No dose missed	Cited	21	80.8	<0.01	Cited	22	75.6	<0.01	Cited	27	58.0	0.73	Cited	15	82.6	<0.01
	Not cited		62.5		Not cited		55.1		Not cited		55.1		Not cited		46.3	

*Answers prompted by investigator's questions.

study) when parents admitted to initiating their own trial off medication.

While poor adherence to inhaled medication has previously been described in this age group,[17] to our knowledge this study is the first to describe the relationship between parental reasons given for non-adherence and electronically measured adherence. Adherence was lower than adherence reported in a similar but smaller study where adherence was monitored for a 1-month period,[13] but comparable to adherence of children of similar age in a recent 18-month-long study with children using dry powder inhalers.[18] Adherence decreased during the course of our study, and as participants were not blinded to the fact that their adherence was being monitored, the lower adherence in the final 3–6 months of the study more likely represent 'true' adherence. As adherence monitoring was not blinded, the measured adherence would be expected to be at least as good as 'real world' adherence.

As adherence can range from zero to 100%, discretion is needed by clinicians to determine patients' true adherence. Factors that prevent patients from being adherent to their prescribed medications are complex. Previous studies[19] have shown that reasons for non-adherence include prolonged and complex medication regimens, and concerns about adverse effects.[20–23] Barriers to adherence that relate to the doctor include lack of continuity in medical care providers, perceived clinician disinterest, and the doctor appearing too busy.[19] Children from low-income families are less likely to adhere to prescribed treatment than children from higher-income families.[24] Low-income and minority patients report that medication cost, difficulty in obtaining medication, daily life hassles, and a general distrust of the medical establishment influence their adherence to medication.[20] Younger and less educated mothers are more likely to report a reason for not administering their children's medication.[25] An established daily routine has been shown to be a marker for better adherence.[26]

In our study various reasons for non-adherence given by parents are described, and parents trying their children off medication was an important reason for non-adherence. Intentional parental non-adherence has previously been described.[27] When parents have doubts regarding the usefulness of medications,[20] or when they misunderstand the role of inhaled corticosteroids, adherence may be reduced.[28] However, both parents and doctors generally overestimate asthma control in children.[29 30] Parents of children with asthma may believe that their children's asthma is under good control and not severe enough to require daily treatment despite high asthma-related morbidity.[7 20 29] In our study other reasons for non-adherence given by parents were statistically related to measured non-adherence at specific time points, but not throughout the study: in these instances the possibility of a type 2 error cannot be excluded.

In conclusion, our data confirm that adherence to prescribed asthma medication is extremely variable in young children. Based on parental response to the question 'Did you miss any doses?', doctors can gain a modest degree of insight into their patients' true adherence to prescribed medication.

Contributors AS participated in the planning of this study, gathered the data, and participated in the analysis and reporting of the results, and is responsible for the overall content as guarantor. PDS contributed to the planning of the study and provided critical advice during the writing of the study. GZ advised on all statistics used and also performed the generalised estimating equations analysis. AV participated in the reporting of the results. SGD contributed to the planning of the study, running of the clinical trial, and provided critical advice during the writing of the study. PNIS participated in the planning of the study, and provided critical advice on terms of data analysis and reporting of results.

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Competing interests The fluticasone pMDIs used in the study were supplied by GlaxoSmithKline, Australia. The valved holding chambers used in the study were partially sponsored by Visiomed, Australia. The sponsors did not have access to the data and played no part in the analyses or interpretation of the data.

Ethics approval This study was approved by Princess Margaret Hospital Research and Ethics Committee (933/EP).

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