



Compliance with inhaled corticosteroid treatment: rates reported by guardians and measured by the pharmacy

Laura M. L. B. F. Lasmar,¹ Paulo A. M. Camargos,² Leila F. Costa,³
Maria Teresa M. Fonseca,¹ Maria Jussara F. Fontes,¹ Cassio C. Ibiapina,⁴
Cristina G. Alvim,⁵ José A. R. Moura,⁶ Eugenio M. A. Goulart,⁷ Emilia Sakurai⁸

Abstract

Objective: There is elevated morbidity associated with asthma, particularly in developing countries, and failure to comply with inhaled corticosteroid treatment contributes to this morbidity. The objective of this study is to compare rates of compliance with beclomethasone treatment reported by parents or guardians with those measured by pharmacy dispensing records.

Methods: A concurrent cohort study of 12 months' duration was carried out, enrolling 106 asthmatic children and adolescents, selected at random. Linear regression was used to compare rates of compliance reported by parents or guardians with the pharmacy dispensing records at the service, every 4 months after enrollment on the study.

Results: Compliance rates reported by parents and/or guardians were always higher ($p < 0.001$) and exhibited a weak correlation with pharmacy records during the period studied; fourth ($r = 0.37$) and twelfth ($r = 0.31$) months of follow-up.

Conclusions: The rates of compliance reported by parents were overestimated during all study periods. The compliance rates of children with asthma should also be monitored by other methods and, in this case, pharmacy records effectively revealed compliance failures. Given its low cost, this method is indicated for verification of these compliance rates.

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Introduction

The safety and efficacy of inhaled corticosteroid for the control of the asthmatic inflammatory process is fully recognized.^{1,2} However, low rates of compliance with treatment using these medications has been associated with an elevated

frequency of hospital admissions and visits to emergency services.³

There are many methods for evaluating whether patients are using their inhaled corticosteroid, including electronic

1. Professora adjunta. Doutora, Disciplina de Pneumologia Pediátrica, Departamento de Pediatria, Faculdade de Medicina, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil.
2. Professor titular. Disciplina de Pneumologia Pediátrica, Departamento de Pediatria, Faculdade de Medicina, UFMG, Belo Horizonte, MG, Brazil.
3. Médica. Especialista em Pneumologia Pediátrica.
4. Professor adjunto. Doutor, Disciplina de Pneumologia Pediátrica, Departamento de Pediatria, Faculdade de Medicina, UFMG, Belo Horizonte, MG, Brazil.
5. Professor adjunto. Especialista em Pneumologia Pediátrica, Departamento de Pediatria, Faculdade de Medicina, UFMG, Belo Horizonte, MG, Brazil.
6. Professor adjunto. Doutor, Departamento de Pediatria, Faculdade de Medicina, UFMG, Belo Horizonte, MG, Brazil.
7. Doutora. Professora adjunta, Departamento de Estatística, Instituto de Ciências Exatas, UFMG, Belo Horizonte, MG, Brazil.
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measuring devices, periodic weighing of metered dose inhalers on electronic balances, review of the dispensing records of pharmacies at health services and the reports of patients or their parents or guardians.⁴

Despite the low sensitivity and specificity of rates of compliance reported by parents and/or guardians, this is the method most often used in clinical practice to verify patients' compliance. In contrast, studies recommend that methods be employed which are objective and of low cost, with emphasis on the use of records of drug consumption over a period of time (generally days) that corresponds to the number of shots in an unused inhaler.^{5,6}

We performed a bibliographic search and did not identify any research into compliance in the pediatric age group in Brazil.

The objective of this study was to compare rates of compliance with beclomethasone treatment reported by parents and/or guardians with those measured by the pharmacy at the service where the study was carried out over 12 months.

Methods

This was a concurrent cohort study of 106 patients diagnosed and selected at random at the pediatric pulmonology clinic at the Campos Sales Healthcare Center (HC), a secondary care service affiliated to the Municipal Health Department (Secretaria Municipal de Saúde) of Belo Horizonte. This clinic is a referral center for patients with moderate and severe asthma and is part of the "Wheezing Child" asthma control program run in this state capital.

All patients were followed without interruption for 12 months after prescription of beclomethasone. Diagnosis of asthma and classification of severity was based on the criteria proposed by the Global Initiative for Asthma (GINA).⁷

Patients

The study enrolled asthmatic children and adolescents aged 3 to 12 years, who had not previously received inhaled prophylactic treatment and who agreed to have their medication exclusively dispensed by the pharmacy at Campos Sales HC, while the presence of other subjacent diseases or opting for dispensation at a different pharmacy on the program were exclusion criteria.

