

Review Article

Methods of assessing adherence to inhaled corticosteroid therapy in children and adolescents: adherence rates and their implications for clinical practice*

Métodos empregados na verificação da adesão à corticoterapia inalatória em crianças e adolescentes: taxas encontradas e suas implicações para a prática clínica

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Abstract

Nonadherence to inhaled corticosteroid therapy is common and has a negative effect on clinical control, as well as increasing morbidity rates, mortality rates and health care costs. This review was conducted using direct searches, together with the following sources: Medline; HighWire; and the Latin American and Caribbean Health Sciences Literature database. Searches included articles published between 1992 and 2008. The following methods of assessing adherence, listed in ascending order by degree of objectivity, were identified: patient or family reports; clinical judgment; weighing/dispensing of medication, electronic medication monitoring; and (rarely) biochemical analysis. Adherence rates ranged from 30 to 70%. It is recognized that the degree of adherence determined by patient/family reports or by clinical judgment is exaggerated in comparison with that obtained using electronic medication monitors. Physicians should bear in mind that true adherence rates are lower than those reported by patients, and this should be considered in cases of poor clinical control. Weighing the spray quantifies the medication and infers adherence. However, there can be deliberate emptying of inhalers and medication sharing. In some countries, pharmacies provide the dates on which the medication was dispensed and refilled. This strategy is valid and should be used in Brazil. The use of electronic medication monitors, which provide the date and time of each triggering of the medication device, although costly, is the most accurate method of assessing adherence. The results obtained with such monitors demonstrate that adherence was lower than expected. Physicians should improve their knowledge on patient adherence and use accurate methods of assessing such adherence.

Keywords: Patient compliance; Asthma/therapy; Asthma/prevention & control.

Resumo

Adesão inadequada à corticoterapia inalatória é comum e contribui para um controle clínico insatisfatório, aumento da morbidade, mortalidade e dos custos do setor. Este artigo de revisão foi conduzido utilizando-se bancos de dados Medline, HighWire, Literatura Latino-Americana e do Caribe em Ciências da Saúde e pesquisa direta, entre 1992 e 2008. Os métodos para avaliar a adesão, citados em ordem crescente de sua objetividade, são: relato do paciente ou seus familiares, julgamento clínico, pesagem da medicação, dispensação de medicação, dosadores eletrônicos e análise bioquímica (pouco utilizada). As taxas de adesão variaram de 30 a 70%. A adesão determinada pelo relato do paciente/familiares e julgamento clínico é reconhecidamente exagerada quando comparada à obtida através do dosador eletrônico. O clínico deve sempre lembrar que as taxas reais de adesão são menores do que as relatadas pelo paciente e isso deve ser considerado, se não houver bom controle da doença. A pesagem do *spray* quantifica a medicação e infere adesão, porém pode ocorrer esvaziamento deliberado e compartilhamento da medicação. A farmácia fornece datas de dispensação e recarga da medicação. Esta estratégia é válida e deveria ser utilizada em nosso meio. O uso de dosador eletrônico é o método mais acurado para avaliar adesão, ele fornece a data e horário de cada disparo na utilização da medicação, porém é oneroso. Os resultados obtidos com dosadores demonstraram que a adesão foi menor que a esperada. Melhorar o conhecimento do médico sobre a adesão do seu paciente e utilizar métodos acurados para acessá-la é um caminho a seguir.

Descritores: Cooperação do paciente; Asma/terapia; Asma/prevenção & controle.

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Introduction

The control of inflammatory processes is one of the objectives of asthma treatment, which is why the use of inhaled corticosteroid therapy has been endorsed by Brazilian and international consensus on asthma management.⁽¹⁾ Adequate adherence to treatment is considered one of the most important factors for reducing mortality rates, morbidity rates and health care costs.^(2,3) In developing countries, easy access to inhaled corticosteroid therapy is unavailable for most of the population, and studies on adherence to treatment with this type of medication are rare.⁽⁴⁾

Adherence can be classified as adequate or inadequate (nonadherence), and the latter can be classified as intentional or unintentional. Intentional nonadherence occurs when an individual does not take any of the medication prescribed or effectively changes the prescription, by reducing the frequency of doses or by discontinuing the medication prior to completing the course. Therefore, the prescription is understood but not followed. Unintentional nonadherence occurs when patients/caregivers do not properly understand the prescription or the use of the medication, as well as when they forget or are unable to administer the inhaled medication.⁽⁵⁾ It is sometimes difficult to classify nonadherence as intentional or unintentional because there might be factors from both categories. However, unintentional nonadherence is related to memory deficit and other disabilities, whereas intentional nonadherence is related to a lack of patient motivation to initiate or continue the treatment.^(6,7)

Rates of adherence to inhaled asthma medication therapy ranging from 30 to 70% have been reported in various studies involving children and adolescents.⁽⁸⁾ Quantitatively, there is a tendency to consider 70% (adherence) the cut-off point to differentiate between adherence and nonadherence.

