Hyperventilation and angina pectoris

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Hyperventilation is frequently regarded as a troublesome neuropsychiatric problem which usually occurs in the absence of organic disease. Attention has already been drawn to the fact that it produces chest pain which is very similar to that of ischaemic heart disease, so that much unnecessary coronary arteriography is performed [1]. Many people deny the incidence of hyperventilation in coronary artery disease. We consider that is a common and confusing problem in the assessment of patients with angina pectoris. We decided to investigate the incidence of hyperventilation in a group of patients with severe exercise-induced angina and its effect, if any, on their subsequent angina as measured by ST Holter monitoring. The findings were compared with normal controls and with patients suffering angina-like chest pain, but with normal coronary arteriograms.

Subjects

Fifty-three subjects were studied; 13 normal control (NC) patients and 40 consecutive patients undergoing diagnostic coronary arteriography. Thirty patients had symptomatic angina pectoris with frequent attacks of angina and ST segment depression on exercise. All had marked coronary narrowings seen at arteriography (over 70 per cent reduction in internal diameter); two patients had disease only of the left anterior descending artery, eight patients had two vessel disease and 20 patients had involvement of all three major arteries, which included the left main stem in one patient. The mean left ventricular end diastolic pressure (LVEDP) in the patients with coronary artery disease (CAD) was in all cases less than 15 mmHg (mean 6.43 mmHg), confirming the absence of heart failure. The remaining 10 patients were investigated for angina pectoris but were found to have completely normal coronary arteriograms (CPNCA). Four of these subjects had ST segment depression (>1mm) with exercise and a mean LVEDP of 11.3 ± 1.02. In all subjects studied, the resting electrocardiogram was in sinus rhythm without conduction abnormalities or voltage criteria for left ventricular hypertrophy. No patient was taking any drugs known to influence the ST segment (e.g. digoxin) and all anti-anginal medication (except sublingual GTN) was stopped for 72 hours prior to and during the testing.

Methods

Hyperventilation

The incidence of hyperventilation was sought in two ways. First, a forced hyperventilation provocation test (FHVPT) with concomitant monitoring of expired carbon dioxide (PetCO₂), heart rate and electrocardiogram, was performed. The resting PetCO₂ was determined using an IL200 infra-red mass spectrometer, calibrated using 5 per cent CO₂ corrected daily for barometric pressure. Tracings at 25 mm/sec paper speed were checked to ensure that an alveolar plateau developed. No patient had any evidence of obstructive airways disease as judged by peak flow measurements. Forced hyperventilation was performed at 60 breaths per minute for 3 minutes, during which time the PetCO₂ was required to fall below 19 mmHg. The rate of return of the PetCO₂ was plotted for 3 minutes following cessation of FHVPT and a ratio derived from the PetCO₂ (per cent) at rest/ PetCO₂ (per cent) 3 minutes following cessation of FHVPT. According to the criteria of Hardonk and Beumer [2], if this is equal to or greater than 1.5, hyperventilation is considered to be present. Patients were asked if they recognised any symptoms produced by the hyperventilation or if they developed their typical chest pain. All patients completed the 60-item General Health Questionnaire to assess concomitant psychiatric morbidity [3].
Second, symptoms of hyperventilation were assessed from the St. Bartholomew’s 106-item questionnaire [4]. This questionnaire has been validated in two stages. First, a factor analysis has identified a ‘hyperventilation’ symptom cluster made up of items that previous workers have found associated with their hyperventilation patients. Second, discriminant function analysis, has shown that a scale made up from the items in this symptom cluster is, by itself, sufficient to identify accurately patients already diagnosed as hyperventilating by a group of clinicians using a number of diagnostic criteria [5]. A score of greater than 24.6 on this hyperventilation scale has then been regarded as correctly identifying these patients. This has given an overall accuracy of 82.5 per cent.

Assessment of angina pectoris

Ambulatory ST Holter monitoring was performed, using the Oxford Medilog 2 System to document episodes of ST segment depression during periods of monitoring. Comprehensive diaries were kept by the patients to record all symptoms of angina and activities during the time that they wore the monitor. In addition, patients were specifically asked to document any episodes of ‘difficulty in breathing/inability to get enough air into the lungs/awareness of their breathing’ that they might experience, in the absence of their normal anginal symptoms.

The 30 patients with coronary artery disease underwent two 48-hour periods of ambulatory ST monitoring, choosing an inferior lead and the precordial lead which had shown the maximum ST segment depression during exercise. The 10 patients with chest pain but angiographically normal coronary arteries and five of the normal controls, only had 48 hours of monitoring. Tapes were analysed at 60 times real time. Significant ST segment depression was considered to be present if there was 1 mm planar or downslipping ST segment depression occurring 80 msec after the J point and lasting for one minute or more. Episodes of ST segment depression were either correlated with diary entries of chest pain (or the patient’s ‘normal’ equivalent symptoms) or with magnetic marks on the tape, produced when the patient pressed the ‘event’ button. ST segment depression in the absence of any recorded symptom was called ‘silent’. Any other diary entries were noted.

