Validation of Morning Dip of Peak Expiratory Flow as an Indicator of the Severity of Nocturnal Asthma*

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Overnight falls in peak expiratory flow (PEF) (with the morning dip of the index) may be considered the hallmark of nocturnal asthma. To validate the morning dip a quantitative marker of the degree of nocturnal bronchoconstriction, the dip was measured in 11 subjects (six with a history consistent with nocturnal asthma) undergoing all-night monitoring of lower respiratory resistance by a double-catheter method. In six subjects, marked and recurrent increases in resistance were recorded, along with morning dips higher than 20 percent; however, on the following morning, only two of them reported having suffered significant breathlessness and wheeze. Peak and average values for resistance, as well as the duration for which resistance was increased, were closely correlated with the magnitude of morning dips. Therefore, unlike the subjective report, PEF may be considered a reliable quantitative indicator of nocturnal bronchoconstriction.

Nocturnal exacerbations of asthma are very common, occurring in the majority of asthmatic patients and resulting in the early morning dip in peak expiratory flow (PEF). Recognition and evaluation of nocturnal asthma is important because of the unfavorable prognostic implications of the phenomenon, both in hospitalized patients with unstable asthma and in outpatients with stable asthma. Whereas the importance of the larger swings in PEF as indicators of increased instability of the airways has been emphasized, so far no objective evaluation of the relationship between the severity of nocturnal attacks and the magnitude of morning dips has been reported.

The present study is aimed at investigating whether the extent of the morning dip of PEF may be a reliable quantitative indicator of the severity of nocturnal asthma by evaluating the behavior of PEF in subjects submitted to all-night monitoring of lower airway resistance.

**Materials and Methods**

The following subjects volunteered for the study: (1) four healthy men aged 27 to 36 years (two smokers and two nonsmokers); and (2) seven asthmatic inpatients aged 18 to 44 years (four men and three women; two smokers and five nonsmokers). Four had extrinsic asthma with sensitization to Dermatophagoides pteronyssinus; three had intrinsic asthma. All but one reported the frequent occurrence of nocturnal chest tightness and wheeze; one of them (case 1) had a ventilatory arrest, which was treated in the emergency room, three weeks before the study.

All of the patients were currently taking sympathomimetics or antimuscarinic inhaled bronchodilators, beclomethasone, and theophylline preparations; four of the patients were also submitted to oral administration of steroids. In all subjects but one, all therapy was withheld 12 hours before the study; in case 1, because of the cited recent episode of arrest, treatment was kept unchanged.

During the two weeks preceding the study, all of subjects were instructed to record PEF hourly from getting up in the morning to the time of going to bed in the evening; the measurement was performed in the standing position in triplicate, and the highest value was recorded on a diary chart. The morning dip of PEF was calculated as the percentage ratio of the early morning to the maximum daily value of the day of study.

Each subject slept for two consecutive nights in the sleep laboratory: the first night being aimed at acclimatizing the subject; only data from the second night were analyzed.

In order to monitor patency of the lower airways and to rule out the occurrence of sleep-related upper airway occlusive events, we measured upper airway resistance, as well as lower respiratory resistance, using a partially modified version of the technique proposed by Hudgel et al.6

The following measurements were recorded both on paper for immediate control and on magnetic tape for further processing: (1) electroencephalogram, electro-oculogram, and submental electromyogram by conventional techniques to perform sleep staging; (2) inspiratory and expiratory flows by a pneumotachograph (Fleisch No. 2) attached to an airtight face mask; (3) volumes by electronic integration of flow signal; (4) esophageal pressure by a balloon-tipped catheter placed in the lower third of the esophagus and connected to one port of a differential transducer (Sanborn); (5) supraglottic pressure (Psg) by a second balloon-tipped catheter introduced through the nares and placed at a 15- to 17-cm distance at the supraglottic level; the catheter was connected to a port of a second pressure transducer (Sanborn); and (6) mouth pressure (Pm) by a catheter placed in the face mask and connected to the second port of both the previously cited transducers to obtain differential pressures.

Total lung resistance (Rl) was measured by the isovolume
method, referring transpulmonary pressure to different flows at equal pulmonary volumes; this method allows one to keep the elastic component constant and to refer any pressure change to the flow-resistive properties. Gas inertial phenomena were considered as negligible at low respiratory frequencies. Supraglottic resistance \((R_{sc})\) was calculated as the ratio, \((P_{sc} - P_{na})/V\). Lower airway resistance \((R_{la})\) was calculated as the difference, \(R_{na} - R_{sc}\).

RESULTS

Monitoring was performed over a total experimental time of 351 ± 77 minutes (mean ± SD). On the average, sleep accounted for 43 percent of the total experimental time (150 ± 63 minutes), with all rapid-eye-movement (REM) and non-REM stages being represented.