Nonadherence implies partial control of the disease and can cause persistent symptoms, increasing school absenteeism and visits to emergency rooms, with a higher risk of a fatal exacerbation. Understanding the factors that influence adherence to asthma treatment can help families take better care of their children and reduce morbidity. Patient characteristics such as gender, race, socioeconomic level and personality are unreliable predictors of adherence.⁽⁹⁻¹⁰⁾ The objective of this study was to

review the literature published between 1992 and 2008 regarding the available methods of assessing adherence to inhaled corticosteroid therapy in children and adolescents, the characteristics of these studies and the adherence rates reported. To that end, we used medical databases (Medline, HighWire and the Latin American and Caribbean Health Sciences Literature) and direct searches.

Review studies and meta-analyses on adherence

Haynes et al.⁽¹¹⁾ reviewed 17 studies published in the literature between 1977 and 1987 and drew attention to the ideal parameters for a study on adherence: randomization, a follow-up period of at least six months, adherence assessment by using multiple methods simultaneously and the inclusion of at least 50 individuals for significance of results. In 10 of the 17 studies in that review, the factors that increased adherence rates were clear instructions provided by health professionals, social support, discussion groups (in order to promote better understanding of the disease) and active measures of maintaining contact with patients.

In 1998, Roter et al.⁽¹²⁾ conducted a meta-analysis including 153 studies on adherence to the treatment of various diseases and 15 studies on adherence to asthma treatment, all 168 studies published between 1979 and 1994. The authors adopted the following inclusion criteria: control group consisting of at least 10 participants, adherence assessment by direct methods, such as biochemical analysis, and indirect methods, such as patient reports, canister weighing and date on which medication was dispensed. The authors found that adherence increased when the approach was based on education and behavior.

Peterson et al.,⁽¹³⁾ in a meta-analysis including 66 studies on interventions to increase adherence, found an increase in adherence rates ranging from 4 to 11%, assessed by patient reports and canister weighing. Educational interventions aimed at improving the understanding of the disease and treatment, whereas behavioral interventions aimed at changes in the routine and the development of asthma management skills.

Bender et al. reviewed 205 studies on adherence to inhaled corticosteroid therapy and concluded that there was no change in adherence rates after experimental interventions in half of the studies

in the review. In addition, in those in which there were behavioral changes, treatment success rates remained unchanged.⁽¹⁴⁾

Guevara et al. evaluated the effectiveness of educational programs in 32 studies accounting for 3,706 participants from 2 to 18 years of age. The authors concluded that educational interventions reduced morbidity due to asthma. Consequently, school absenteeism, sleep alterations and the number of visits to emergency rooms decreased. In addition, the pulmonary function and the physical activity of patients improved.⁽¹⁵⁾

Holgate et al. evaluated the perspective of patients regarding asthma management based on 24 studies.⁽¹⁶⁾ The authors concluded that the knowledge of patients on the disease was insufficient and that treatment options, as well as adherence, were inadequate.

Available methods for adherence assessment

The following methods of assessing adherence, listed in ascending order by degree of objectivity, were identified: patient or family reports; clinical judgment; weighing of canisters; registration of the dates on which medication is dispensed; electronic medication monitoring; and biochemical monitoring. Biochemical monitoring can be considered a direct method, whereas the other methods are indirect, and their degree of reliability regarding the use of medication can only be inferred.

Chart 1 shows the general characteristics of the available methods for the assessment of adherence to asthma treatment.

Biochemical monitoring

Biochemical monitoring can be classified as a direct method, having the advantage of confirming the presence of the medication in blood, urine or saliva. However, there are some disadvantages, such as the need for repeated determinations, high costs and difficulties in medication detection due to rapid or limited systemic absorption of some substances, such as inhaled corticosteroids.

