

## Compliance with inhaled medication and self-treatment guidelines following a self-management programme in adult asthmatics

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**ABSTRACT:** Two of the principal components of self-management are compliance with medication and adherence to self-treatment guidelines. The aim of this study was to evaluate compliance objectively.

Twenty two adult asthmatics attended a self-management programme. During a 2 week run-in period, compliance with inhaled steroids and peak expiratory flow (PEF) were electronically-registered. For PEF this resulted in a personal best value (PBV). Subsequently, patients attended four educational group sessions. During the four weeks of follow-up, patients were instructed to measure their PEF on a fixed day of the week and when they experienced an increase in symptoms. If PEF fell below 80% of PBV, patients had to double their use of inhaled steroids; if PEF fell below 60%, they had to start a short course of oral steroids.

During run-in, mean compliance was 83% and compliance per patient varied from 6 to 106%. During follow-up, on days without exacerbation, compliance with inhaled steroids increased by 12% (95% confidence interval (95% CI) 3–21%) compared to run-in, ranging 21–200%. On days when patients should have doubled their inhaled steroids, compliance decreased by 28% (95% CI -39 to -17), and compliance ranged 46–94%. Of the 10 patients who should have doubled their medication, only three did so, whilst four increased the use of inhaled steroids but only by one or two puffs; three patients did not alter their behaviour. In five patients (24%) PEF fell below 60% of their PBV, after which four started prednisolone (self-report). In conclusion, even after a formal self-management programme, patients with asthma comply only partially to self-treatment guidelines. Most are willing to increase, but not double, their inhaled steroids. This suggests that more emphasis is needed to reassure patients about the safety of inhaled steroids.

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During the last decade, many programmes have been developed to improve self-management behaviour among adult asthmatic patients [1–6]. In this paper, good self-management is defined as: effective behaviour with regard to asthma based on sufficient knowledge about asthma and its provoking factors; adequate coping behaviour; compliance with inhaled medication; attention to changes in the severity of the disease; recognition of symptoms; adequate inhalation technique; and the correct use of a peak flow meter. An indispensable component of self-management is self-treatment, which in this paper is defined as the self-adjustment of the medical therapy to changes in disease severity and/or the environment, based on a set of written guidelines provided by a physician [2]. These guidelines, in turn, are based on changes in peak expiratory flow (PEF) values and/or symptoms. By including self-treatment in the definition of self-management, both psychosocial and pharmacotherapeutic aspects of asthma are involved [7–11].

Two of the principal components of self-management are compliance with inhaled medication and adherence

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to the written guidelines pertaining to self-initiated changes in the medical management. Compliance with inhaled medication (defined as the number of actual inhalations divided by the number of prescribed inhalations×100%) in asthmatics ranges 30–95%, with compliance regarding bronchodilators being somewhat better than with inhaled steroids [12–15]. Inadequate compliance with prescribed medication can lead to failure of treatment, excessive use of medication, unnecessary costs, life-threatening exacerbations, and ultimately death [16].

The aim of the present study was to objectively monitor treatment compliance as part of self-treatment behaviour in a self-management programme in adult asthmatics. Various studies have evaluated compliance with inhaled medication in different ways; results of these studies depend partly upon the way in which compliance is measured. Notably, self-reported compliance and, to a lesser extent, pill-counts and weighing of canisters, tend to overestimate use of medication [12–15, 17–22]. To overcome these problems, all inhaled steroids were administered *via* an electronic inhalation device (Nebulizer

Chronolog (NC); Medtrac, Lakewood, CO 80215, USA; and Electronic Diskhaler (ED)). In this way, overestimation of medication use could be avoided. Furthermore, compliance with PEF measurements is notably poor. A recent study found that, when patients were asked to measure their PEF with an electronic peak flow meter twice daily for a period of approximately 3 months, this was done on only 34% of days and 22% of all values were invented [23]. In moderate-to-severe asthmatic patients, it is advised to use PEF measurements as part of a self-management plan, preferentially during periods of unstable asthma rather than during periods of good control [24]. In the present study, PEF was also registered with an electronic peak flow meter (DiaryCard; SensorMedics Corp., Yorba Linda, CA, USA). Because patients were recommended to use the electronic peak flow meter on a fixed day of the week and when they experienced an increase in symptoms, we could partially monitor compliance with the self-treatment guidelines, by combining the inhaler and peak flow data.