Procedures

The inhaled corticosteroid chosen as the standard medication for the "Wheezing Child" was beclomethasone dipropionate, in a 200-dose canister, each shot containing 250 µg of the drug. The medication was administered using valved spacing devices (Flumax®, Flumax Medical Equipments, Brazil) fitted to a face mask or mouthpiece, depending on the age of the patient. Both medication and spacer were provided to patients free of charge.

Reported and measured compliance rates – Lasmar LM et al.

Since each canister contained 200 doses and the mean daily dose was two shots per day, each inhaler would be emptied, on average, in 3 months and 10 days and, for this reason, it was decided to check compliance after the period needed to use up all of the doses. All of the patients enrolled were followed up for 12 months. Two medical consultations and one assessment by the pharmacist were scheduled in each four-month period.

In addition to the clinical medical records, a pharmaceutical record was also designed, containing identification data, information on medication, number of canisters dispensed, posology, dates of dispensation and return date to collect the new inhaler. The health center pharmacy would only provide a new canister when the patient returned the previous one completely empty.

Rates of compliance were calculated by two methods and formulae, as follows:

- 1) Percentage rate according to the pharmaceutical medical record, calculated using the following formula: number of doses dispensed/number of doses that should have been used between the date the medication was provided and the actual date of return x 100.⁸
- 2) According to the information provided by parents or guardians: the difference between the number of days on which medication should have been given and the number of days that the parent or guardian reported it had not been administered/number of days between the date the medication was provided and the actual date of return x 100.⁶

Statistical considerations

Sample size

Estimating a prevalence of reported compliance rate of 90%,⁶ an alpha error of 5% and a margin of error of ± 3%, the sample size was calculated as 100 patients. In order to compensate for possible losses and dropouts, the final sample included 106 patients, who were selected by simple random sampling.

Statistical analysis

The dependent variable was the rate of compliance reported by parents and/or guardians at the fourth, eighth and twelfth months.

Means were calculated together with their respective 95% confidence intervals. Comparisons between means were made using Student's *t* test for paired samples.

We also employed: 1) Pearson's correlation coefficient to evaluate a correlation between the two variables. This coefficient tells us the degree of association between the two variables and varies from -1 to +1; 2) simple linear regression, where the response variable was the rate of compliance reported by parents and/or guardians, and the independent variable the rate of compliance measured by pharmacy

records, providing the angular coefficient and coefficients of determination. The level of significance was $p < 0.05$.

Ethical considerations

The study protocol and the informed consent form were approved by the Research Ethics Committee at the Universidade Federal de Minas Gerais.

Results

The majority of the children were male and 84.9% of them presented with the persistent severe form of asthma. The median age was 70 months. At the start of the study the person responsible for 60.4% of the children was the mother and/or father and passive smoking was present in 62.3% of homes. Morbidity was elevated, with 83% of the children reporting exacerbations once or twice a month before enrollment on the study.

Table 1 contains descriptive characteristics of the patients at enrollment.

Figures 1 and 2 illustrate the reported compliance and compliance measure by pharmacy records during the 12 months of follow-up.

Figures 1 and 2 illustrate the positive, although weak, correlation between the reported compliance rates and those measured by the pharmacy, demonstrated by the value of Pearson's correlation coefficient at the fourth ($r = 0.37$) and twelfth months ($r = 0.31$).

It will also be observed, in the adjusted linear regression, by the angular coefficient, that it is expected that reported compliance is 0.316 and 0.204 times compliance recorded by the pharmacy at the fourth and twelfth months, respectively, which confirms that reported compliance is greater than that measured by the pharmacy.

We observed, by means of the coefficients of determination (R^2), that the variability in compliance in the data from the pharmacy explains just 14 and 10% of the variation in reported compliance at the fourth and twelfth months, respectively.

Table 2 lists the distribution of compliance rates over the 12 months of follow-up.

There was a statistically significant difference when the rates obtained from the pharmacy data were compared with those obtained from parents and/or guardians' reports for all periods.

Discussion

This study has demonstrated that rates of compliance, as measured by pharmacy dispensing records, declined over the 12-month follow-up period and that during this period the rates reported by parents and/or guardians were always higher than those recorded by the pharmacist.

Table 1 - Descriptive characteristics of the study sample (n = 106)

Variables	n	%	95%CI	Median (amplitude)
Sex				
Male	73	68.9		
Female	33	31.1		
Age group (years)				70 (37-147)
3 to 6	57	53.8		
7 to 12	49	46.2		
Maternal age (years)				31 (17-48)
17-30	51	48.1		
31-48	55	51.9		
Child's guardian				
Mother/father	64	60.4		
Other	42	39.6		
Guardian changed during study?				
No	67	63.2		
Yes	39	36.8		
Passive smoking				
Yes	66	62.3		
No	40	37.4		
Asthma-related variables*				
Severe persistent asthma	90	84.9		
Moderate persistent asthma	16	13.1		
Number of exacerbations/month [†]				2 (1-8)
Once/month	51	48.1		
Twice/month	37	34.9		
Three or more times /month	18	17.0		

