Standardization of ambulatory peak flow monitoring: the importance of recent β_2-agonist inhalation

H.K. Reddel, S.I. Ware, C.M. Salome, G.B. Marks, C.R. Jenkins, A.J. Woolcock

Standardization of ambulatory peak flow monitoring: the importance of recent β_2-agonist inhalation. H.K. Reddel, S.I. Ware, C.M. Salome, G.B. Marks, C.R. Jenkins, A.J. Woolcock. ©ERS Journals Ltd 1998.

ABSTRACT: Standardization of conditions for peak expiratory flow (PEF) monitoring is much more difficult in practice than for laboratory spirometry. Patients are usually asked to record PEF before medication.

The aim of this study was to determine the effect of prior bronchodilator use on PEF outcome measures in a clinical trial.

Electronic PEF records from 43 subjects with poorly controlled asthma were examined to determine the frequency with which β_2-agonist was inhaled <4 h before PEF measurement, as such PEF are potentially "postbronchodilator". The effect of inclusion of such PEF values on improvement in PEF outcome measures after 8 weeks of inhaled budesonide was calculated. Subjects were asked to record PEF before medication.

During run-in, the median frequency of postbronchodilator PEF was 29%, falling to 0% after 8 weeks of budesonide. Inclusion of postbronchodilator PEF led to an overestimation of average morning, evening and daily PEF during run-in (p<0.001). Improvement in these indices with treatment was, therefore, underestimated. Minimum morning PEF expressed as per cent personal best was unaffected.

Subjects may not be able to withhold β_2-agonist for 4 h before every peak flow reading. This may change as the level of asthma control changes, leading to a systematic bias in clinical trial end-points or inaccuracy in individual treatment decisions. Simple changes to peak expiratory flow instructions and analysis are proposed.
Eur Respir J 1998; 12: 309–314.

Institute of Respiratory Medicine at the Royal Alfred Hospital and the University of Sydney, Camperdown, New South Wales, Australia.

Correspondence: H.K. Reddel
Institute of Respiratory Medicine
P.O. Box M77, Missenden Rd
Camperdown, NSW 2050
Australia
Fax: 61 295506115

Peak expiratory flow (PEF) monitoring is now frequently recommended in asthma guidelines for assessing the severity of asthma [1–3] and response to treatment [4, 5], as it allows assessment of asthma over a period of time with a degree of objectivity which is not necessarily available from symptom reporting alone. In addition, PEF indices are used in many clinical asthma trials as outcome measures that may contribute to critically important therapeutic recommendations and PEF data may lead to acute changes in medication with the implementation of an asthma crisis plan [6]. Quality-control issues are, therefore, important in PEF monitoring.

Assessment of spirometry in clinical trials is usually carefully standardized, with rescheduling of appointments if they fall outside a time-window or if bronchodilator has not been withheld for 6–8 h before the measurement. While similar standardization of the conditions under which ambulatory PEF monitoring is performed would be ideal, electronic diary cards have demonstrated that the reality of long-term PEF monitoring is very different, even if careful attention is paid to patient instructions; for example, considerable variation has been seen in the times of PEF recordings between weekdays and weekends [7]. In an attempt to standardize PEF data for bronchodilator use, guidelines for ambulatory monitoring of PEF recommend

that morning PEF be measured before medication [3, 8, 9] and this is also a requirement in most clinical trial protocols. Ideally, subjects will comply with all instructions, but it would be unrealistic to expect that those requiring frequent inhalation of β_2-agonist for relief of symptoms would be able or willing to withhold bronchodilator until after every scheduled PEF recording. Therefore, even if subjects are asked to record PEF before medication, some PEF values may be, to some extent, "postbronchodilator" (postbronchodilator PEF).