### Methods

Twenty four adults aged 18–65 yrs from the out-patient clinic of the Medisch Spectrum Twente in Enschede, The Netherlands, were enrolled in an experimental self-management programme. The patients had stable asthma and required regular treatment with corticosteroids.

#### *Electronic devices*

The NC contains a microprocessor, which registers the date and time of each actuation of the canister containing the medication. Up to 4,000 actuations can be stored in its memory. The ED also contains a microprocessor and a pressure-sensitive sensor, which lists the date and time whenever a blister is perforated. An integrated flow-sensor observes whether perforating the blister is followed by an inspiratory flow. The electronic peak flow meter logs PEF and also records the date and time of use.

#### *Run-in period*

During a 2 week run-in period, baseline data regarding compliance with inhaled steroids were electronically-registered, as were daily PEF recordings. All patients were instructed in the correct use of their inhaler and of the electronic peak flow meter, by well-trained lung function technicians. Twenty two patients inhaled their steroids with the NC and two patients used an ED. Patients were told that the number of inhalations with NC or ED were counted by the inhalers and that the PEF was registered. They were unaware that the date and time were logged as well.

#### *Follow-up*

Following the run-in period, patients were educated in four small group sessions (5–8 patients per group)

about asthma characteristics (*e.g.* symptoms, provoking factors), and different drugs and their mode of action. Furthermore, they were instructed in the proper use of their inhaled medication. Each session lasted approximately 90 min and all patients attended all four sessions. During the last group session, patients were given personal written guidelines and were asked to adjust their medical regimen according to the recommended steps during the next 4 weeks. An important directive was that, during the 4 weeks of follow-up, patients were asked to measure their PEF on a fixed day of the week and if they experienced an increase in symptoms. Patients were told to inhale their drugs as prescribed, as long as they were almost symptom-free or their PEF was above 80% of their personal best value (PBV). This personal best value was the highest morning PEF registered before the use of bronchodilators, during the 2 week run-in period. If PEF fell between 60 and 80% of their PBV on two consecutive mornings, patients were to double their dose of inhaled steroids until they returned to values above 80%, after which they were to continue inhaling the doubled dose for another week. Below 60% of their PBV, patients had to start a 1 week course of oral prednisolone. Compliance with oral steroids was based on self-report. Patients were to contact their chest physician if PEF values fell below 50% of their PBV.

Two analyses will be presented. The first analysis ("standard compliance") evaluated compliance with inhaled medication during the run-in phase, as well as compliance during the follow-up period on days when patients were symptom-free and/or PEF values were above 80% of their PBV. Compliance is defined as the number of actual inhalations taken divided by the number of inhalations prescribed  $\times 100\%$ , and was deemed good if it was 75–125%, and poor if below 75%. The second analysis ("self-treatment compliance") evaluated compliance with inhaled medication during the follow-up period only, on days when patients experienced symptoms and used their peak flow meter and PEF values were 60–80% of their PBV for two consecutive days. If this was the case, patients were instructed to double the number of inhalations of inhaled steroids.

To assess changes in compliance prior to and following the educational sessions, 95% confidence intervals (95% CI) of the differences will be presented. Because the follow-up period was longer than the run-in period, the number of patient days in the run-in period was compared with an equal number of days at the end of the follow-up period. Another reason for this approach was that patients would have had time to adapt to the new guidelines, and that the possible initial "enthusiastic" effect may have overestimated compliance.

The protocol was approved by the hospital's Medical Ethics Committee.

### Results

Twenty six patients were asked to participate, of whom two declined. The data of three patients could not be analysed during the run-in phase and/or follow-up period due to malfunction of the NCs. The average ( $\pm$ SD) age of the remaining 21 patients (11 males and 10 females) was  $42 \pm 13$  yrs (range 21–63 yrs), and they had had asthma

on average  $16 \pm 12$  yrs (range 1–40 yrs). Most had been attending the out-patient clinic for a number of years. The mean level of beclomethasone use by metered-dose inhaler (MDI) was  $578 \mu\text{g}\cdot\text{day}^{-1}$  (range 200–1,600  $\mu\text{g}\cdot\text{day}^{-1}$ ). Ten patients used  $\beta_2$ -agonists "as needed", while for the other 14 the mean daily (MDI) dose was  $485 \mu\text{g}$  (range 200–1,000  $\mu\text{g}$ ).

