Failure of perception of hypocapnia: physiological and clinical implications

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Summary

Hyperventilation causes hypocapnia and respiratory alkalosis and thereby predisposes to coronary vasoconstriction and cardiac arrhythmia. Diagnostic methods for use between episodes have not been established.

In this study of 100 patients and 25 control subjects the resting end-tidal P_{CO_2} (Pet CO_2) levels and the results of a forced hyperventilation test did not show a significant difference between the groups. However the patients hyperventilated more profoundly in response to emotional stimulation, and were less aware of inappropriate breathing and hypocapnia.

It is suggested that these differences should be accommodated in cardiac rehabilitation.

Introduction

A wide variety of psychophysiological disturbances can be produced by hyperventilating or breathing in excess of metabolic needs[1,2]. The form these disturbances present is influenced by the severity and duration of the hyperventilation, by depletion of the body's alkali reserve in chronic cases[1,3], by emotional arousal[1,4-6], and by variations in individual sensitivity to hypocapnia and respiratory alkalosis. They have an important place in cardiovascular medicine: hypocapnia and alkalosis can precipitate dangerous cardiac arrhythmia[7] and probably provide the major pathways[8] by which 'personally-relevant mental stressors' can cause myocardial ischaemia[9] and 'emotionally-charged experiences' sudden death[10] in vulnerable individuals.

A major problem of prevention is created by the fact that patients can develop symptoms and even bring themselves to the edge of a serious cardiovascular event without being aware of the preceding overbreathing and hypocapnia. As Lewis wrote about the hyperventilation syndrome: 'Another feature is the patient's curious lack of awareness of his overbreathing, or when he is aware of it, his usual insistence that it was the result of the attack and did not develop until after the episode was well underway'[11].

The purpose of this paper is to report a study of this failure of perception.

Subjects

In order to assess the phenomenon of failure of perception we studied 100 consecutive patients (61 men, 39 women; with a mean age of 45.3 years±14.0; range 20-86) referred to a cardiology clinic where a clinical diagnosis of hyperventilation was made on the basis of Lum's[1] and Magarian's[2] descriptions. The cardinal symptoms are loss of ability to make and sustain effort associated with fatigue, breathlessness, chest pain[12] and palpitations. Wakening at 03.00 or 04.00 h with anxiety, and finding it very difficult to relax during the day are common consequences of hyperventilation[3,6] as are headaches, giddiness and paraesthesiae. The signs are the disordered breathing patterns described by Lum[1]. The term 'effort syndrome' is considered appropriate where the hyperventilation is due to effort and anxiety[13].

Of the 100 patients recruited, 10 were excluded (seven had abnormal lung function, one had a vasovagal episode under testing, one could not follow instructions, one had an inadequate tracing). The results are therefore presented from the remaining 90 patients (56 men, 34 women), mean age 45 years±13.9 (range 20-86). Sixty-one were considered to have effort syndrome without organic disease, and 29 had evidence of organic conditions. These included old pulmonary embolism (1); pulmonary stenosis (1); heart valve replacement (1); mitral valve prolapse (2); hypertension (15); ischaemic heart disease (9) comprising angina pectoris (3), myocardial infarction (2), illness after coronary bypass surgery (3) or coronary angioplasty (1).

A control group of 25 asymptomatic volunteers (15 men, 10 women) was recruited from hospital staff. They had a mean age of 42 years±15.6 (range 20-72). All subjects gave their informed consent to the testing, but were not told about its aims and no information about hyperventilation was given or suggested indirectly.

Methods

Peak flow-measurements were used to exclude obstructive airways disease. End-tidal carbon dioxide levels were recorded by means of an IL 200 infrared mass spectrophotometer, a capnograph, analysing the air drawn continuously through a fine bore plastic tube held within the dominant nostril by a lightweight headband while the subject sat in a comfortable chair.

The capnograph was calibrated by means of a Corning calibration cylinder (5% CO_2, 12% O_2, 83% N_2) with a daily correction for barometric pressure to permit Pet CO_2 to be measured on a mmHg scale. Pet CO_2 recordings were taken with a 2-channel Devices recorder.

