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Assessment of variability of exercise tolerance limited by breathlessness

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ABSTRACT A sequence of questions was designed to quantify the within subject variation of exercise tolerance limited by breathlessness, to serve as a guide to variation in airflow limitation for epidemiological purposes. The questions seek answers about breathlessness in relation to various levels of attempted activity when the subjects are at their best and at their worst. The difference between exercise tolerance at best and exercise tolerance at worst (variation in exercise tolerance) was expressed on a scale ranging from 0 (no variation) to 6 (greatest variation). The effectiveness of these questions has been assessed in 68 patients with airflow limitation attending a chest clinic, by comparing the results with variation in peak expiratory flow rate (PEF). Variation in PEF was expressed as the standard deviation of the first 24 PEF recordings from each patient (equivalent to four days' recordings). There was a highly significant relation between the measure of variation in exercise tolerance obtained from the questionnaire and PEF variation, though each point on the scale of variation in exercise tolerance covered a wide range of variation in PEF. The questions give some guide to the variation in airflow limitation and in combination with other questions may be helpful in epidemiological studies.

Introduction

Recent reports[1,2] of attempts to diagnose asthma in the general population by questionnaire have indicated that positive responses to questions on wheezing or whistling in the chest enable the recognition of most individuals with bronchial hyperreactivity, an objectively measured response thought to be closely related to asthma. Some subjects without hyperreactivity also answer positively to these questions,[2] and some of these probably have non-asthmatic airflow limitation or non-pulmonary disease. It would be helpful if supplementary questions could aid the distinction of subjects with asthma from those with other diseases.

Identification of asthma is also hampered by the lack of a generally accepted definition of the condition, though variable airflow limitation is agreed to be a cardinal feature.[3] Recognition of the symptoms resulting from variable airflow limitation by questionnaire would be helpful. As variability in airflow limitation is commonly accompanied by variation in breathlessness, the epidemiologist might be able to estimate approximately the degree of variability of airflow limitation in an individual by asking a series of questions about variation in breathlessness, just as in a clinical setting the physician may ask similar though less rigidly structured questions.

We describe an attempt to assess the variability of airflow limitation in patients with airflow limitation by a sequence of questions designed to quantify variability of exercise tolerance limited by breathlessness. We have compared the answers to the questions with serial measurements of peak expiratory flow (PEF), since these measurements are less invasive and may reflect more closely the symptoms of which the asthmatic patient complains than do bronchial reactivity tests. We administered the questions to subjects with chest disease, who also recorded serial PEF measurements. The variability of exercise tolerance due to breathlessness as assessed by questionnaire has been compared with the variability of airflow limitation as assessed by serial PEF measurements.

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Methods

SUBJECTS

Seventy four consecutive patients attending an adult chest clinic, with a diagnosis (made by the physician) of asthma or chronic obstructive bronchitis, agreed to participate. Informed, written consent was obtained. All patients had airflow obstruction with an FEV_1 of less than 80% of the predicted value, or an increase in FEV_1 of at least 20% after an inhaled beta agonist. Subjects with other chest or cardiac diseases were excluded.

QUESTIONNAIRE

The questionnaire was designed to elicit from patients detailed clinical information relevant to the diagnosis of asthma, but this paper is concerned with only one part—a sequence of questions about the grade of exercise tolerance limited by breathlessness when their chest was at its best and a similar sequence about when it was at its worst (table 1).

The questions were adapted from the Medical Research Council questionnaire on respiratory symptoms.[4] From these questions breathlessness ranging from "at best" to "at worst" can be graded on a scale of 1–7. A numerical scale of variation of breathlessness was derived by subtracting the numerical value of the grade "at best" from the grade "at worst," and this was used in the analysis.

The questionnaire was initially tested for comprehensibility in a different chest clinic, and modified in the light of this experience. It was administered to all patients by one of us (ETP) according to a strict protocol.

Each patient was also asked to measure his PEF (mini Wright peak flow meter) six times daily for two weeks and to record the best of three attempts on each occasion. Only patients who recorded consecutive, or nearly consecutive, readings for a total of 24 readings (equivalent to four days) were included in the analysis.