Clinical judgment

This might be the most employed and the least reliable method for adherence assessment. Clinical judgment is performed during medical visits. Various studies showed that this method overestimates adherence, with rates ranging from 75 to 95.4%.^(17,18) However, it is frequently used since it is rapid and quite inexpensive. Ideally, this method should be used in conjunction with others, such as canister weighing, registration of dates on which medication was dispensed in the pharmacy or the use of electronic medication monitors, in order to increase its reliability. The skill of the physician during visits and the physician-patient relationship are relevant factors for improving the reliability of the data obtained. It should be borne in mind that the actual adherence rates are always lower than those perceived by the physician. One reason for false, overestimated adherence reported by patients and families is that questions, such as how often the medication is administered, what is expected from the efficacy of treatment and what impediments might be present (financial, psychosocial and

Chart 1 – Characteristics of the methods available for assessing adherence to asthma treatment.

Method	Description	Advantages	Disadvantages
Clinical judgment	Medical visits and clinical examination	Rapid, inexpensive	Overestimated adherence is frequent
Patient/family reports	Clinical interviews and patient/family member reports	Rapid, simple, inexpensive	Limited by memory bias, overestimated adherence
Canister weighing	Weighing of the canister on a digital scale	Simple, easy to perform	Susceptible to intentional sharing and emptying of medication canister; costly
Medication dispensing	Registry on a spreadsheet by the pharmacist	Simple, easy to perform, inexpensive	Susceptible to sharing and emptying of medication canister
Electronic medication monitoring	Date and time of administration are registered	Provides daily information on medication use	No guarantee that the medication was effectively administered, costly

cultural problems, such as corticosteroid phobia), are not systematically and rigorously asked. If clinicians always remember the gap between reported and actual adherence, higher doses of inhaled corticosteroids or the prescription of long-acting β_2 -agonists will be avoided, as will the unnecessary increase in treatment costs and in the complexity of the therapeutic regimen. Exaggerated adherence estimates can occur due to memory bias and the willingness of patients to please their physicians. However, if asthma is under control, physicians often forget to ask whether the medication was administered or not.

Formal recording of medication use data provided by patients or family members

Formal recording of medication use data provided by patients or family members can be carried out using questionnaires, interviews or diaries. This method is fast, inexpensive and frequently used. In addition to medication use, frequency of symptoms, use of rescue medications, variations in peak expiratory flow, incidence of sleep alterations and school absenteeism can also be recorded. The use of diaries to record data regarding the administration of medication is usually subject to exaggerated adherence estimates when compared to other methods, such as the concomitant use of electronic medication monitors.⁽¹⁹⁻²²⁾ In two different studies, adherence rates were found to be 90 and 95.4%, respectively, when based on patient/family reports, compared with 34 and 13.7%, respectively, when electronic medication monitors were used.^(23,24)

There is considerable variation in the accuracy of patient reports. However, when this method is carefully carried out, it can help determine adherence rates and identify problems associated with partial adherence.

Registration of dispensed medication in pharmacies

This method is objective, practical, valid and inexpensive. Using this method, information on the amount of medication dispensed and the dose schedule can be obtained, as can the date on which the inhaler should be replaced. The daily percentage of the administered dose can be calculated, and the date when the medication was dispensed can be

compared using other methods, such as electronic medication monitoring. Registration of the medication dispensed and canister weighing are strategies that are subject to deliberate emptying of the inhaler or sharing of the medication with another patient, which can mask a lower adherence rate.

However, the data available in pharmacies only refer to the dates of medication dispensing and return of the inhalers, which might not indicate the actual quantity of medication administered. These data can be even less reliable if medication was dispensed in more than one pharmacy. Therefore, patients should be instructed to obtain their medication from a single pharmacy.⁽²⁵⁻²⁷⁾

Adherence rates based on pharmacy dispensing records ranged from 41 to 61%,^(28,29) whereas those based on canister weighing ranged from 44 to 69%.^(30,31)

Sherman et al. calculated the adherence rates of 116 children by telephoning 55 pharmacies in order to obtain their medication dispensing records. The mean adherence rate was 61%. The accuracy of pharmacy records was 92%, which was confirmed by cost reimbursement records of the health care insurance companies.⁽²⁹⁾

Canister weighing

Canister weighing is a simple but more costly method, due to the need to acquire a digital scale. This method also requires that the exact dates on which the medication was dispensed and the exact number of inhalers provided for patients. For example, the 250- μ g/dose Clenil® canister weighs 25 g (10 g for the canister itself and 15 g for the medication accounting for 200 doses). Therefore, the average weight of a single dose is 75 mg. The adherence rate is calculated by determining the mean daily use of the medication, which can be determined by successive determinations of the canister weight. This method presents limitations, such as the need for skilled personnel to handle the digital scale. The medication can also be shared with other family members suffering from the disease, and there can be the intentional triggering of the device without the actual administration of the medication. Two studies were conducted by Rand et al., which included children and adolescents. In the first of the studies, the authors found adherence rates of 72 and 70%, respectively, based on patient reports

and canister weighing. In the second study, adherence rates were 70, 62 and 15%, respectively, based on patient reports, canister weighing and electronic medication monitoring.^(30,31)