Tracings at a paper speed of 25 mm/s were examined to ensure that alveolar plateaux developed in each case. Under these conditions the differences between Pet CO_2 and arterial P_{CO_2} (Pa CO_2) are minimal[14]. Thereafter, a paper speed of 0.1 mm/s was used for the testing which had four parts:

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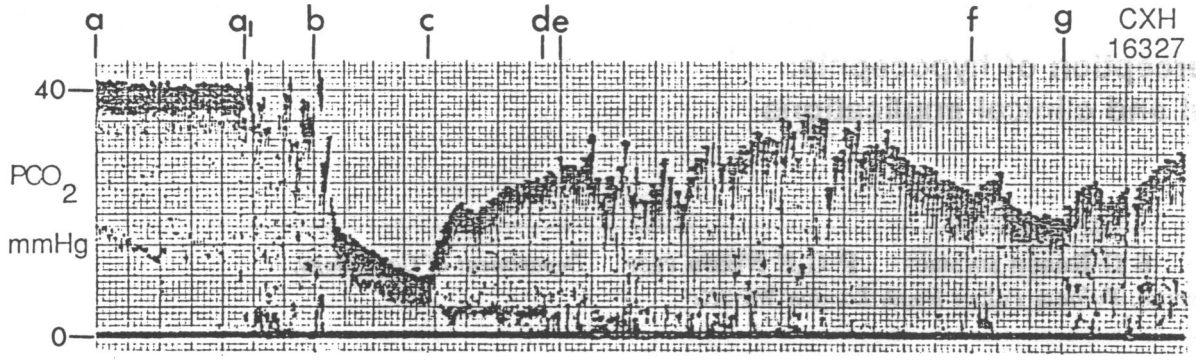

Figure 1. A capnogram from a patient. a-a_1: resting period, patient not talking (Pet CO_2=41 mmHg). a_1-b: resting period, patient talking. b-c: 3 min forced hyperventilation provocation test (FHPT). c-d: 3 min period of recovery from FHPT (Pet CO_2 at d=25 mmHg). e: patient closes eyes. e-f: patient invited to think about anger at home, the effects of fatigue and his lack of control of his predicament (Pet CO_2 nadir=24 mmHg). f: patient invited to open eyes and to relax. g: breathing signalled as normal (Pet CO_2=20 mmHg)

(1) The resting Pet CO_2 was noted, and a value of 29 mmHg or less was deemed positive for hypocapnia[14].
(2) A forced hyperventilation provocation test (FHPT) was performed to assess the individual's tendency to continue to overbreathe after stimulation by breathing deeply and rapidly for 3 min and reducing the Pet CO_2 to 20 mmHg or less[14]. Three minutes after cessation of overbreathing the Pet CO_2 was noted and expressed as a percentage of the resting Pet CO_2 level. In accordance with Hardonk and Beumer values below 66% were considered positive[14].
(3) Between 3 and 4 min from the end of the FHPT, the subjects were asked to close their eyes for the 'think test'[15].

The 'think test' recorded the capnographic consequences of stimulation by recall of personally-relevant mental stressors or emotionally-charged experiences chosen by watching the patient for breathing clues during the medical history taking. It was carried out immediately after FHPT because the overbreathing involved in that was considered likely to reduce inhibition of respiratory responses to emotional stimulation. The lowest point (nadir) of Pet CO_2 reached in the 'think test' was noted and expressed as a percentage of the resting Pet CO_2. In this study, the 'think test' was considered positive if the Pet CO_2 fell by 10 mmHg or more from a starting level of 30 mmHg or above, or fell 6 mmHg if the starting level was 29 mmHg or below.
(4) At the end of the 'think test', each subject was asked to open his eyes, to relax, and to signal by raising a hand as soon as the breathing felt normal. The Pet CO_2 at this level was noted and expressed as a percentage of the resting Pet CO_2.

This perception test was arbitrarily considered positive if the Pet CO_2 at the 'normal' signal was $\leq$80% of the resting level.

The testing of the control group followed the procedure adopted for the patients. After the FHPT they were asked to think about personally-relevant mental stressors and emotionally-charged experiences associated with anger, despair, fear and happiness.

An example of a test record is shown in Figure 1.

Statistical analysis
t-tests were used.

Results

The results from the 90 patients and 25 controls are presented in Table 1. The mean levels of Pet CO_2 at rest and 3 min after FHPT in controls and patients differed by 1 mmHg of each other. At the nadir of the 'think test', the mean Pet CO_2 for all patients (n=90) was significantly lower than the mean Pet CO_2 for the controls (n=25). The perception of normality was also significantly different.