This possibility has been raised in relation to the methodology of population PEF studies, but the difficulties of standardization and the expected low frequency of affected values have led to a decision to make no recommendation to subjects in such studies about the timing of PEF relative to medication use [10]. Intermittent use of bronchodilators is recognized as a confounding factor in guidelines relating to the diagnosis of occupational asthma from two hourly PEF records [11]. However, for clinical trials and clinical asthma practice there are no published data reporting the frequency with which postbronchodilator PEF occur, nor are there published guidelines about control for this effect in study design or in clinical practice.

The aim of the present study was to determine, in the setting of a clinical trial in which subjects were asked to

record PEF before medication, the frequency with which PEF were actually performed <4 h after inhalation of a short-acting β_2-agonist and to assess the effect of such potentially postbronchodilator PEF values on calculated PEF end-points. The investigation was built into the first 8 weeks of a clinical asthma study of inhaled corticosteroids in subjects with poorly controlled asthma who used electronic diary card spirometers twice daily.

Methods

Subjects

Prior to enrolment in the clinical trial all subjects had poorly controlled asthma, as indicated by symptoms, bronchodilator use and peak flows, for at least 3 months, with a daily dose of inhaled steroid of 0–1,200 μg. Exclusion criteria included current smoking, use of long-acting β_2-agonists and exacerbation of asthma or change of inhaled corticosteroid dosage (if used) in the previous month. Baseline characteristics of the subjects are summarized in table 1.

Study design

At the time of analysis, 43 subjects with moderate-to-severe asthma had completed run-in (9–28 days) and the first eight week treatment period of the clinical trial, which was a long-term study of budesonide given by Turbuhaler® (Astra Draco AB, Lund, Sweden). Subjects inhaled terbutaline or salbutamol as needed for the relief of asthma symptoms, but oral bronchodilators and long-acting β_2-agonists were not permitted. Data were analysed from the last 7 days of run-in and the last 7 days of the first 8 week treatment period. The protocol was approved by the hospital Ethics Committee and written informed consent was given by all subjects. At clinic visits spirometry was carried out using a pressure-differential heated pneumotach (Jaeger Masterscope version 4.17; Erich Jaeger, Wuerzburg, Germany). Baseline airway hyperresponsiveness to histamine was assessed using the rapid method [12].

Electronic diary card recordings

Subjects were given written and verbal instructions for using a hand-held electronic diary card/spirometer (Micro Medical DiaryCard, Rochester, Kent, UK) immediately upon waking and in the evening. They were asked to record PEF "before taking medication", either β_2-agonist or inhaled corticosteroid. Questions which appeared on the electronic diary card screen included occasions (not actuations) of β_2-agonist use since the previous scheduled electronic diary card entry and whether β_2-agonist had been inhaled in the previous 4 h. If the response to the latter question was "yes", the PEF was regarded as being "postbronchodilator". During each of three prompted spirometric manoeuvres, PEF, forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were recorded and PEF was displayed on the screen in L·min^{-1}. Data were downloaded for analysis and the first 2 days were excluded for learning effect [4]. Reproducibility and quality-control data have been reported elsewhere [7].

The best PEF from each set of three spirometry manoeuvres was selected. The following peak flow indices which are used as end-points in clinical asthma trials were calculated: 1) average morning PEF; 2) average evening PEF; 3) average daily PEF; 4) diurnal variability calculated as amplitude per cent mean, i.e. (maximum PEF - minimum PEF)/mean PEF (%) for each day, averaged over 7 days; and 5) minimum morning PEF per cent personal best i.e. minimum morning PEF over 7 days, expressed as per cent of personal best PEF [13, 14]. Personal best PEF was defined as the best PEF that the subject had recorded at any time in the previous 12 months on the same electronic spirometer. For each of the PEF indices in the two periods, results were calculated firstly using all PEF values, and secondly with exclusion of postbronchodilator PEF. The former method would reproduce the typical situation in which no information is available about prior bronchodilator use, whereas the latter method would calculate PEF indices based on essentially prebronchodilator values only.

