Hyperventilation in patients with recurrent functional symptoms

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SUMMARY. In view of the similarity between the reported effects of hyperventilation and recurrent functional symptom presented in primary care, a study was undertaken to establish whether such symptoms are attributable to hyperventilation. Twenty patients with two or more recurrent functional symptoms which their doctors found difficult to diagnose or treat, and 30 controls, were studied using symptom questionnaires and a series of hyperventilation provocation tests during which the partial pressure of carbon dioxide (PCO_2) and symptoms were recorded. Sixteen cases (80%) had unexplained breathlessness compared with two of the controls (7%). All of the cases recognized familiar functional symptoms during provoked hyperventilation, and in 16 (80%), these included primary physical symptoms; only 23% of the controls recognized any previously experienced symptom. Considerable overlap of PCO_2 values between groups meant that absolute values of PCO_2 were not useful in differentiating between groups, but cases were more likely than controls to have a PCO_2 of less than 4 kPa at rest, three minutes after hyperventilation, or during mental stress (75% of cases fulfilled one or more of these criteria versus 40% of controls). This is the first study in primary care to examine the effect of hyperventilation in a group of patients with multiple somatic symptoms. The findings have implications for the recognition and management of such patients.

Keywords: hyperventilation; dyspnoea; somatization.

Introduction

HYPERVENTILATION, defined as physiologically inappropriate over-breathing,[1] has been recognized for many years as a cause of a wide range of symptoms. These include breathlessness, chest and abdominal pain, light-headedness and other neurological symptoms, palpitations, and panic attacks.[2] Since the advent of capnography for measuring the end-tidal partial pressure of carbon dioxide (PCO_2) in expired air, and recognition of its close correlation with arterial PCO_2, assessment of hyperventilation using both laboratory and clinical techniques has been possible.[3]

Hospital based studies have demonstrated low levels of end-tidal PCO_2 in patients with symptoms suggesting hyperventilation.[3] Despite this, no clearly definable hyperventilation syndrome has emerged,[1,4] reflecting the difficulty in integrating physiological measurements with widely experienced but differing symptoms. The poor correlation between symptoms and arbitrary laboratory standards has been used both to argue that symptoms are a poor predictor of hyperventilation[5] and to doubt the usefulness of PCO_2 as a criterion for the diagnosis of the hyperventilation syndrome.[6] Some workers have now abandoned this label in favour of 'symptomatic hyperventilation'[7] but still argue the case for some form of PCO_2 measurement.[4]

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The symptoms described in hospital studies appear to overlap with the type of functional symptoms frequently presented to general practitioners. Patients with functional symptoms may be difficult to treat, as disability can seem at odds with normal findings, and explanation of the symptoms may be unsatisfactory. Despite this, to date there have been no formal studies of hyperventilation in general practice.

The aim of this study was to establish whether patients in general practice have recurrent functional symptoms attributable to hyperventilation, by using both symptom questionnaires and measurement of end-tidal PCO_2.

Method

The study was carried out between March 1991 and April 1992 in a three partner, rural practice with a list size of approximately 5000 patients. The protocol for the study was approved by the relevant ethics committees and informed written consent was obtained from all subjects.

Potential subjects for the study were identified by all the doctors in the practice, either from memory or at the time of consultation. Patients were invited to participate as cases if they had attended with two or more physical symptoms for which there was no apparent pathological cause on two or more occasions in the preceding year and their general practitioner found these symptoms difficult to diagnose or treat. Controls were recruited from patients who had recently had injuries or operations, patients with inflammatory joint or bowel disease, and health promotion clinic attenders. No attempt was made to include all the patients who might have met either set of criteria in the study.

Patients whose main reported symptoms were psychological, and those with depression characterized by anhedonia and diurnal mood variation were excluded; those with lesser psychological symptoms in addition to their physical ones were included. Although potential controls were not invited if they had a history of anxiety or depression warranting treatment, they were not screened in advance for functional symptoms and several reported such symptoms at interview. Anyone with proven cardiac or neurological disease was excluded, as was any individual receiving medication for respiratory problems.

The interview was conducted by the author after a brief explanation of the test in which emphasis was placed on testing the equipment, not the patients, and there was no suggestion of hyperventilation. Subjects were asked to describe up to two troublesome physical symptoms (primary symptoms) and were then asked five questions about breathlessness and five about other symptoms (paraesthesiae, light-headedness, a feeling of being about to die, disturbed sleep and fatigue). Breathlessness was enquired about on exertion, at rest, when anxious, during primary symptoms or if there were no primary symptoms, during other past symptoms, and in association with a feeling of being unable to get a deep breath. An arbitrary score of three out of five positive answers, was taken to represent significant breathlessness.