*Compliance with medication during the run-in period (2 weeks) (tables 1–3)*

The 21 patients had used their inhalers on 247 patient days ( $11.8 \text{ days}\cdot\text{patient}^{-1}$ ). Mean compliance was 83% and ranged 6–106%. Six patients had an average com-

pliance below 75%, and they inhaled their steroids with good compliance on 27% of the days. The 15 patients with an average good compliance showed this on 91% of the days.

*Compliance with medication during the follow-up period (4 weeks)*

The 21 patients used their inhalers on 531 patient days ( $25.3 \text{ days}\cdot\text{patient}^{-1}$ ) (table 1).

*Standard compliance.* Mean compliance was 92% (table 1). To assess changes in compliance, patient days from the run-in period were compared with an equal number

Table 1. – Compliance with inhaled medication

	Days* n	Mean compliance‡ %	<75%	Compliance % <sup>#</sup> 75–125%	>125%
Run-in period	247	$83 \pm 38$ (0–200)	24	73	3
Follow-up Standard days <sup>§</sup>	387	$92 \pm 52$ (0–550)	27	63	10
Self-treatment days <sup>†</sup>	144	$65 \pm 30$ (0–200)	63	35	2

\*: total number of days on which 21 patients inhaled their medication; ‡: compliance (number of actual inhalations/number of prescribed inhalations $\times 100$  %) presented as mean $\pm$ sd, and range in parenthesis; #: percentage of days on which compliance was <75%, 75–125% and >125%; §: days on which the standard dose of inhaled steroids had to be used; †: days on which the doubled dose of inhaled steroids had to be used.

Table 2. – Ranking of patients in order of mean compliance (number of days), before (Run-in) and after (Follow-up) the self-management programme

Pt No.	Age yrs	Sex	Run-in		Follow-up			
			Compliance %	Days n	Standard <sup>#</sup> Compliance %	days n	Doubled <sup>‡</sup> Compliance	days n
1	51	M	106	13	73	24	-	
2	56	M	104	13	132	15	94	8
3	21	F	102	13	106	24	-	
4	50	F	102	13	99	24	-	
5	40	M	102	13	97	25	-	
6	49	M	102	13	102	23	-	
7	62	M	100	13	104	24	-	
8	51	F	100	6	115	30	-	
9	27	F	100	13	100	7	50	17
10	51	F	100	13	77	8	60	17
11	35	F	100	6	100	1	46	28
12	31	M	96	13	138	78	82	17
13	48	F	92	13	82	16	49	9
14	44	M	92	13	200	1	77	24
15	28	F	77	15	92	15	66	7
16	31	M	68	7	21	39	-	
17	35	M	67	6	79	29	-	
18	22	M	67	13	109	11	94	8
19	56	F	39	13	137	15	56	9
20	61	F	35	13	89	26	-	
21	27	M	6	13	92	22	-	

Results of the 21 patients, whose data were available both for run-in and follow-up period are reported. Values are presented as mean compliance, and number of days (n). #: days on which the standard dose of inhaled steroids had to be used; ‡: days on which the doubled dose of inhaled steroids had to be used. Pt: patient; M: male; F: female.

Table 3. – Percentage of days on which compliance was <75, 75–125 and >125% before (Run-in) and after (Follow-up) the self-management programme