Data analysis

The mean difference in each PEF index between the two methods of calculation (i.e. the bias) was calculated

Table 1. – Baseline data from the run-in period of a clinical trial of inhaled corticosteroids for subjects with poorly controlled asthma and from additional subjects who performed 1 month of electronic monitoring under the same conditions

	Clinical trial subjects	Additional subjects	All subjects
n	43	27	70
Males n (%)	25 (58)	17 (63)	42 (60)
Age yrs*	41.0±12.6	44.5±12.4	42.4±12.6
Atopic n (%)	42 (98)	22 (81)	64 (91)
Past smoker n (%)	8 (19)	13 (48)	21 (30)
FEV1 % pred*	73.6±17.6	82.0±17.0	78.0±2.2
PD20 μmol histamine†	0.11	1.15	0.27
	(0.07, 0.27)	(0.61, 5.40)	(0.09, 1.15)
β_2-agonist use occasions·day^{-1}†	3.0	0.5	2.1
	(1.9, 4.6)	(0.15, 1.6)	(0.8, 3.8)
Postbronchodilator PEF‡ % total	28.6	0.0	14.3
PEF records†	(9.7, 40.7)	(0.0, 7.7)	(0.0, 30.8)

*: mean±SD; †: median (interquartile range); ‡: postbronchodilator peak expiratory flow (PEF) performed <4 h after inhalation of β_2-agonist, even though subjects were asked to record PEF before medication. FEV1: forced expiratory volume in one second; PD20: provocative dose causing a 20% fall in FEV1.

and tested by paired t-tests. The limits of agreement, *i.e.* the range within which 95% of differences between pairs of observations would be expected to lie, were calculated by the method of BLAND and ALTMAN [15]. Rank correlations were calculated using Spearman correlation coefficients. In order to determine the frequency of β_2-agonist inhalation which best identified subjects with greater than 10% postbronchodilator PEF, a receiver operator characteristic (ROC) curve [16] was constructed. Because β_2-agonist use at entry into the clinical trial was considerably higher than β_2-agonist use reported by people with asthma randomly selected from a community sample [17], the sample for the ROC curve was supplemented with data from an additional 27 subjects (total 70 subjects) to give a more representative range of β_2-agonist use. These additional subjects were not selected for asthma severity, but otherwise had the same entry criteria, monitoring instructions, electronic diary card questions and baseline investigations as subjects enrolled in the clinical trial, and written informed consent and ethics approval were obtained. The final 7 days of 1 month of electronic diary card recordings were used. Baseline characteristics are recorded in table 1.

Results

During the run-in period of the clinical trial (table 1), median β_2-agonist use was 3.2 occasions·day^{-1} and 29% of PEF values were postbronchodilator. The effects of inclusion and exclusion of these postbronchodilator PEF on several calculated PEF indices are shown in table 2. Average morning PEF, average evening PEF and average daily PEF were significantly higher if postbronchodilator PEF were included than if only prebronchodilator PEF values were used, with moderate agreement between the two measures. Although there was no systematic bias between the two measures for amplitude per cent mean, there was very poor agreement for this index (group mean 20%, limits of agreement -13% to +13%). For minimum morning PEF % personal best there was no significant bias and agreement between the two measures was good.

After the first 8 weeks of inhaled corticosteroids, median use of β_2-agonist had fallen from 3.2 to 0.7 occasions·day^{-1} (p<0.0001) and the median proportion of postbronchodilator PEF from 29% to 0% (p<0.00001), although for six subjects (14%) more than 10% of PEF were still postbronchodilator, usually in the evening. By this time, all PEF indices had improved significantly compared

with run-in (fig. 1). However, the improvements in average morning PEF, average evening PEF and average daily PEF compared with run-in were substantially underestimated if postbronchodilator PEF were included in the calculations; improvement in minimum morning PEF % personal best was not significantly affected. The limits of agreement for amplitude per cent mean were still wide after 8 weeks of budesonide.