After the interview, patients were connected to a Normocap 200® capnograph (Datex Instrument Corporation) by a fine-bore sampling line taped inside one nostril. Values for PCO_2 were noted from the monitor at set times and a printed record of values and trends was obtained. At each session the calibration of the

monitor was checked. In all cases, plateaux of the PCO_2 waveform were obtained at measurement times suggesting that alveolar air was being adequately sampled.

After an initial period of at least three minutes of recording, during which subjects were allowed to read, a baseline value was calculated by taking the mean of PCO_2 recordings at 10 second intervals over a further minute. Further tests were then carried out, during which values for PCO_2 were recorded and symptoms noted. Symptoms were grouped as follows: primary symptoms, other familiar symptom, other unfamiliar symptom and no symptom noted.

There were three tests. In the 20 breath test, as described by Howell,[8] participants were asked to take 20 consecutive deep breaths and then to breathe normally. The PCO_2 attained at the end of the 20 breaths, and three minutes thereafter were recorded. Subjects were then asked to describe anything they had felt. A further period was allowed, if necessary, to allow the PCO_2 to return to over 4.0 kPa and at least 90% of the baseline value.

In the one minute forced hyperventilation test, a shortened version of the standard three minute test,[6] subjects were made to over-breathe for one minute during which they were encouraged to reach and maintain a PCO_2 of less than 2.9 kPa. The lowest PCO_2 values at the end of the minute, and three minutes thereafter were recorded, as were symptoms.

In the think test,[9] when PCO_2 had returned to near baseline, subjects were asked to envisage a series of situations while PCO_2 was recorded. Each lasted a minute and they comprised, in order, a relaxed situation (for example, on a beach), a situation when primary (or other) symptoms had been severe, a return to the relaxed situation and one which made the subject 'frustrated or upset'. At the end of this, subjects were asked to indicate when breathing was felt to be normal and the PCO_2 was noted. Any symptoms experienced during the think test were recorded.

Analysis

The results obtained were compared between groups using appropriate chi square tests for discrete variables and Kruskal-Wallis one way analysis of variance for continuous variables. Calculations were carried out using the *Epi info 5* package.[10]

Results

Fifty six patients were invited to take part. Four potential controls declined or were unable to attend, one potential case had minor electrocardiogram abnormalities in association with atypical chest pain and another had responded to antidepressant medication between the invitation and attendance for study and so were excluded. Although their primary symptoms were physical and there were no signs of severe depression, four cases were taking antidepressant medication; one of these had, in retrospect, a fairly short-lived agitated depression and symptoms cleared quickly. Twenty cases and 30 controls were recruited. Seven cases and eight controls were men. The mean age of the cases was 39 years (standard deviation (SD) 12 years, range 20–59 years) and the mean age of the controls was 41 years (SD nine years, range 22–55 years).

Interview

When asked to state their two primary symptoms, 10 cases reported neurological symptoms (for example, a light-headed or dizzy feeling), nine reported fatigue, six chest pain, five abdominal pain, five musculoskeletal pain, and five reported panic/palpitations. Thirteen controls were recruited from health promotion clinics. Eight reported primary symptoms as a a result of recent injury or operation; six from arthritis and three from inflammatory bowel disease. Additional primary symptoms reported by controls were neurological symptoms (three subjects), abdominal pain two, panic/palpitations two, musculoskeletal pain (one) and fatigue (one). Seven controls reported no primary symptoms.

Almost all the symptoms reported (all of the cases' symptoms) had been brought to medical attention and several cases had undergone hospital investigations. Two had had coronary angiography with normal results and one had been diagnosed as suffering from chronic fatigue syndrome.

The results of the direct questions about breathlessness and other symptoms are shown in Table 1. There were significant differences between the groups in the numbers of positive responses except in reporting disturbed sleep. Sixteen cases (80%) reported dyspnoea in three or more of the situations, compared with two of the controls (7%) (Yates corrected chi square = 24.9, $P<0.001$).

Capnography

Two cases did not complete the PCO_2 monitoring: one had a PCO_2 of 3.8 kPa at the beginning of the test which fell further, in association with primary symptoms, without voluntary hyperventilation and the other was distressed by the 20 breath test and moved directly to the think test. Patients' PCO_2 values as a result of the tests are shown in Table 2. There was no significant difference between cases and controls in PCO_2 except that during the stress stages of the think tests, the mean values were significantly lower for cases than controls. The mean PCO_2 at rest was significantly lower in subjects reporting fatigue than in those not doing so (mean 4.6 kPa, SD 0.37 versus 4.9 kPa, SD 0.53, $P<0.05$). There was no such difference between subjects reporting and not reporting breathlessness in three or more situations.