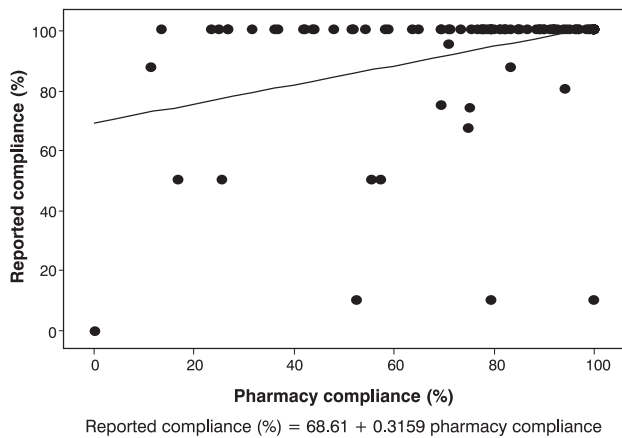
* On enrollment.

[†] During the 12 months prior to enrollment on the study

The rates of compliance reported by parents and/or guardians began with a mean proportion of 92.4% (95%CI 91.9-92.8), in the fourth month of the study, remaining high (93.2%; 95%CI 92.8-93.6) in the twelfth month. In contrast, the compliance rates obtained from pharmacy dispensing data began at a mean of 75.4% (95%CI 74.9-75.8) and reduced to 61.0% (95%CI 60.4-61.6) in the twelfth month of the study.

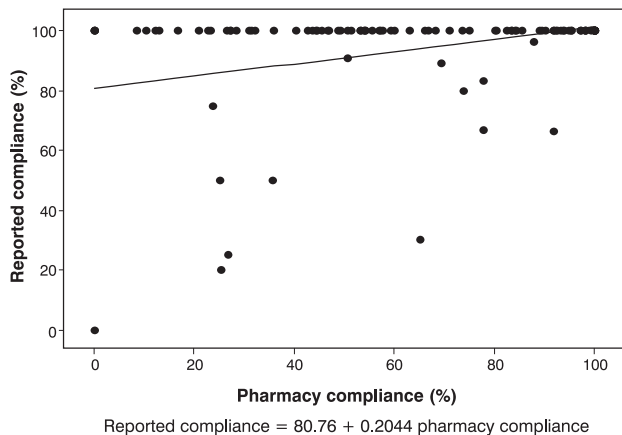
These results are consistent with the international literature, which has demonstrated that compliance reported by parents overestimates compliance rates, and that rates obtained by more objective methods decline over time. Nevertheless, both suffer certain variations resulting from method of compliance measurement, study design and follow-up period.

Celano et al. studied 34 African American children for 3 months and did not find agreement between rates measured



Pearson's correlation coefficient ($r = 0.37$).
 $R^2 = 0.14$;
 R^2 adjusted = 13%.

Figure 1 - Compliance reported by guardians and measured by the pharmacy after 4 months
 Reported compliance (%) = 68.61 + 0.3159 pharmacy compliance
 Pharmacy compliance (%)
 Reported compliance (%)



Pearson's correlation coefficient ($r = 0.31$).
 $R^2 = 0.10$;
 R^2 adjusted = 8.6%.
 R^2 = coefficient of determination;
 R^2 adjusted (coefficient of determination adjusted).

Figure 2 - Compliance reported by guardians and measured by the pharmacy after 12 months
 Reported compliance = 80.76 + 0.2044 pharmacy compliance
 Pharmacy compliance (%)
 Reported compliance (%)

by weighing canisters (44%) and those reported by parents and guardians (96%).⁹

Milgrom et al. compared data from 24 children in the form of data from diaries and data measured electronically. These authors found that more than 90% of the patients overestimated their compliance rates during the 4 months of study.¹⁰

Bender et al., in a prospective study lasting 6 months and involving 27 children, found an electronically measured rate of compliance of 58%, while rates reported by mothers varied from 70 to 100%.¹¹

Coutts et al. studied 14 children for periods of 2 to 6 months. They found a 52% rate of compliance via electronic monitoring and, despite the symptoms, parents reported rates of 90%.¹²

The reported compliance rates that we observed are consistent with the literature with variation between 90 and 96%.

We employed data generated by the pharmacy system in order to calculate compliance rates. This is a method that has been widely used in the literature, providing a good estimate of true compliance. Nevertheless, it has its limitations because it assumes administration of the prescribed medication and that the metered dose aerosol will be exclusively activated for the purposes of inhaling the medication and is not applicable to patients who use dry powder inhalers. Since the method provides data on the period between the date medication is provided and the date patients return for more, it does not inform on the way in which the patient has used the medication.⁴

Despite these limitations, the use of data generated by pharmacy systems is a useful method for detecting patients with partial compliance and has great potential for assessment of compliance rates in public health. Its limitations are minimized when the rates of compliance calculated by the pharmacy system are analyzed in conjunction with clinical assessment.^{4,5}

The possibility that patients will acquire their medication outside of the "Program Wheezing Child" pharmacy system is small.³ The children in this study have insufficient family income to purchase the medication and the inhaled corticosteroid dispensation registration system does not allow registration at more than one pharmacy.