Analysis of the predictive value of β_2-agonist frequency was carried out with data from 70 subjects (see Methods). For the combined group, median β_2-agonist use was 2.1 occasions·day^{-1} and 14% of PEF were postbronchodilator (table 1). As expected, there was a strong correlation between frequency of β_2-agonist inhalation and frequency of postbronchodilator-PEF (r=0.78, p<0.0001) (fig. 2). Subjects with greater airway hyperresponsiveness had a higher frequency of morning postbronchodilator PEF (r=0.50, p<0.0001) associated with more frequent nocturnal asthma, but the frequency of evening postbronchodilator PEF correlated poorly with airway hyperresponsiveness (r=0.27, p=0.02). From the ROC curve (fig. 3), β_2-agonist inhalation of Š2.2 occasions·day^{-1} was best able to identify subjects with more than 10% postbronchodilator PEF val-
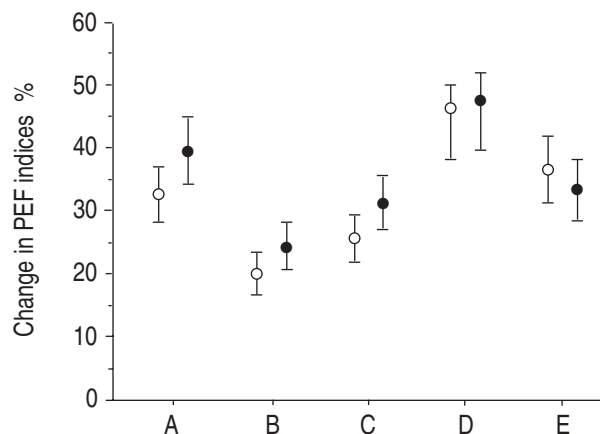

Fig. 1. – Improvement in peak expiratory flow (PEF) indices after the first 8 weeks of inhaled corticosteroid treatment (n=43). A: average waking PEF (p=0.0004); B: average evening PEF (p=0.02); C: average daily PEF (p=0.0003); D: amplitude % mean (p=0.2); and E: minimum waking PEF % personal best (p>0.1). ○: shows the improvement if each PEF index was based on all PEF values (including postbronchodilator PEF, where β_2-agonist had been inhaled in the previous 4 h); ●: shows the improvement if each PEF index was based only on strictly prebronchodilator values. Error bars show 95% confidence intervals. The p-values are for paired t-tests comparing the two methods of analysis.

Table 2. – Comparison of calculated peak expiratory flow (PEF) indices for subjects (n=43) with poorly controlled asthma, using all PEF values (including postbronchodilator PEF, where β_2-agonist had been inhaled in the previous 4 h) and using only strictly prebronchodilator values

	Group mean PEF index		Mean bias	95% limits of agreement
	with post-BD	pre-BD only		
Mean morning PEF L·min^{-1}	358.5	342.9	15.6***	-33.7, +66.0
Mean evening PEF L·min^{-1}	402.2	385.8	13.7***	-35.1, +63.5
Mean daily PEF L·min^{-1}	379.9	362.9	17.0***	-29.4, +64.3
Amplitude % mean % (n=33)	20.4	19.9	-0.5	-13.4, +12.7
Minimum morning PEF expressed as % personal best	59.1	60.2	-1.3	-10.6, +8.2