Variables derived from the first 24 PEF recordings from each subject were analysed. PEF "variability," assumed to be a continuous variable, was analysed initially for each individual in three ways: (1) the difference between the maximum and minimum PEF values; (2) the difference between the mean of the three best values and the mean of the three worst values (PEF range); (3) the standard deviation of all values.

There was a close correlation between the different measures of variation; for instance, the correlation coefficient of PEF range with PEF SD was 0·944 (fig 1). Since SD was based on all the data we decided to use this as the measure of variation in PEF.

The mean PEF reading was used as a measure of the average level of airflow obstruction. Variation in PEF was compared with variation in exercise tolerance, the influence of age being taken into account. As the potential for variation in exercise tolerance is inevitably influenced by the level of exercise tolerance when the subject is at his or her best, the grade of exercise tolerance at best was also taken into account.

Apparent associations were investigated by means of ordinary least squares multiple linear regression, the numerical values for grade of exercise tolerance at best and variation in exercise tolerance being used as continuous variables.

Table 1 *Questions designed for estimating exercise tolerance at best and at worst**

PREAMBLE: *I want you to think about your best and worst times from the point of view of your chest*

	Grades of exercise tolerance						
	1	*2*	*3*	*4*	*5*	*6*	*7*
	Required answers						
1 At your best are you confined to bed or chair?						N	Y
2 At your best are you confined to the house?					N	Y	
3 At your best can you walk at your own pace?				Y	N		
4 At your best can you walk with other people of your own age on level ground?			Y	N			
5 At your best can you hurry on level ground or walk up a steep hill?		Y	N				
6 At your best can you run?	Y	N					
7 At your worst are you confined to bed or chair?							
8 At your worst are you confined to the house?							
9 At your worst can you walk at your own pace?							
10 At your worst can you walk with other people of your own age on level ground?							
11 At your worst can you hurry on level ground or walk up a steep hill?							
12 At your worst can you run?							

*Routing instructions, and instructions for excluding subjects disabled by musculoskeletal disease, have not been shown, but are advisable in the use of the questionnaire. From the answers to questions 1–6 and also 7–12 gradings of exercise tolerance at best and at worst respectively can be derived on scales of 1–7 (note that the logic of the yes/no answers changes through the sequence). The gradings attributed to combinations of answers to the first six questions are shown on the right. By subtraction of the grading at best from the grading at worst a grading of variation in exercise tolerance on a scale of 0–6 can be derived. Higher grades indicate greater variability.

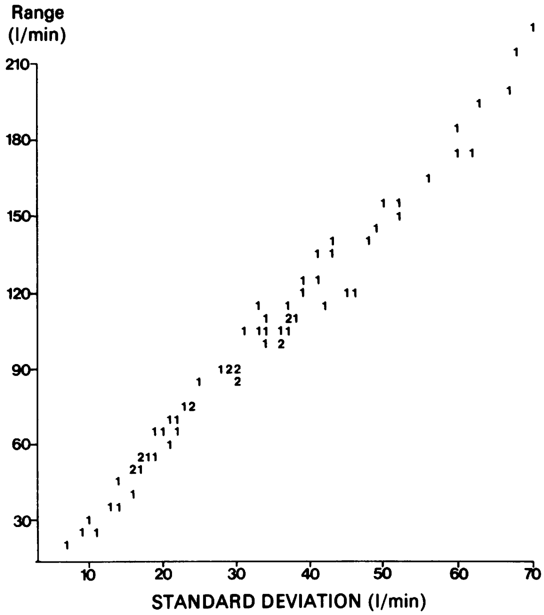

Fig 1 *Relation between two measures of variation in peak expiratory flow (PEF) over four days in 68 subjects. "Range" is the difference between the mean of the highest three and the lowest three PEF recordings.*

The answers to the question "Does your chest ever make a wheezing or whistling sound?" were also noted.

Results

Seventy four subjects completed the questionnaire and measured their PEF. Three were excluded from the analysis because they provided fewer than 24 PEF measurements, and a further three because (through misunderstanding or misrecording) they reported being more limited by breathlessness when at their best than when at their worst. Details of the remaining 68 subjects (39 men, 29 women) are shown in table 2.