Electronic medication monitoring

In the past 20 years, computer technology has allowed the development of an additional method for adherence assessment: the use of electronic medication monitors. These devices both record and store the date and time of medication administration. While connected to the inhaler, it registers the data whenever the device is triggered. Some of these monitors have an alarm mechanism that informs and alerts the patient when the number of doses remaining reaches a critical point. The use of electronic medication monitors can improve the accuracy of adherence assessment, and such monitors can be used without interruption for prolonged periods. However, they are costly. Adherence rates assessed using this method range from 13.7 to 50%.⁽³²⁻³⁸⁾

The use of these monitors can improve the accuracy of adherence assessment because they continuously record the number of doses administered over prolonged periods. Most of these monitors are able to detect up to 200 doses; therefore, if two daily doses are prescribed, the use of a given inhaled corticosteroid will be covered over a period of 100 days. Some monitors can record

up to a one-year follow-up period. Nonadherent patients can be identified, and an intervention plan can be carried out. The major disadvantages of electronic medication monitors are their unavailability in developing countries and their costs, since each monitor costs an average of US\$ 33 plus import duties. This precludes the large-scale use of these monitors in developing countries, where they are used primarily in clinical studies. The most well known commercial monitors are made in the USA: Chronolog[®] (Medtrac Technologies, Lakewood, CO, USA); Doser[®] (Meditrack Products, Hudson, MA, USA); and Smartinhaler[®] (Nexus6 Ltd, Dayton, OH, USA).

Bender et al. evaluated 27 children submitted to inhaled corticosteroid therapy during a six-month follow-up period. The authors reported mean adherence rates of 80, 69 and 50%, respectively, assessed by means of legal guardian reports, canister weighing and the use of the Doser[®].⁽³³⁾

Milgrom et al.⁽³⁴⁾ compared the adherence to inhaled corticosteroid therapy of 24 children ranging from 8 to 12 years of age. After a follow-up period of 13 weeks, mean adherence rates were 95.4 and 58.4%, respectively, based on patient reports and electronic medication monitors. Using the Chronolog[®], Jonasson et al. calculated adherence rates of 122 children and adolescents ranging from 7 to 16 years of age during a follow-up

Table 1 – Studies on adherence to treatment of children and adolescents, conducted using different methods, and their respective adherence rates.

Author	Year	Number of participants	Duration (months)	Method			
				Patient/legal guardian reports	Medication dispensing registered by pharmacists	Canister weighing	Electronic medication monitors
Adherence rate (%)							
Milgrom et al. ⁽³⁴⁾	1996	24	4	95.4	-	-	13.7
Bender et al. ⁽⁴⁰⁾	1997	131	4	-	-	-	45.0
Celano et al. ⁽³²⁾	1998	55	5	75.0	-	44.0	-
Jónasson et al. ⁽³⁵⁾	2000	122	27	-	-	-	43.7
Carter et al. ⁽³⁷⁾	2003	141	6	-	41.0	-	-
Sherman et al. ⁽²⁹⁾	2000	116	8	-	61.0	-	-
Bender et al. ⁽³³⁾	2000	27	6	80.0	-	69.0	50.0
Butz et al. ⁽³⁶⁾	2005	221	6	75.0	-	-	27.0
Bollinger et al. ⁽³⁸⁾	2006	53	18	64.5	49.1	-	-
Lasmar et al. ⁽⁴²⁾	2007	106	12	93.2	61.0	-	-
Mudd et al. ⁽³⁹⁾	2008	221	12	-	57.2	-	-

period of 27 months. The mean adherence rate at 3 months was 76.7%, compared with approximately 44% at the end of the study.⁽³⁵⁾ Table 1 shows the studies that met the inclusion criteria, using various methods for adherence assessment, as well as the names of authors, year of publication, number of participants, follow-up period (in months) and adherence rates. Of those, nine studies were conducted in the United States,^(32,33,36-41) one in Norway,⁽³⁵⁾ and one in Brazil.⁽⁴²⁾