The mean difference between the two methods of calculation for the whole group is shown as mean bias. The 95% limits of agreement were calculated by the method of BLAND and ALTMAN [15] and show the magnitude of variation between the two methods of calculation of PEF indices. BD: bronchodilator. ***: pð0.001.
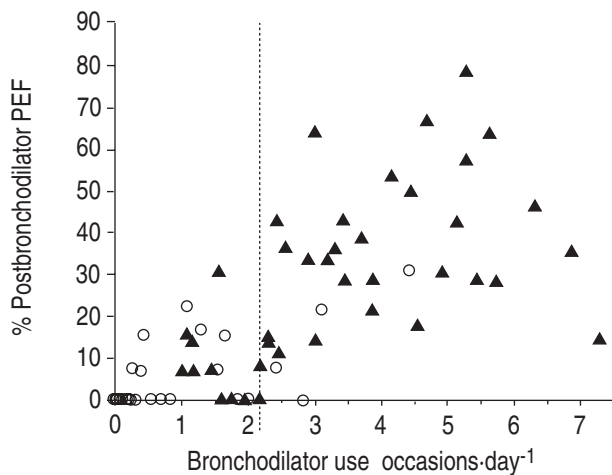
Fig. 2. – Correlation between β_2-agonist inhalation (occasions·day^{-1}) and the proportion of peak expiratory flow (PEF) measurements performed <4 h after inhalation of β_2-agonist, when subjects were asked to record PEF before medication (r=0.78, p<0.0001). The sample from the clinical trial (n=43, ▲) was supplemented with an additional 27 subjects (○) in order to give a representative range of β_2-agonist use. For β_2-agonist use of Š2.2 occasions·day^{-1} (········), a median of 31% of PEF values were postbronchodilator, compared with 0% for β_2-agonist use of <2.2 occasions·day^{-1}.
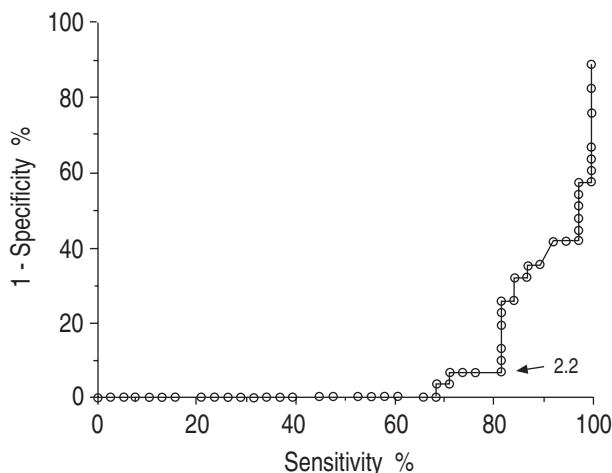

Fig. 3. – From the receiver operator characteristic (ROC) curve it was found that a level of β_2-agonist inhalation of Š2.2 occasions·day^{-1} had the best combination of sensitivity and specificity for identification of subjects for whom >10% of peak expiratory flow values were postbronchodilator (β_2-agonist inhaled within the previous 4 h).

ues. The median frequency of postbronchodilator PEF was 31% for subjects inhaling β_2-agonist on Š2.2 occasions·day^{-1} and 0% for subjects inhaling β_2-agonist on <2.2 occasions·day^{-1} (p<0.0001).

Discussion

This study showed that when subjects with poorly controlled asthma were asked to record PEF twice daily before medication, a high proportion of PEF values were potentially postbronchodilator because of inhalation of short-acting β_2-agonist <4 h previously, and that inclusion of such PEF values into calculated PEF indices would introduce significant measurement bias into the assessment of therapeutic response in a clinical trial. As expec-

ted, the frequency of postbronchodilator PEF correlated strongly with the frequency of β_2-agonist inhalation, and study of a larger group of subjects showed that almost one-third of PEF data can be expected to be postbronchodilator if β_2-agonist use is Š2.2 occasions·day^{-1}.

The instructions given to subjects in this study are clearly crucial to the significance of the results. Written directions reinforced the standard verbal instruction to perform PEF "before taking medication". If subjects were unable to withhold β_2-agonist for 4 h before recording PEF, the prior bronchodilator use was to be noted on the electronic diary. Because this question may have given implied permission for performance of a postbronchodilator PEF, the observed frequency may have been lower if these data had been collected covertly, for example with a logging metered-dose inhaler. However, the present results are mathematically predictable, in that if β_2-agonist was inhaled even once during the daytime the probability of a postbronchodilator evening PEF would be approximately one in three. The results are also psychologically plausible, in that it would be unrealistic to expect that subjects woken by asthma during the night would refrain from using β_2-agonist until the time of scheduled morning PEF.

