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Short communication

Peak expiratory flow variation and bronchial hyperresponsiveness in asthmatic children during periods of antigen avoidance and reexposure

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Changes of diurnal variation of peak expiratory flow rate (%PEF variation) and their relationship with bronchial hyperresponsiveness (BHR) to methacholine (PC_{20}) were evaluated in 12 children with mild-to-moderate asthma and house-dust mite allergy, during successive periods of stay in a mite-free environment at high altitude (1756 m) and at their home at sea level. The children remained at the high altitude from October until the end of December; then they spent a 3-week period at home and returned to high altitude residence in January. PEF was measured daily, in the morning and in the evening, during the 3 months' stay at high altitude and then for 10 days after the return in January. PC_{20} was assessed in 8/12 children, once a month from October to December, and at the return in January. Mean absolute PEF values did not change significantly throughout the study. From October to December, patients showed a significant decrease of mean %PEF variation ($P = 0.04$), while PC_{20} showed an increase ($P = 0.05$). After the 3 weeks at home, both %PEF variation ($P = 0.03$) and PC_{20} ($P = 0.05$) significantly worsened. The correlation between PC_{20} values and mean %PEF variation in the 2 days before and after each methacholine test was $r = -0.63$ ($P = 0.001$). Our data suggest that there is a beneficial effect of a prolonged stay in a mite-free environment, on both PEF variability and BHR, also in asthmatic children with good pulmonary function. PEF variability and bronchial responsiveness to methacholine were significantly correlated also for small changes of the two variables.

E. A. Valletta [1], A. Comis [2], G. Del Col [2], E. Spezia [1], A. L. Boner [1]

[1] Pediatric Clinic, University of Verona, Verona, and [2] Istituto Pio XII, Misurina, Italy

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A. L. Boner, MD
Clinica Pediatrica
Policlinico B. Roma
37134 Verona
Italy

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Bronchial hyperresponsiveness (BHR) to various stimuli is a main physiologic feature of patients with asthma. In allergic subjects, BHR is increased during antigen exposure (1), while prolonged allergen avoidance has been reported to be associated with a decrease of BHR (2, 7). Diurnal (within a day) variation of peak expiratory flow rate (PEF) in asthmatics was shown to be a good indicator of changes in bronchial lability (4) and to be positively related to the degree of BHR (3, 5, 9, 10).

The aim of the present study was to investigate, 1) the modifications of PEF variability and of bronchial responsiveness, and 2) the relationship between these two variables in a group of children with asthma and house-dust mite allergy, during successive periods of mite avoidance at high altitude and reexposure at sea level in their home environment.

Material and methods

Twelve children (mean age 11.1 ± 1.1 years) with mild-to-moderate asthma, allergic to house-dust mites, were studied. All the patients had skin prick tests clearly positive for *Dermatophagoides pteronyssinus* and/or *D. farinae*. In the first week of October, the children were admitted to the Residential House Istituto Pio XII of Misurina (1756 m above sea level) in the Italian Alps, where they remained until the last

10 days of December. Then, they spent a 3-week period at home during the Christmas holidays, during which they were likely to be exposed to their home allergens and pollutants. All the children lived at the sea level in a rather limited area of northeastern Italy, the climate of which, in winter, is usually cold, damp, and foggy. No pets were present in the houses of those children who were known to be sensitized to cat or dog antigens. The children were again admitted to the clinic in January.

PEF measurements were performed daily by a Wright peak flow meter (Airmed, UK), in the morning (0800–0900) and in the evening (2000–2100) during the first 3 months of stay at high altitude and then for 10 days after the readmission in January. The PEF measurement was always performed prior to any drug administration, under the supervision of a physician or a nurse, and the best of three efforts was always recorded. The within-day variability of PEF for each patient was calculated as follows: %PEF variation = (highest −lowest reading)/mean reading of the day × 100 (3, 5).

BHR was evaluated by methacholine challenge at the admission and then once a month during the stay at the clinic. In January, the challenge was performed at the readmission after the Christmas holidays. Methacholine was delivered by a dosimeter (ME.FAR, Brescia, Italy) which can nebulize 10 µl of solution in 1.2 s. Five puffs of increasing concentrations of methacholine (buffer, 0.075, 0.15, 0.31, 0.61, 1.25, 2.5, 5, 10, and 25 mg/ml) were administered at intervals of 2 min. After every series of puffs, lung function (FEV_1, FEF_{25-75}, PEF) was evaluated, and the best of three efforts was recorded. After buffer inhalation, the test was continued only if the FEV_1 drop was less than 10% of basal value, and it was stopped when there was a decrease > 20% of the FEV_1 value measured after buffer inhalation. The methacholine concentration which caused a 20% (determined by interpolation) decrease of FEV_1 values was considered to be PC_{20}-FEV_1. All inhaled drugs were withheld for at least 12 h before any challenge. Long-acting β_2-agonists and theophylline preparations were discontinued at least 24 and 48 h, respectively, before the first test in October. Methacholine challenge was performed only if the baseline FEV_1 value was > 80% of predicted values. The protocol was approved by the hospital ethics committee, and informed consent from children's parents was always obtained.