There was a positive relationship between variation in exercise tolerance and PEF variation (fig 2), though for each point on the scale for variation in exercise tolerance there was a wide range of values for PEF variation.

Table 3 shows the relation between variation in exercise tolerance and exercise tolerance at best and how each of these is related to mean PEF and variation in PEF. PEF variation was related to variation in exercise tolerance for all grades of exercise tolerance at best, though subjects with severely impaired exercise tolerance at best inevitably had a limited scale on which to measure variation in exercise tolerance. There was a tendency for variation in exercise tolerance to be inversely related to PEF in some groups, but this was not consistent.

Table 2 *Variables derived from serial peak expiratory flow rate recordings*

	Mean	*SD*	*Range*
Age (y)	52	14	15– 73
Peak flow (l/min):			
Mean	264	88	97–522
Maximum minus minimum	125	58	20–260
Range (average of maximum three minus average of minimum three)	101	48	18–223
Variation (standard deviation)	33	16	7– 70

The influence of age, variation in exercise tolerance, and exercise tolerance at best on PEF variation and mean PEF was examined by multiple regression (table 4). After allowance had been made for age and exercise tolerance at best variation in exercise tolerance was significantly related to PEF variation ($p < 0.001$). After allowance had been made for PEF variation age and exercise tolerance at best did not have significant effects.

Mean PEF was inversely related to exercise tolerance at best and showed a weakly significant inverse relation to variation in exercise tolerance (the lower the mean PEF the worse the exercise tolerance at best and the greater the variation in exercise tolerance).

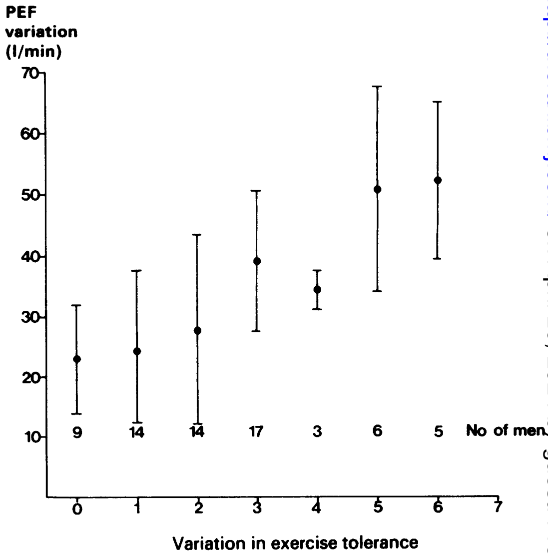

Fig 2 *Mean and standard deviations of peak expiratory flow (PEF) variation according to reported variation in exercise tolerance. PEF variation is the standard deviation of all the PEF readings for each subject.*

Table 3 *Means of derived peak expiratory flow (PEF) measurements according to grades of exercise tolerance at best and of variation in exercise tolerance**

Grade of exercise tolerance at best:	*Grade of variation in exercise tolerance* 0	1	2	3	4	5	6
1	0	2	3	3	4	5	0
	—	419	327	333	275	297	—
	—	36	32	46	51	52	—
2	2	3	5	2	1	2	0
	295	332	276	315	283	292	—
	19	34	32	41	31	50	—
3	2	4	2	9	2	0	0
	253	200	177	284	154	—	—
	16	18	26	35	36	—	—
4	4	4	4	3	0	0	0
	254	248	146	232	—	—	—
	25	22	21	42	—	—	—
5	0	1	0	0	0	0	0
	—	168	—	—	—	—	—
	—	10	—	—	—	—	—
6	1	0	0	0	0	0	0
	192	—	—	—	—	—	—
	37	—	—	—	—	—	—
7	0	0	0	0	0	0	0
	—	—	—	—	—	—	—
	—	—	—	—	—	—	—

No subjects reported the most severe grade of impairment of exercise tolerance at best (grade 7: confined to bed or chair), but, as implied by the table, seven subjects reported this grade when at their worst.
*Each cell contains number of subjects, PEF mean level in l/min, and PEF mean variation in l/min. Standard deviations are not shown because of the small size of the groups.