Pt No.	Run-in days %			Follow-up days %					
	<75%	75–125%	>125%	<75%	Standard# 75–125%	>125%	<75%	Doubled‡ 75–125%	>125%
1	0	92	8	42	54	4	0	0	0
2	8	84	8	0	80	20	25	62	13
3	0	100	0	33	38	29	0	0	0
4	0	100	0	13	83	4	0	0	0
5	0	100	0	12	84	4	0	0	0
6	0	100	0	0	96	4	0	0	0
7	0	100	0	0	96	4	0	0	0
8	0	100	0	0	73	27	0	0	0
9	0	100	0	0	100	0	100	0	0
10	8	84	8	50	50	0	59	35	6
11	0	100	0	0	100	0	100	0	0
12	8	92	0	0	63	37	18	82	0
13	15	85	0	38	62	0	100	0	0
14	23	69	8	0	0	100	33	63	4
15	47	53	0	40	47	13	71	29	0
16	72	14	14	90	10	0	0	0	0
17	67	33	0	55	31	14	0	0	0
18	46	46	8	27	36	37	13	87	0
19	62	38	0	0	80	20	89	11	0
20	69	31	0	27	69	4	0	0	0
21	100	0	0	9	91	0	0	0	0

Results of the 21 patients, whose data were available both for run-in and follow-up period are reported. #: days on which the standard dose of inhaled steroids has to be used; ‡: days on which the doubled dose of inhaled steroids had to be used. Pt: patient.

of days at the end of the follow-up period, because the follow-up period was longer than the run-in period. Following the educational sessions, based on 172 patient days when patients should have inhaled their preventive medication as prescribed, compliance increased by 12% (95% CI 3–12%), from 81% during the run-in to 93% in the follow-up period.

Compliance per patient ranged 21–200% (table 2). Two patients had an average compliance below 75%, inhaling their medication with good compliance on 27% of the days. Fifteen patients demonstrated good average compliance and showed this on 69% of the days, whilst four patients inhaled more than 125% of the prescribed amount of inhaled steroids. They were compliant on 74% of the days.

*Self-treatment compliance.* For 10 patients, a PEF of 60–80% of their PBV was registered and, therefore, they should have inhaled their steroid in a doubled dose. Mean compliance was 65% (table 1). Again, to assess changes in compliance, patient days in the run-in period were compared with an equal number of days at the end of the follow-up period. After the self-management programme, based on 75 patient days when patients should have doubled their inhaled steroids, compliance decreased by 28% (95% CI -39 to -17%), from 88% during run-in to 60% in the follow-up period.

Compliance per patient, based on these 10 patients, ranged 46–94%. Six patients had an average compliance below 75%, inhaling their medication with good compliance on 30% of the days. Four patients demonstrated good average compliance and showed this on 72% of the days. Following a decline in PEF to values below 80%, only three of these 10 patients subsequently doubled the dose of inhaled steroids on most of the days.

After reaching the 80% mark again, they returned to their initial dosage within one or two days. Four patients increased the use of inhaled steroids when indicated, but mostly by one or two puffs. Three patients did not alter their behaviour at all. In 5 of the 21 patients, PEF dropped below 60% of their PBV, after which four of these five patients started an oral course of prednisolone.

**Discussion**

This study measured compliance with inhaled medication among adult asthmatic patients as well as compliance with written self-treatment guidelines, by means of a combination of electronic inhalation devices and electronic peak flow meters. In this way, overestimation of medication use by subjective self-report was avoided [12, 14, 18–20, 25]. Compared to other studies, it would seem that baseline compliance levels in the present study population were high. These findings of individual compliance with inhaled steroids during the run-in period (mean±SD 83±27%, range 6–106%) are almost identical to another Dutch study by DOMPELING *et al.* [22]. Their corresponding results were 82±30% (range 8–126%). Their definition of compliance, however, was slightly more stringent, with good compliance ranging 80–120%, and compliance was assessed by pill count. APTER *et al.* [13] used NCs to monitor compliance with inhaled steroids, and reported an average±SD compliance of 64±30% (range 11–106%). In a study by MAWHINNEY *et al.* [26], also using NCs, patients took their inhaled medication as instructed on a mean of 37% of the days. In this study, patients were only considered compliant if they took 100% of the prescribed dose. If we applied the same strict definition, our patients would

be compliant on 66% of the days. BOSLEY and co-workers [27, 28], who used Turbuhaler Inhalation Computers, reported that average compliance with inhaled steroids as well as with beta-agonists was 60–70%, and that 51% of their patients showed poor compliance (less than 70% of the prescribed dose). In the present study, only 32% showed a mean compliance below 75%.