It was expected that the frequency of postbronchodilator PEF would be determined by asthma severity because of the higher frequency of β_2-agonist inhalation, and it was found that for morning PEF, the frequency of postbronchodilator PEF correlated with airway hyperresponsiveness, consistent with the effect of nocturnal asthma. However, the correlation with airway hyperresponsiveness was poor for evening postbronchodilator PEF, suggesting that other factors such as convenience may have influenced the time at which β_2-agonist was inhaled or PEF was recorded in the evening.

Postbronchodilator PEF had clear effects on some commonly used PEF indices (table 2, fig. 1). Inclusion of postbronchodilator values in the calculations led to significant positive bias in average morning PEF, average evening PEF and average daily PEF during run-in and significant underestimation of the extent of improvement in these PEF indices after 8 weeks of inhaled corticosteroids when the frequency of postbronchodilator PEF had fallen dramatically. Although there was no systematic difference in amplitude per cent mean calculated by the two methods, there was very poor agreement between the two values both during run-in and after treatment.

The findings of the present study may appear obvious to the point of superfluity. However, a search of clinical asthma trials reported in major respiratory and general journals in the past 12 months suggests that this confounding effect has not usually been taken into account in either protocol design or analysis. Twenty clinical asthma trials reporting PEF end-points were identified, with PEF said to have been performed before medication in eight. Eleven studies reported a significant change in frequency of bronchodilator use, but the potential impact of this change on PEF outcome measures was discussed in only two studies. It, therefore, appears that there has often been an underlying assumption either that subjects would always be able to withhold bronchodilator prior to PEF, or that PEF values were equally likely to be affected by prior bronchodilator use during the run-in and treatment periods. The present study has demonstrated the magnitude of the potential effect, with a decrease in median frequency

of postbronchodilator PEF from 29% to 0% in 8 weeks. It can be postulated that there may have been systematic bias in the reported therapeutic effectiveness of interventions in studies in which potential changes in the frequency of postbronchodilator PEF have not been considered.

Application to clinical asthma trial protocols

Some clinical trial protocols may be more vulnerable than others to bias in PEF outcome measures. Current enrolment criteria often include a level of symptoms and bronchodilator use consistent with poorly controlled asthma in order to allow detection of a therapeutic response [18], but an effective intervention in such subjects is likely to result in a significant change in β_2-agonist use. If enrolment criteria were changed to include only subjects able to withhold β_2-agonist prior to all PEF recordings, this would reduce the generalizability of the findings of such studies for subjects with less well-controlled asthma. An alternative clinical trial design, in which subjects with initially well-controlled asthma are destabilized, with "survival analysis" of elapsed time to exacerbation [19], may also be vulnerable to confounding by changes in bronchodilator use; a requirement for a PEF criterion to be met on consecutive days may lead to late detection of an exacerbation if a postbronchodilator PEF is recorded. In the past, clinical trials have required PEF to be recorded both before and after bronchodilator, two to three times daily. It is possible that routine use of β_2-agonist at regular intervals in past studies may have reduced on-demand inhalation of β_2-agonist in the 4 h before PEF measurements, resulting in a lower frequency of postbronchodilator PEF during these studies. It should be noted that the present results do not necessarily apply to studies in which long-acting β_2-agonists are used.

Some studies have required all subjects to withhold β_2-agonist for 4 or even 6 h before every scheduled PEF. Although this would not be onerous for short periods or for subjects with well-controlled asthma, for subjects with more frequent β_2-agonist usage a requirement to delay β_2-agonist use for some time after onset of asthma symptoms could change other outcome measures such as symptom severity or duration, and could result in reduced adherence with monitoring, as it is well recognized that inconvenience and practical difficulties are significant contributors to poor adherence with medical instructions [20, 21] and that patients may selectively adhere to some medical instructions but not to others [22]. If subjects were to be withdrawn during the course of a clinical trial if they became unable to withhold β_2-agonist before PEF measurements, this would have the very undesirable effect of introducing substantial selection bias into the study.