Sixteen cases (80%) recognized primary symptoms, and four (20%) recognized other familiar symptoms during one or more stages of the tests. Two controls (7%) recognized primary symptoms, five (17%) recognized other familiar symptoms, 11 (37%) experienced unfamiliar symptoms and 12 (40%) experienced no symptoms during hyperventilation.

The mean PCO_2 of patients who experienced their primary symptom at some stage of the hyperventilation testing and those who either experienced symptoms which they did not recognize from prior experience (for example, light-headedness), or who had no symptoms at all were compared (Table 2). Significantly

Table 1. Percentage of subjects in cases and control groups reporting symptoms.

Symptom	% experiencing symptoms: Cases (n = 20)	Controls (n = 30)
Dyspnoea on exertion	70	30 **
Dyspnoea at rest	50	0 ***
Dyspnoea when anxious	85	20 ***
Dyspnoea during primary or other symptoms	85	17 ***
Dyspnoea and unable to take a deep breath	60	10 ***
Three or more of the above	80	7 ***
Light-headed with primary or other symptoms	75	27 **
Paraesthesiae with primary or other symptoms	70	17 ***
Sometimes feel as if dying	65	27 *
Disturbed sleep	70	47
Fatigue	80	27 ***

n = number of patients in group. P value calculated from Yates corrected chi squares (Fisher's exact test used to test dyspnoea at rest); *$P<0.05$, **$P<.01$, *** $P<.001$.

Table 2. Partial pressure of CO_2 at different stages of testing among cases and controls and among those experiencing primary symptoms and those experiencing no symptoms or unfamiliar symptoms.

	Mean partial pressure of CO_2 (kPa) (standard deviation)			
Stage of test	Cases (n = 19)	Controls (n = 30)	Experiencing primary symptoms (n = 18)	Experiencing no familiar symptoms (n = 23)
At rest[a]	4.6 (0.4)	4.9 (0.5)	4.6 (0.4)	4.9 (0.5)
After 20 breaths	2.9 (0.4)	2.8 (0.4)	2.9 (0.4)	2.8 (0.4)
Three minutes after 20 breaths	4.1 (0.4)	4.5 (0.7)	4.1 (0.4)	4.7 (0.7) *
After one minute hyperventilation[b]	2.7 (0.3)	2.7 (0.2)	2.7 (0.3)	2.7 (0.2)
Three minutes after hyperventilation[b]	4.0 (0.4)	4.3 (0.6)	4.1 (0.4)	4.5 (0.6)
End of first period of relaxation	4.6 (0.3)	4.7 (0.5)	4.6 (0.3)	4.8 (0.5)
End of first period of mental stress	4.1 (0.4)	4.5 (0.7) **	4.1 (0.4)	4.6 (0.7) *
End of second period of relaxation	4.5 (0.3)	4.7 (0.6)	4.5 (0.4)	4.8 (0.6)
End of second period of mental stress	4.0 (0.5)	4.5 (0.8) *	4.0 (0.5)	4.5 (0.8) *

n = number of patients in group. [a]number of cases = 20. [b]number of cases = 18. Kruskal Wallis one way analysis of variance; *P<0.05, **P<0.01.

lower PCO_2 values were found among those recognizing primary symptoms compared with those either experiencing symptoms they did not recognize or who had no symptoms at all three minutes after 20 breaths, and at the end of two periods of mental stress.

Despite the difference between means, the considerable overlap between groups meant that absolute values of PCO_2 did not appear to be useful in differentiating between groups. However, when an arbitrary cut-off point for low PCO_2 was applied (PCO_2 <4.0 kPa at rest, three minutes after either period of hyperventilation, or during the stress phases of the think test), 15 cases (75%) fulfilled one or more of the criteria, compared with 12 controls (40%).

Combined results

The combined test results using the criteria of breathlessness in at least three out of five situations, reproduction of recognized symptoms (either primary or other familiar), and PCO_2 less than 4.0 kPa in one or more of the situations previously described are shown in Table 3. All subjects who met the criteria for breathlessness recognized symptoms during testing, irrespective of PCO_2. While low PCO_2 or recognition of any symptoms was not confined to cases, combining any two measures discriminated better between the groups. In particular, dyspnoea and two short hyperventilation tests appeared to differentiate well between the groups.