When the last days of the follow-up period are compared with the run-in period, the absolute number of inhalations per day has increased dramatically, to 102% of prescribed. This is mainly due to the 10 patients who had to double their inhaled medication. In patients whose asthma had been under control throughout the entire follow-up period, only a moderate increase in compliance was observed. Given the high levels of baseline compliance, a large improvement was not to be expected.

When the self-treatment guidelines are also considered, among those whose PEF fell below 80% on one or more occasions, compliance with the doubled dose of inhaled steroids was 65%. This means that patients increased the number of inhalations as compared to the standard days. We believe that the observed increase in compliance is due to the self-management programme.

In contrast to the three patients who doubled their medication, three patients did not alter their behaviour at all, although this was clearly indicated in the self-treatment guidelines. The other four increased the amount of inhaled steroids but erratically, and never actually doubled the dose. During the educational sessions, patients were instructed to double the dose of inhaled steroids when PEF was below 80% on two consecutive days. Within one or two days of returning above the 80% mark, they returned to their initial dosage, contrary to the recommendations. It seems that patients are willing to act "more or less" according to the guidelines, but are apprehensive of what they perceive to be too high a dosage of inhaled steroids. During exit interviews, patients also indicated that they felt that, instead of actually doubling their inhaled steroids, it would be enough to "take just a little bit more". Although there is no proof of the efficacy of doubling inhaled steroids, it is our impression that the procedure can be effective. Therefore, the importance of following the guidelines clearly needs to receive particular emphasis during the educational sessions. During the follow-up period, patients had to measure their PEF on a fixed day of the week and when they noticed an increase in symptoms. We wanted to approximate "real life" as much as possible, and, in practice there are only very few patients who will measure PEF on a daily basis when they are symptom-free, and compliance with PEF measurements decreases over time [23]. This did not allow us to assess compliance with the assessment of the severity of asthma based on symptoms. Patients might recognize symptoms but might decide not to act. This would have led to an overestimation of compliance with the self-treatment guidelines. Also, if patients were poor perceivers of their asthma severity, they would not measure their PEF and, therefore, we would not know whether patients had missed a period of poorly controlled asthma. We tried to circumvent this problem by weekly PEF measurements. Unfortunately, patients were not compliant with this directive. This might have resulted in insufficient asthma control. However, a study by CHARLTON *et*

*al.* [29] showed that self-treatment based on symptom perception was as effective as self-treatment based on PEF measurements.

It is striking that four out of the five patients whose PEF fell below 60% of their PBV started a course of oral prednisolone, although they admitted to being concerned about the possible side-effects. The data on prednisolone are based on self-report, so that they have to be interpreted with caution. The relatively high number of patients requiring a course of oral steroids reflected the severity of asthma.

Caution is also necessary when interpreting data obtained with the NC, because it is not possible with NC to distinguish between dumping the medicine (spraying it in the air, or removing the canister and flicking the switch manually) and actually inhaling more. Using the Electronic Diskhaler, this distinction can be made because perforating the blister has to be followed by an airflow. One of the two patients who were given an ED used it every day, but in 32% of all perforations this was not followed by an airflow. This clearly calls for more research with this kind of inhaler.

In conclusion, it is obvious that baseline compliance with inhaled medication was reasonably good in the present study population. After a formal self-management programme, patients complied only partially to self-treatment guidelines; most were willing to increase, but not double, their inhaled steroids when symptoms increased or PEF fell below 80% of their PBV, but they stopped immediately after returning to normal values. It might be beneficial to place particular emphasis on doubling the dose of inhaled steroids when PEF falls below 80%, and to instruct patients to stay at this level for a fixed period (*e.g.* 14 days). Furthermore, we might not have succeeded sufficiently in reassuring patients about the absence of serious side-effects of inhaled steroids, although about one hour was spent on discussing the side-effects of inhaled and oral steroids. It is possible that more time was spent on oral steroids because, during the educational sessions, patients very often showed concerns about this type of medication. Nevertheless, side-effects of inhaled steroids were also discussed and patients were told that, with proper rinsing of the mouth after inhaling, or, even better, by using a large inhalation chamber, very few side-effects would occur. Given the fact that 7 out of 10 patients were reluctant to double their inhaled steroids, we feel that more effort should be made to reassure patients about the safety of (doubling) inhaled steroids.

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