If data about prior bronchodilator use have been collected in a study, prebronchodilator PEF indices could be calculated, with the exclusion of postbronchodilator PEF values. The present study has shown that this would eliminate a potential source of significant measurement bias. However, this approach may, instead, introduce selection bias, by the exclusion of "sick days" when β_2-agonist use was higher. Alternatively, during analysis the calculated PEF indices could be adjusted for β_2-agonist usage, but this may be inappropriate as β_2-agonist usage is, in itself, an outcome measure for clinical asthma trials.

The preferred solution to the problem of bias in PEF outcome measures in clinical asthma trials is a pragmatic approach which recognizes both the need for standardization and the practical difficulties of achieving this during long-term monitoring without the loss of compliance. Subjects should still be asked to record PEF before bronchodilator if possible and the frequency of as-needed β_2-agonist use should always be recorded. The PEF diary cards should include a check box to be marked if bronchodilator was inhaled in the previous 4 h, so that the magnitude of potential bias can be calculated. During analysis, all of the available PEF data should be used, but a calculated PEF index which is relatively independent of β_2-agonist usage should be selected as the outcome measure. The lowest morning PEF over 1 week, expressed as per cent personal best [13, 14], showed no significant bias due to inclusion of postbronchodilator PEF, had satisfactory limits of agreement and was responsive to change in asthma control over a period of 8 weeks in the present study. This index requires only morning PEF, which in the present study was recorded more frequently than evening PEF (p<0.0002, unpublished data). Of the PEF indices studied, amplitude per cent mean was the most vulnerable to bias by bronchodilator effect, possibly explaining recent reports of poor correlation of this index with other measures of asthma severity [14]; the use of amplitude per cent mean cannot now be recommended when PEF is recorded only twice daily.

Application to asthma guidelines

Patients will often present for review of asthma medication during a time when their β_2-agonist requirements are high. In this situation, postbronchodilator PEF values may mask the severity of asthma, and assessment of the extent of subsequent improvement in PEF with treatment may be biased by a reduction in β_2-agonist requirements. Physicians should ask patients to circle PEF values if bronchodilator was inhaled in the previous 4 h, so that potential bronchodilator augmentation can be recognized. The physician should also be aware that β_2-agonist use and, therefore, the likelihood of postbronchodilator PEF, will tend to be higher on "sick days" and that this may delay implementation of an asthma crisis plan based on PEF. During an exacerbation, it may be preferable to record PEF immediately before inhalation of bronchodilator, rather than at scheduled times [3].

Conclusions

Standardization of conditions under which ambulatory peak expiratory flow monitoring is carried out is clearly important, because of the implications for therapeutic recommendations and for individual patient treatment decisions. Clinical trial protocols and asthma guidelines have attempted to minimize the effect of prior bronchodilator use by asking patients to record peak expiratory flow before medication. It appears from published reports that it has often been assumed either that patients should always be able to adhere with this requirement, or that the effect of prior bronchodilator use will be uniform throughout a study. The present study has demonstrated under

actual clinical trial conditions that neither of these assumptions is correct for patients who inhale β_2-agonist more than twice daily and that the resulting bias may significantly alter the ability of a clinical trial to demonstrate a therapeutic effect. Based on the findings of this study, simple changes to peak expiratory flow monitoring are proposed which can reduce the confounding effect of prior short-acting bronchodilator use on peak expiratory flow end-points without placing an excessive burden on patients or reducing patient compliance. Standardization of ambulatory peak expiratory flow monitoring requires a careful balance between ideal conditions and the practicalities of their implementation by patients.

References

1. The British Thoracic Society, The National Asthma Campaign and The Royal College of Physicians of London in association with the General Practitioner in Asthma Group, The British Association of Accident and Emergency Medicine, The British Paediatric Respiratory Society and the Royal College of Paediatric and Child Health. 1995 Review and Position statement. *Thorax* 1996; 52: Suppl. 1, S1–S21.