Individual PEF measurements and %PEF variation data were respectively analyzed, considering all the results recorded by each child in each month of the study. The Wilcoxon signed rank test was employed to compare mean values of PEF, %PEF variation, and PC_{20} obtained in December with those in October or January. The correlation between mean %PEF variation recorded in the 2 days before and after each methacholine test and the corresponding PC_{20} value was assessed by the Spearman rank correlation coefficient.

Results

Because of the high altitude and favorable conditions of climate which allowed a mite-free environment (6), regular sodium cromoglycate, nedocromil, inhaled corticosteroid, or theophylline could be progressively withdrawn within the first 3–4 weeks of the study. Then the children were treated only if needed. During the 3-week period at home, an individualized treatment was prescribed, depending on the previous clinical history. Some clinical features of the patients are shown in Table 1.

For each one of the two daily measurements (morning and evening) of PEF in the 12 children studied, 353 observations were available in October (that is, 95% of the maximum possible number), 222 in December (93%), and 98 (82%) in January. Corresponding values of %PEF variation were available. Good cooperation in performing bronchial provocation tests was obtained in eight of the 12 children. Thus, eight PC_{20} methacholine values were available for each one of the 3 months considered.

Mean (± SD) normal PEF value for height in the 12 children was 363 ± 56 l/min (8). No significant change in mean PEF values was observed either during the stay at the clinic (October: morning 379 ± 45 l/min, evening 409 ± 50 l/min; December: 378 ± 56 l/min, 408 ± 55 l/min) or after the 3-week interval at home (January: 374 ± 51 l/min, 402 ± 46 l/min). Mean %PEF variation and PC_{20} showed a better defined trend (Table 2). During the October–December period, mean %PEF variation significantly decreased ($P = 0.04$) while PC_{20} increased

Table 1. Clinical features of 12 children studied

Patient no.	Age (years)	Sex	Therapy at admission in October	Therapy during 3-week period at home
1	11	M	IC	IB
2	9	M	IC, IB	IB
3	12	M	IC	IB
4	13	F	IC, IB	IB
5	11	M	IC	IB
6	10	M	IC, NS	NS
7	12	F	IC	NS, IC
8	12	M	Th	NS, IC
9	10	F	Th	Th
10	12	F	IC, IB, Th	Th, IC
11	10	F	IC	IB
12	12	M	IC, SCG	SCG

IC: inhaled corticosteroid (beclomethasone, 300–750 µg/day); IB: intermittent β_2-agonist (salbutamol); NS: nedocromil sodium (4 mg tid); SCG, sodium cromoglycate (10 mg qid); Th: theophylline (dose to achieve serum level of 10–20 µg/ml).

Table 2. Mean monthly %PEF variation (12 children) and PC_{20} methacholine (mg/ml) (eight children) during stay at high altitude (October and December) and after 3-week period at home (January)

Patient no.	October		December		January	
	%PEF var.	PC_{20}	%PEF var.	PC_{20}	%PEF var.	PC_{20}
1	6.4	3.25	5.8	4.25	5.6	2
2	14.5	1.2	9.3	1.87	13.5	1.08
3	7.6	0.43	6.9	1.81	13.6	1.62
4	12.8	–	12.1	–	12.5	–
5	3.8	8	2	25	3.2	12
6	4.7	2.5	4.9	3	7.3	2
7	13.9	2.37	13.1	3.25	9.7	4.25
8	11.2	–	11.7	–	11.2	–
9	14.2	–	16.3	–	21.9	–
10	5.4	0.68	4.7	4.75	7.5	2.31
11	12.5	3.25	10.7	2.3	16.5	1.75
12	10	–	4.9	–	8.8	–
Median	10.6	2.4	8.1[§§]	3.1[f #]	10.4	2

%PEF var.: [b]: vs October, $P=0.04$; [§]: vs January, $P=0.03$.
PC_{20}: [f]: vs October, $P=0.05$; [#]: vs January, $P=0.05$.

($P=0.05$). In January, when the children were readmitted to the clinic, a worsening of both %PEF variation ($P=0.03$) and PC_{20} ($P=0.05$) was observed if compared with values recorded in December. When PC_{20} values in the eight children were plotted against the corresponding mean %PEF variations (see Material and methods section), a correlation coefficient $r=-0.63$ ($P=0.001$) was obtained.