Figure 2 shows each subject's resting Pet CO_2 mmHg and the level at which he signalled that the breathing was perceived as normal. Using each subject as his own control in this way the mean for the patient and control group was calculated. The patient group showed a significantly greater fall, compared with the control group (−8 mmHg±6.8 vs −1±4.5, P=0.001).

Table 2 presents the frequency of positive results in the four procedures.

The level at which the breathing was signalled normal did not appear to be a function of the nadir of the 'think test', which might be regarded as its initial value, because the signal was lower than the

Table 1. Mean Pet CO_2 values from the four tests

Measurements		*Controls* (25)	*Patients* (90)
Resting level	Pet CO_2 mmHg	35±4.0 (28-45)	34±4.6 (22-44)
3 min after 3-min forced hyperventilation provocation test	Pet CO_2 mmHg	28±5.7 (15-36)	27±6.5 (11-42)
	% resting Pet CO_2	80	79
'Think test'	Pet CO_2 nadir mmHg	28±5.0 (17-37)	* 23±5.3 (10-36)
	% resting Pet CO_2	80	68
Breathing signalled normal	Pet CO_2 mmHg	34±4.7 (22-40)	* 26±5.3 (15-42)
	% resting Pet CO_2	97	76

*P<0.001

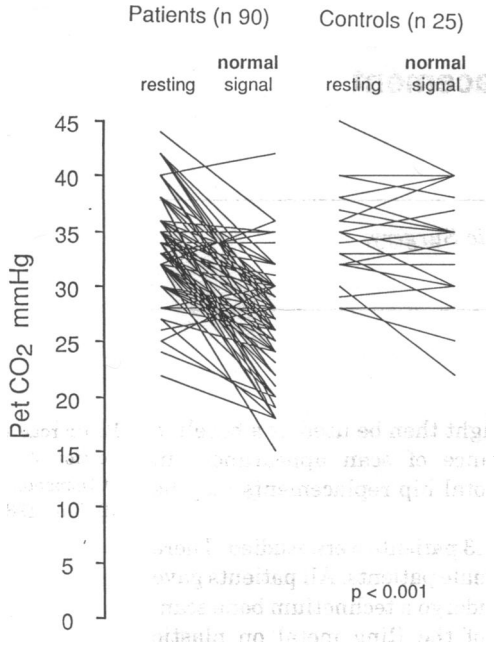

Figure 2. Pet CO_2 values at rest and at the normal signal in the patients and the controls

Table 2. The frequency of positive results in four tests

Test	*Positive in controls*	*Positive in patients*
Resting Pet CO_2 ≤29 mmHg	12% (3/25)	13% (12/90)
3 min after 3 min forced hyperventilation provocation test	20% (5/25)	18% (16/90)
'Think test'	36% (9/25)	79% (71/90)
Breathing signalled normal ≤80%	4% (1/25)	53% (48/90)

nadir in seven patients, and had no constancy of relationship in the remainder.

Discussion

This study supports the observation[11] that failure of perception of hypocapnia can be deep enough and sufficiently frequent among hyperventilators to merit inclusion with chronicity[1,3] and emotional arousal[1,4-6] as an important determinant of the clinical outcome.

The results indicate that patients cannot be separated from controls by reference to the resting Pet CO_2 or the FHPT. The FHPT, formerly thought of as a tool for distinguishing between populations of hyperventilators and non-hyperventilators, might now be more usefully employed to sensitize the subject for the 'think test' than to attempt to discriminate in a binary fashion between abnormal and normal individuals.

Normal human beings hyperventilate when their circumstances or predicament call for this response[6], and our study suggests that those who suffer from the psychophysiological disturbances of hyperventilation overbreathe more profoundly and for longer periods in response to personally-relevant mental stressors and emotionally-charged experiences, and have a greater insensitivity to hypocapnia than their fellows. We agree with Wientjes *et al.*[16], in their view that it is not feasible to categorize people as hyperventilators or non-hyperventilators.

From a therapeutic point of view, the ability to identify disturbing and potentially dangerous stimuli with the 'think test' enables us to teach the patient how to defend himself against hypocapnic instability of the internal milieu, and set up safeguards against the dynamic factors that can precipitate cardiac arrhythmia, myocardial ischaemia and sudden cardiac death[7-10,12].

We believe that hyperventilation should be considered when clinicians deal with angina pectoris[17] or organize cardiac rehabilitation[18]. The capnograph is a useful instrument for checking the patient's acquisition of self-help skills.

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