2. GINA (Global initiative for asthma). Asthma management and prevention, NIH Publication No. 96-3659A. Bethesda, MD, NHLBI, 1995.

3. NAEPP Expert Panel Report 2. Guidelines for the diagnosis and management of asthma, NIH Publication No. 97-4051. Bethesda, MD, NHLBI, 1997.

4. Quackenboss JJ, Liebowitz MD, Krzyzanowski M. The normal range of diurnal changes in peak expiratory flow rates. Relationship to symptoms and respiratory disease. *Am Rev Respir Dis* 1991; 143: 323–330.

5. van Aalderen WM, Postma DS, Koëter GH, Knol K. The effect of reduction of maintenance treatment on circadian variation in peak expiratory flow rates in asthmatic children. *Acta Paediatr Scand* 1988; 77: 269–274.

6. Beasley R, Cushley M, Holgate ST. A self-management plan in the treatment of adult asthma. *Thorax* 1989; 44: 200–204.

7. Reddel HK, Ware SI, Salome CM, *et al.* Pitfalls in processing electronic spirometric data in asthma. *Eur Respir J* 1998; 12: (in press).

8. Enright PL, Lebowitz MD, Cockroft DW. Physiologic measures: pulmonary function tests. *In*: NIH Workshop on measures for use in asthma clinical research. *Am J Respir Crit Care Med* 1994; 149: S1–S8.

9. American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med* 1995; 152: 1107–1136.

10. Britton J. Measurement of peak flow variability in community populations: methodology. *Eur Respir J* 1997; 10: Suppl. 24, 42s–44s.

11. Gannon PFG, Burge PS. Serial peak expiratory flow measurement in the diagnosis of occupational asthma. *Eur Respir J* 1997; 10: Suppl. 24, 57s–63s.

12. Yan K, Salome CM, Woolcock AJ. Rapid method for measurement of bronchial responsiveness. *Thorax* 1983; 38: 760–765.

13. Reddel HK, Salome CM, Peat JK, Woolcock AJ. Which index of peak expiratory flow is most useful in the management of stable asthma? *Am J Respir Crit Care Med* 1995; 151: 1320–1325.

14. Brand P, Duiverman E, Postma D, *et al.* Peak flow variation in childhood asthma: relationship to symptoms, atopy, airways obstruction and hyperresponsiveness. *Eur Respir J* 1997; 10: 1242–1247.

15. Bland JM, Altman DG. Statistical method for assessing agreement between two methods of clinical measurement. *Lancet* 1986; i: 307–310.

16. Green DM, Swets JA. Signal Detection Theory and Psychophysics, Rev. Edn. Huntington, NY, USA, Krieger, 1974.

17. Marks GB, Mellis CM, Peat JK, *et al.* A profile of asthma and its management in a New South Wales provincial centre. *Med J Aust* 1994; 160: 260–268.

18. Cockcroft DW. Asthma control *versus* asthma severity. *J Allergy Clin Immunol* 1996; 98: 1016–1018.

19. Toogood JH, Andreaou P, Baskerville J. A methodological assessment of diurnal variability of peak flow as a basis for comparing different inhaled steroid formulations. *J Allergy Clin Immunol* 1996; 98: 555–562.

20. Di Matteo M. Enhancing patient adherence to medical recommendations. *JAMA* 1994; 271: 79–83.

21. Rand C, Wise R, Adherence with asthma therapy in the management of asthma: review and clinical guidelines. *In*: Szefler S, Leung D, eds. Severe Asthma: Pathogenesis and Clinical Management. New York, Marcel Dekker, 1995; pp. 435–464.

22. DiMatteo MR, Hays RD, Gritz ER, *et al.* Patient adherence to cancer control regimens: scale development and initial validation. *Psychol Assess* 1993; 5: 102–112.