Table 3. Cases and controls meeting various study criteria.

Criteria	No. of cases (n = 20)	No. of controls (n = 30)
Low PCO_2[a]	15	12
Dyspnoea[b]	16	2
Dyspnoea plus any symptom recognized during first two breathing tests	16	1
Dyspnoea plus any symptom recognized during 20 breath test	13	0
Primary symptoms reproduced in any test	16	2
Any symptom reproduced by any test	20	7
Low PCO_2 plus recognized symptom at any stage of test	15	5
Any two of low PCO_2, dyspnoea and any recognized symptom on testing.	19	6

n = total number of patients in group. [a]<4.0 kPa at rest, three minutes after voluntary hyperventilation, or during mental stress test. [b]In at least three out of the five situations described.

Six controls had 'abnormal' results in two or more categories. Of these, four had reported (and two had experienced during testing) primary symptoms which may have been functional: two with panic attacks, one with pelvic pain and one with symptoms not easily explicable by Crohn's disease. While not meeting the entry criteria for cases, these patients appeared to have some functional symptoms elicited on questioning. No control had only unexplained breathlessness.

Discussion

This study, the first of hyperventilation induced symptoms in general practice, has shown that 80% of a selected group of 20 patients with two or more functional symptoms recognized at least one of these symptoms during brief voluntary hyperventilation. The remaining four experienced non-specific symptoms which had occurred previously. Sixteen cases reported breathlessness suggestive of psychogenic dyspnoea. Despite the wide difference in symptom experience, there was considerable overlap between cases and controls in actual PCO_2 values.

There are a number of potential sources of error in this study. Subjectivity was introduced by the doctors putting forward patients they found difficult to diagnose or treat. Selection and testing were carried out by the same person, who was also many of the subjects' own general practitioner. To reduce personal influence, inclusion of patients and controls was according to firm criteria and verbal and non-verbal communication during the tests was minimized.

As this is the first formal study of hyperventilation in general practice, no comparable data are available. As both respiratory and psychiatric illness may cause hyperventilation,[11,12] attempts were made to exclude patients with these, although no formal respiratory or psychometric tests were performed. In hospital studies, few patients with even severe hyperventilation appear to have unexpected respiratory disease,[11] and doubt has been expressed about the validity of routine respiratory measurements in patients who hyperventilate.[13] Several of the cases may have met the diagnostic criteria for somatization disorder[14] but this was not specifically looked for.

The proportion of cases reporting functional breathlessness (80%) is higher than that demonstrated in hospital studies of patients with atypical chest pain (Bass and colleagues reported 33%[15] and Hornsveld and colleagues reported 48%[16]) although

slightly different questionnaires were used. The questions in this study appear valid however, as only two controls reported unexplained breathlessness and both of these reported functional symptoms in addition to the reason for recruitment as controls. The incidence of reported symptoms among cases during hyperventilation was also high, but this probably reflects the fact that recognition of one symptom, rather than a combination of symptoms, was counted.

This study used provocation testing protocols, of 20 breaths and one minute of hyperventilation, that were both shorter than the usual three minute test. Although the tests used in the study have not been fully validated elsewhere, they used similar principles to the traditional tests. The reproducibility,[17] the validity of applying strict numerical criteria,[6] and the specificity of the standard tests[16] have been criticized and in this context, the shorter tests were developed to be applicable to routine primary care consultations.

There is evidence that experience of symptoms owing to hyperventilation is both common[6] and non-specific,[16] and it has been argued that the interpretation put on symptoms, rather than the severity of metabolic change, is the critical factor in the perception of ill health in this context.[18] The considerable overlap in PCO_2 values between groups in this study contrasts with the wide differences in symptoms experienced, and supports this notion. Rather than a physiologically discrete hyperventilation syndrome, this study suggests a model wherein hyperventilation triggers recognized somatic symptoms in some patients, often at PCO_2 levels which may be tolerated by others. In this model, measurement of PCO_2 becomes less important than the demonstration to the patient of the effect of hyperventilation, which can be used as a simple but practical way of relating symptoms to psychological factors, and provide a basis for simple behavioural treatment.

This study has demonstrated that hyperventilation induced symptoms and inappropriate breathlessness were common among a group of patients with recurrent functional symptoms which their doctors found difficult to diagnose or treat. Whether or not the reduced PCO_2 caused the symptoms, it suggests a practical way of recognizing and demonstrating their functional nature. Further investigation is needed to validate the tests described, and evaluate methods of explanation and treatment based on the recognition of the effects of hyperventilation.

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