Patient reports were compared to data obtained by means of electronic medication monitors in three studies. Mean adherence rates obtained from patient reports were 95.4, 75 and 80%, respectively, whereas those obtained from electronic medication monitors were 13.7, 27 and 50%, respectively.⁽³²⁻³⁴⁾ Patient reports were compared to data obtained by means of canister weighing in two studies. Mean adherence rates obtained from patient reports were 75 and 80%, respectively, whereas those obtained from canister weighing were 44 and 69%, respectively.^(32,33) Patient reports were compared to data obtained from medication dispensing records in two studies. Mean reported adherence rates obtained from patient reports were 64.5 and 93.2%, respectively, whereas those obtained from medication dispensing records were 49.1 and 61%, respectively.^(38,42) In one study, medication dispensing records were compared to the use of electronic medication monitors. Mean adherence rates were 75 and 27%, respectively.⁽³⁶⁾ In two studies based on medication dispensing records to calculate adherence rates, with no comparison with other methods, mean adherence rates were 57.2 and 61%, respectively.^(29,39)

Therefore, we can conclude that the highest adherence rates were found using patient reports; intermediate rates were found using dispensing records and canister weighing; and the lowest rates were found using electronic medication monitoring.

Although there is an increase in the perception of the importance of educating patients and their families, adherence to asthma treatment is still a problem in the treatment of these patients. Table 1 shows that, on average, only half of the prescribed medication is correctly administered.

In many studies, the follow-up period was short (between one and six months). However, it is widely recognized that adherence decreases over time, and that studies with longer follow-up periods, although

necessary, would make research more costly and even impracticable. Exaggerated patient reports and deliberate emptying of the canisters prior to medical visits are common characteristics of most studies on adherence.^(43,44)

The level of knowledge regarding the method and the timing of administering the medication can influence adherence, as can the degree to which an individual understands inhaled therapy. In addition, parents often have a less complete understanding of this therapy than do health care professionals.

Adherence can vary according to the number of prescribed doses, frequency of administration and number of medications in the therapeutic regimen. Other factors, such as the complexity of the therapeutic regimen, route of administration and duration of inhaled medication use, also affect adherence, as do social, cultural and psychological factors.⁽⁴⁵⁻⁴⁷⁾ Improvements in adherence have been associated with proper family organization and quality of life.

Physicians, in order to increase adherence rates, should explore all of the abovementioned factors.

In order to improve adherence, it is necessary to evaluate each child and family separately, educating and negotiating with them, as well as rationalizing and individualizing treatment.

Final comments

In any given context, the best method of evaluating adherence can only be determined by evaluating the availability of time and equipment, as well as financial and human resources of physicians and health care staff. Clinical judgment and patient/family reports are inexpensive methods and, although they overestimate adherence, are applicable in the everyday clinical practice. Therefore, they should be used as part of the routine. Physicians should bear in mind that adherence reported by patients and family members is always exaggerated, and this must be taken into consideration when proper clinical control of the disease is not achieved. Prior to changing the medication, increasing the dose of inhaled corticosteroids or prescribing long-acting β_2 -agonists, physicians need to make sure that problems in adherence to treatment have been corrected.

Canister weighing and the use of electronic medication monitors are costly and are out of the reach of most Brazilians. However, further studies

using these methods, especially electronic medication monitoring, should be conducted in Brazil, since they can more reliably portray adherence.

In terms of public health, using pharmacy records regarding medication dispensing is a method that could be more frequently used in everyday clinical practice, since it is a simple, inexpensive procedure. These records should be carefully registered in order to be reliable.

In the Brazilian cities where there are asthma programs, data on medication dispensing has a practical application, since these data can be used in order to monitor adherence rates. This method not only facilitates the active search for missing patients but also improves the quality of treatment of asthma patients.⁽⁴²⁾ Adherence determined by pharmacy records on medication dispensing can be carried out at most health care facilities, since this method can be easily executed, improving treatment. It should be included in the routine practice as an instrument to improve the quality of the management of patients with asthma. Physicians in private medical offices and in outpatient clinics, even those not working directly with pharmacists, can also note the date of purchase of medications and calculate the number of remaining doses, promoting adherence in an individualized fashion and, consequently, improving the physician-patient relationship.

The practical implication of monitoring medication dispensing is that reliable and reproducible data can be obtained, which makes this strategy adequate for determining adherence rates. This could also bring medical, pharmaceutical and nursing teams closer together. In terms of public health, all of the professionals involved in dispensing inhaled corticosteroids should be encouraged to record medication dispensing data in order to monitor adherence.

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