In the six patients with a positive history for nocturnal asthma, dramatic recurrent increases in \(R_{la}\) were recorded throughout the night, reaching an average maximum increase of 409 percent with respect to the baseline value recorded in the supine position before the onset of sleep. By contrast, in the seventh patient and in the healthy subjects, the increase in \(R_{la}\), although noticeable, was far less marked (on the average, 227 percent). In only four out of the six patients with marked nocturnal exacerbations did one or more of these episodes result in an awakening, which, in turn, was accompanied by the subjective awareness of breathlessness and wheeze in only two subjects. On the following morning, only these two subjects reported experiencing nocturnal asthma.

In the six patients who underwent nocturnal attacks, morning dips of PEF ranged from 20 to 50 percent, whereas values from 1 to 12 percent were recorded in the remaining five subjects. A close linear correlation was found between the magnitude of the morning dips and, respectively, the following (Fig 1): (1) the highest \(R_{la}\) attained in the night \((r = 0.90; p<0.001)\); (2) the average \(R_{la}\) measured throughout the night \((r = 0.835; p<0.001)\); (3) the time spent in the most marked bronchoconstriction \(ie, at \ R_{la} \) levels increased by more than 200 percent with respect to the baseline value \((r = 0.956; p<0.001)\); and (4) the time elapsed from the last peak increase in \(R_{la}\) to the morning awakening when the measurement of PEF was performed \((r = -0.996; p<0.001)\). All together, the previously mentioned factors accounted for a coefficient of multiple correlation equal to 0.978, thus indicating that more than 95 percent of the variance of morning falls in PEF was related to the examined variables.

Awakening resulted in the brisk resumption of airway patency, so that if measurements of PEF were repeated even as early as 30 minutes after the awakening, a definite and significant \((p<0.01)\) increase in PEF occurred; if these latter values had been used for the calculation of morning dips, an average underestimation by nearly 30 percent would have resulted.

DISCUSSION

Morning dipping of the PEF has long been recognized as being associated with nocturnal exacerbations of asthma; however, attention has mainly focused on its value as a marker of bronchial asthma or as an indicator of poorer prognosis; by contrast, the sign has never been submitted to an objective scrutiny of its relationship with the severity of causative phenomenon, ie, nocturnal bronchoconstriction.

The results of the present study point out that the magnitude of morning falls in PEF, provided its recording is made as early as possible and in standardized fashion, may be regarded as a reliable marker of the severity of nocturnal attacks. In fact, the index proves sensitive to the overall trend of airway obstruction at night, since it correlated not only to the highest attained peak, but also to the longitudinal course of bronchial obstruction as expressed by the mean resistance value and the duration of the obstructive events.

The growing interest toward the treatment of nocturnal asthma warrants the search for reliable methods to be used in formal controlled trials; the results of the present study demonstrate the acceptability of PEF monitoring for this purpose. In addition, they allow the selection of a suitable criterion for inclusion in such trials; in fact, the 20 percent value of the morning dip, which has been selected in some studies merely on clinical grounds, proves to be more suitable than other thresholds (such as 15
percent or 25 percent in picking up subjects undergoing nocturnal asthmatic attacks.

Nevertheless, valuable as it is, morning dip is a gross index just reflecting the tail of nocturnal phenomena which at the time of the measurement more or less rapidly are undergoing a progressive attenuation. As such, it is critically affected by an early or late awakening in the morning, since the greater the time elapsed since the last obstructive event, the less sensitive the test.

Moreover, because of the manifold influences that the state of wakefulness and physical activities may exert upon the control of airway smooth muscle, a sharp increase in airway patency occurs in the period immediately following awakening; as a consequence, delaying the morning measurement of PEF, even for only half an hour, results in a blunting of the morning dip and in some underestimation of nocturnal asthma. Therefore, it must be recommended that the measurement be made as the very first thing in the morning; moreover, if comparisons from one period to another are to be made (eg, to evaluate the effects of treatments), the time for awakening in the morning must be kept as constant as possible.

A final consideration concerns the definition of nocturnal asthma. In a recent report, Hughes suggested the following as a simple and probably the best definition: “wheezing and breathlessness at night.” The obvious merit of this clinical description is confirmed by the fact that all of the six subjects of our series who fulfilled this criterion in their history were objectively confirmed as prone to nocturnal attacks. This widely shared point of view should warrant the attitude of focusing any clinical and therapeutic attention only on patients showing this clinical picture; however, on the study night, two of our six subjects were able to sleep their asthma off, and two more, although awake in the night in connection with peak increases in R_{LBR}, were not aware of the nocturnal attack on the following morning. These results may be interpreted as a consequence of the fact that the arousal response is largely variable, both between and within individuals, in relation to the complex interaction of the resistive load with the sleep stage and other mechanical and chemical variables. Therefore, given the important implications of the syndrome and in order not to miss any case possibly worth treatment, it may be suggested that the definition of nocturnal asthma be somewhat extended, in order to include those cases in whom the evidence of a definite morning dip in PEF is noticed, even though not accompanied by the cited full-blown clinical picture.

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