Table 2 - Distribution of mean compliance rates (%) over the 12-month period

Period	n	Reported compliance (95%CI)	Pharmacy compliance (95%CI)	p
Fourth month	106	92.4 (91.9-92.8)	75.4 (74.9-75.8)	< 0.001
Eighth month	102	91.7 (91.1-92.2)	63.7 (63.1-64.3)	< 0.001
Twelfth month	100	93.2 (92.8-93.6)	61.0 (60.4-61.6)	< 0.001

Data provided by parents and/or guardians are recognized in the literature as leading to overestimation of compliance rates. Nevertheless, in routine assessment of children and adolescents with asthma reported compliance can provide an idea of patterns of compliance failures, such as forgetting to administer during weekends or one of the doses each day, of the number of days on which medication has not been administered and of the reason for not administering it.⁴

Verification of reported compliance provides an opportunity to encourage compliance individually and strengthen the doctor-patient relationship. When performed with care it can provide important information on the pattern of compliance failures. Furthermore, there is no evidence of compliant patients who state that they are noncompliant.⁴

Due to the intense symptomatology and the risks associated with severe uncontrolled asthma, it might be thought that patients with persistent moderate or severe asthma would have greater motivation to comply with treatment and not overestimate their rates. It is possible that, among our patients, there has been memory bias, however, the overestimation by parents of compliance rates cannot be attributed exclusively to memory bias in view of the large disparity between the reported rates and those measured by the pharmacist.

We noticed that a good proportion of the patients classified as having severe persistent asthma at the start of the study were controlling their conditions with lower doses than those prescribed, however, this study was designed to verify compliance and not the efficacy of dosages with relation to severity.

In this study, all patients were treated by the same pediatric pulmonologist and by the same nurse. Whenever one of the children did not attend a consultation, the family was visited at home in order to make another appointment. Additionally all participants received medication free of charge. Even so, guardians' reports overestimated rates of compliance.

Rand et al. stated that reported compliance depends on the characteristics and attitudes of both physician and patient.⁶ It is possible that parents and guardians felt a need to please the treating team by over estimating compliance rates. Notwithstanding, the guardians' reasons for overestimate compliance rates must remain in the realms of speculation, since they knew that rates were being monitored by the pharmacy system. It is probable that research employing qualitative methodology can contribute to explaining this phenomenon.

Monitoring compliance with inhaled corticosteroid therapy by means of pharmacy records may be an appropriate strategy for increasing rates of compliance and has been recommended by the World Health Organization, since compliance failures result in elevated social and financial costs, particularly in developing countries.⁵

This study has practical implications in the context of public health in Brazil. For those Brazilian cities which have asthma control programs and make inhaled corticosteroid available, pharmacy dispensing records can be used to monitor compliance, providing the treating team with a more realistic estimate of rates. This measure also makes it possible to detect patients who do not attend the pharmacy, and who are therefore noncompliant, early on. Pharmacists are the front line in accessing and monitoring compliance.

In the context of private healthcare, the treating physician can estimate rates by means of records of the dates on which medications are bought. The pharmaceutical industry, in turn, could also contribute to this important task of increasing compliance rates by manufacturing inhalers at an accessible price fitted with dose counters. This is not merely in order to assess the cost benefit-ratio, but primarily to avoid risks and psychosocial damage to patients with poorly controlled asthma due to compliance failure.

Measuring compliance rates, particularly when they are low, is of great importance in the context of the challenge of raising those rates. However, healthcare professionals must be aware that the use of more objective compliance rate measurement methods will not by itself increase the rates, and that it is necessary to provide feedback to patients in order that they have the opportunity to improve their own rates.

In conclusion, data reported by parents and/or guardians overestimated compliance rates and measurements by means of the pharmacy system proved to be easily carried out, effective, reproducible and of no extra cost. For these reasons this method should be used to measure compliance rates, concurrently with clinical assessment of patients.

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Correspondence:

Paulo A. M. Camargos
Departamento de Pediatria da Faculdade de Medicina da Universidade Federal de Minas Gerais
Avenida Alfredo Balena 190/4061
CEP 30130-100 – Belo Horizonte, MG – Brazil
Tel.: +55 (31) 3248.9773
Fax: +55 (31) 3248.9664
E-mail: pcamargs@medicina.ufmg.br,
pauloamcamargos@gmail.com