Discussion

The results of the present study show that, in children with asthma and house-dust mite allergy, prolonged antigen avoidance at high altitude significantly improves both diurnal PEF variability and nonspecific bronchial reactivity. An inverse relationship was observed between %PEF variation and PC_{20} methacholine.

It has been suggested that diurnal variation of PEF is a reliable marker of bronchial lability, related to the level of bronchial responsiveness to histamine or methacholine (3, 5, 9, 10). Nevertheless, most of the published studies were cross-sectional reports, and they lacked a prolonged follow-up (5, 9). When the latter was available (3, 10), exposure to specific or nonspecific environmental stimuli was largely casual. With respect to this, the environment in which the present study was performed provided some advantages: the around-the-year analysis of the dust from the clinic in Misurina failed to reveal the presence of mites (6). On the contrary, evaluation of mite content in the dust from houses in the area served by the clinic, performed by guanine test, showed a level of positivity (mean ± SEM) of 1.72 ± 0.076 (of a score ranging from 0 = no mites to 3 = high antigen level).

In our patients, we did not observe any significant change of mean PEF values throughout the study period. Nevertheless, the prolonged stay in a mite-free environment resulted in progressive reduction of diurnal PEF variation and of bronchial response to methacholine challenge. These changes, although small and of limited clinical value, show that, also in patients with mild-to-moderate disease and near-to-optimal pulmonary function (as measured by PEF), a further improvement of bronchial lability and responsiveness can be obtained by reducing children's exposure to the offending allergen.

The significant inverse correlation between PC_{20} methacholine and mean diurnal PEF variation is in keeping with recent observations by Josephs et al. (3) in a mixed group of adults and children. The correlation ($r=-0.60$) found by these authors was similar to our own ($r=-0.63$), and both were stronger than the correlation ($r=-0.41$) observed in the cross-sectional study of Ryan et al. (9) when the presalbutamol variation of PEF was considered. Similarly, Woolcock et al. (10) found a significant correlation ($P<0.01$; r: not given) between PEF variability and PD_{20} histamine in a long-term (1–2 years) follow-up study in adults with asthma. Finally, our data show that, in asthmatic children, such a correlation is present also for small modifications of both PEF variability and BHR and in subjects with good pulmonary function, thus confirming and further extending the observation that PEF variability is a good marker of BHR severity.

References

1. Boulet LP, Cartier A, Thomson NC, Roberts RS, Dolovich J, Hargreave FE. Asthma and increases in non-allergic bronchial responsiveness from seasonal pollen exposure. J Allergy Clin Immunol 1983: 71: 399–406.
2. Boner AL, Niero E, Antolini I, Valletta EA, Gaburro D. Pulmonary function and bronchial hyperreactivity in asthmatic children with house dust mite allergy during prolonged stay in the Italian Alps (Misurina, 1756 m). Ann Allergy 1985: 54: 42–5.
3. Josephs LK, Gregg I, Mullee MA, Holgate ST. Non-specific bronchial reactivity and its relationship to the clinical expression of asthma. A longitudinal study. Am Rev Respir Dis 1989: 140: 350–7.
4. Lebowitz MD. The use of peak expiratory flow rate measurements in respiratory disease. Pediatr Pulmonol 1991: 11: 166–74.
5. Neukirch F, Liard R, Segala C, Korobaeff M, Henry C, Cooreman J. Peak expiratory flow variability and bronchial responsiveness to methacholine. An epidemiological study in 117 workers. Am Rev Respir Dis 1992: 146: 71–5.
6. Piacentini GL, Martinati L, Fornari A, et al. Antigen avoidance in a mountain environment. II. Influence on basophil releasability in children with allergic asthma. J Allergy Clin Immunol 1993: 92: 644–50.
7. Platts-Mills TAE, Tovey ER, Mitchell EB, Moszoro H, Nock P, Wilkins SR. Reduction of bronchial

hyperreactivity during prolonged allergen avoidance. Lancet 1982: ii: 675–8.
8. POLGAR G, PROMADHAT V. Pulmonary function testing in children. Techniques and standards. Philadelphia: WB Saunders, 1971.
9. RYAN G, LATIMER KM, DOLOVICH J, HARGREAVE FE. Bronchial responsiveness to histamine: relationship to diurnal variation of peak flow rate, improvement after bronchodilator, and airway calibre. Thorax 1982: 37: 423–9.
10. WOOLCOCK AJ, YAN K, SALOME CM. Effect of therapy on bronchial hyperresponsiveness in long-term management of asthma. Clin Allergy 1988: 18: 165–76.

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