Statistical methods

The Student’s t test has been used on continuous variables and non-parametric tests on categorical variables. Statistical analysis of the questionnaire is described in the text.

Results

Forced hyperventilation provocation testing

Carbon dioxide results. Resting hypocapnia (<30 mmHg) was present in five (16.6 per cent) patients with coronary artery disease, in one patient with chest pain and normal coronary arteries and in none of the controls. Seventeen patients with CAD (56.7 per cent), six patients with CPNCA (60 per cent) and one NC (7.7 per cent) were considered to be hyperventilators on the basis of a slope ≥ 1.5 [2]. All patients with CAD, nine of 10 patients with CPNCA and 12 of 13 normal controls completed the three minutes of the FHVPT. The rate of return of the PetCO$_2$ following provocation is shown in Figure 1. The rate of return of patients with CAD has been grouped on the basis of the derived slope greater than or less than 1.5. The PetCO$_2$ three minutes post-hyperventilation was significantly different between these two groups (p < 0.007).

Reproduction of symptoms. Twelve CAD patients reproduced symptoms that they recognised as similar to those experienced during daily life, eight experiencing their typical anginal pain. Five CPNCA patients reproduced recognisable symptoms, three having their typical chest pain. The one control patient with a slope > 1.5 also said the test reproduced some sensations that he had experienced during his daily life.

Electrocardiographic findings. The provocation test increased the heart rate of all patients but there was no significant difference between patients who were and were not considered to be hyperventilators. The mean heart rate increase in the patients with CAD was 20 beats per minute and in the patients with chest pain and normal coronary arteries was 16 beats per minute. This is in
keeping with our previous reports of heart rate increases following provocation testing [6].

There were nine electrocardiographic abnormalities in all the CAD patients following FHVPT, seven of whom were hyperventilators. Four patients had marked T-wave inversion. Four other electrocardiographic abnormalities were observed in different patients; 1 mmST segment depression in two, left ventricular ectopy occurring every fourth beat in one, 1 mmST segment elevation in one, and coronary sinus rhythm in one. There were two electrocardiographic abnormalities in CPNCA patients: one developed 1 mmST segment depression and one had multiple ectopic beats. There were no electrocardiographic abnormalities in the control patients.

**Questionnaires**

*Barts hyperventilation questionnaire.* Three questionnaires from the patients with coronary artery disease and three from the patients with chest pain but normal coronary arteries, could not be analysed because they were inadequately filled in or lost. In 27 patients with CAD, 12 (44 per cent) scored more than 24.6 (mean score 34.1; range 27–38) consistent with a diagnosis of hyperventilation. Four (57.1 per cent) CPNCA patients and one NC were also considered hyperventilators as their score was more than 24.6.

*General health questionnaire (GHQ).* A score of ≥ 13 on the 60-item GHQ has been considered to represent a ‘case’, i.e. a patient who is at risk of psychiatric/psychosocial breakdown. The mean score in the 30 CAD patients was 13.13 ± 10.98. However, those patients considered to be hyperventilators on the basis of provocation testing had a lower mean score (11.29) compared with the rest (15.53—difference not significant) suggesting that patients who hyperventilate do not have greater psychiatric morbidity, as might have been thought. The mean score in the 10 patients with CPNCA was 9.8; three patients had a score greater than 13. Those patients considered to be hyperventilators from the FHVPT had a mean score of 6.0, whereas the remaining four patients had a mean score of 17.6—once again underlining the fact that in this group of patients hyperventilation and psychiatric morbidity do not appear to be significantly associated.

**Ambulatory monitoring**

A total of 2,711 hours were analysed in patients with CAD and the total number of ischaemic events, the length of ischaemic time per patient, the number of symptomatic and asymptomatic ST segment depressions were documented (Fig. 2). There was no difference in any of these parameters as to whether the patient was considered to be a hyperventilator or not. However, the number of episodes of chest pain marked in the diary and with the event marker, but not associated with ischaemic ST segment depression was significantly more in patients considered to be hyperventilators (p<0.03 and p<0.000) than in the remaining subjects during both the first 48- and second 48-hour periods of monitoring.

There were 45 episodes of ‘breathing trouble’ reported in the diaries of patients with CAD which occurred in the absence of the normal anginal symptoms, but which were associated with ST segment depression. These patients were more likely to complain of chest pain following FHVPT. (M-W U = 49.5; p<0.04 (corrected for ties z = −2.49; p < 0.02)).