Estimates from a simplified single regression model for variation in exercise tolerance with PEF variation (with no allowance for age or exercise tolerance at best) indicate that the change in PEF variation (measured as SD) between each point on the variation in breathlessness scale is about 5 l/min. For example, someone whose breathlessness does not vary would be predicted to have a PEF standard deviation of about 20 l/min, whereas someone who could run on good days but could not walk at his own pace on bad days would be predicted to have a PEF SD of about 40 l/min.

Only five of the 68 subjects did not admit to wheezing or whistling.

Discussion

We did not expect that either questions on variation in exercise tolerance or serial measurements of PEF would identify individuals with asthma with complete reliability. Even in the clinical setting, the identification of asthma may require evidence from history, physical signs, and physiological measurements over an extended period. Measurement of PEF variation is an attempt to assess the variable airflow limitation that is a cardinal feature of asthma directly. We wished to know whether the questions on variation in exercise tolerance showed some degree of correspondence with PEF variation.

The system of questions we used was a preliminary attempt to grade variation in exercise tolerance due to breathlessness. No doubt the wording can be improved, and we have already modified and simplified the questions described here for use in epidemiological study of wool textile workers.[5] These changes meant some alterations in the wording and sequence of the questions, and the substitution of the questions on confinement to house and to bed or chair with one on breathlessness when resting. We recognise that other causes of variation in exercise tolerance besides asthma could interfere with this assessment, though possibly other questions (not yet explored by us) could identify, for instance, cardiac disease.

Some additional discrepancy might have been expected betwen the questionnaire assessments and the PEF assessments of variation, as the questions did not define the period of interest and the PEF measurements related to only four days. A period of recording longer than four days would probably have given a fuller assessment of the variation in airflow obstruction. Nevertheless, the range of variation of

Table 4 *Multiple regression models for peak expiratory flow (PEF) revised variables*

Variable†	*PEF variation (l/min)* *Coefficient*	$\lvert t \rvert$	*PEF mean level (l/min)* *Coefficient*	$\lvert t \rvert$
Age (years)	−0·09	−0·6	−0·59	−0·7
Exercise tolerance at best (scale 1–7)	−1·89	−1·2	−40·49	−4·2***
Variation in exercise tolerance (scale 0–6)	4·42	3·9***	−13·59	−2·0*
Intercept	32·11	—	432·39	—
Percentage of population variation explained	38	—	26	

†Higher numbers on the scale for exercise tolerance at best indicate more limited exercise tolerance and on the scale for variation in exercise tolerance greater variability than lower values. Age has been retained in the statistical models to illustrate how little it contributes to these relationships after exercise tolerance has been taken into account. $\lvert t \rvert$ is the coefficient divided by the standard error of the estimate. Values of $\lvert t \rvert$ greater than about 2 indicate that the estimated relationship is likely to have arisen by chance less than once in 20 times.
*$0·05 > p > 0·01$. ***$p < 0·001$.

PEF between patients was wide, confirming that adequate comparisons with symptoms could be made.

The population we studied did not include individuals with normal lung function, and we do not know at present what results would have been obtained in a normal population. It is, however, appropriate that the results of the present study refer only to subjects with airflow obstruction, as we envisage that these questions will be used to supplement other questions (such as those on wheezing) identifying abnormal individuals.

Despite these reservations, we have shown a highly significant relation between variation in exercise tolerance assessed by questionnaire and variation in airflow obstruction assessed by serial peak expiratory flow measurements. Confidence in this result is increased by the quite different, and clinically plausible, relation between mean PEF and response to the questions. The questions, or adaptations of them, may be used in epidemiological studies with some degree of confidence that the answers relate to variation in PEF in those with abnormal airflow. As anticipated, in individuals the degree of reliability is not adequate for clinical purposes, but for epidemiological studies the questions are capable of indicating an approximate likelihood of variability of airflow limitation, which may be compared with other factors of interest. Indeed, adaptations of these questions have already enabled the identification of individuals with variable exercise tolerance in a population of wool textile workers[5] whose symptoms were related to their occupation.

We thank Dr G Anderson for permission to study his patients, and the patients themselves for their participation.

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