The 17 CAD patients considered to be hyperventilators on the result of the FHVPT had more episodes of ST

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**Fig. 2.** Bar chart demonstrating the results from ambulatory monitoring in patients with coronary artery disease. **ASYM** = asymptomatic (ie chest pain) ST depression. **SYMP** = symptomatic (ie chest pain) ST depression.
Discussion

This study demonstrates that patients with symptomatic coronary artery disease can and do hyperventilate. Of the patients with CAD, 56.7 per cent were considered to hyperventilate on the basis of the provocation test, a much higher incidence than previously reported [1]. This reflects the employment of the forced hyperventilation provocation test, in addition to measurement of the resting expired carbon dioxide level. The provocation test identifies patients who, once provoked into over-breathing, appear to continue to hyperventilate in a habitual fashion. Subjects who are not susceptible to habitual hyperventilation rapidly return their carbon dioxide level to baseline. In these patients we would advise ECG monitoring during the provocation test, because the test can produce infarction [7] and coronary arterial spasm in vulnerable patients [8,9].

The test is also useful in reproducing symptoms associated with the hyperventilation syndrome, which the patient may recognise as typical of feelings that they have experienced in daily life. Forty per cent of the patients studied reproduced symptoms and this correlated well with the 44 per cent from the questionnaire. Chest pain is a prominent feature of the hyperventilation syndrome [10], but in the patients with coronary artery disease, this may not always be ischaemic in origin. It is interesting to note that CAD patients who recorded episodes of 'breathlessness' in their diary were more likely to suffer chest pain after the provocation test.

The Holter monitoring revealed that anginal patients reported 'breathlessness', but not pain, in relation to ischaemia on some occasions. The cause is probably transient pulmonary oedema, from raised left ventricular end diastolic pressure, which can act as a physiological trigger for hyperventilation. Even though the left ventricular end-diastolic pressure falls back to normal levels with relief of the ischaemia [11], the hyperventilation may persist as a habit and lead to an increased reporting of chest pain. 

Angina pectoris is a symptom but not a measurable disease, and we are compelled to manage the case according to its reported severity. Those who hyperventilate generate more pain and more severe pain, than those who do not, but cannot be distinguished by the 'gold standard' of coronary arteriography, the laboratory testing of ECG responses to physical effort, or by field studies of ambulatory monitoring. They are therefore likely to be subjected to heavier medication and earlier selection for coronary artery bypass grafting. This is an unsatisfactory state of affairs, if only because the untreated hyperventilator is likely to continue to complain about chest pain following surgery, and may be subjected to further angiography to assess the state of his grafts [12]. Furthermore, the much lower GHQ score in the patients considered to hyperventilate means that they cannot be dismissed as neurotic or in need of a liaison psychiatrist.

All of the patients with normal coronary arteries who produced ST segment depression during exercise testing and Holter monitoring were considered to be hyperventilators on the result of the provocation test, and such an association has not previously been reported. The aetiology of the ECG changes in these cases is unclear, but does not appear to be associated with any rise in left ventricular end diastolic pressure, as measured by ambulatory pulmonary artery monitoring [13]. It may reflect autonomic imbalance with asynchronous repolarisation, associated with the hyperventilation.

We have discussed elsewhere the predisposing factors to hyperventilation [14] in patients with ischaemic heart disease and the mechanisms involved in the production of chest pain [10]. It is our experience that this neglected disorder does produce considerable and unacknowledged morbidity in patients with coronary artery disease. We suggest that thinking about hyperventilation and testing for it (by provocation and questionnaire) should become part of the routine assessment of the 'coronary case'. The observation of the patient provides strong clues, particularly when paraesthesiae of the hands are associated with chest pain.

We believe that teaching about the nature of the symptoms, breathing retraining, tactical advice about coping with day to day problems and the management of maladaptive hyperarousal are the chief ingredients of treatment. We have obtained excellent results by delegating the treatment to occupational therapists [15] and nurses [16]. This treatment approach should logically come before further invasive investigations and it should certainly be considered more often where coronary arteriographic findings do not warrant bypass grafting. Reassurance does not reduce morbidity. This is particularly pertinent in patients who are demonstrated to have angiographically normal coronary arteries [17].

Acknowledgements

Leisa J. Freeman was supported by a Charing Cross Governor's Fellowship during the period of this study.

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Book Review

Stroke: Pathophysiology, Diagnosis and Management edited by H. J. M. Barnett, J. P. Mohr, B. M. Stein and F. M. Yatsu. Churchill Livingstone, Edinburgh, 1986. 2 volumes. Price £135.

Cerebrovascular disease has always been an extremely important, even if therapeutically discouraging, field of clinical neurology. However, as the editors of this work point out, attitudes to investigation and management have changed greatly in the past decade, due mainly to rapid advances in diagnostic and research techniques that have led clinicians to look at stroke patients in a new light and to explore much more actively new ways of reducing the occurrence and severity of stroke. Therapeutic nihilism has gradually given way to cautious optimism that, with further understanding of the mechanism of stroke, a better outlook for some stroke syndromes is becoming a realistic possibility. This more positive approach to the problems posed by cerebrovascular disease is actively promoted throughout this major work. Indeed the reader cannot fail to be impressed by the enthusiasm that motivated the four editors to undertake so formidable a task, or fail to sense their enjoyment in fulfilling it.

The book, published as two volumes, sets out to 'provide current information on stroke pathophysiology, diagnosis and therapy in a single reference'. It is composed of five sections that deal successively with pathophysiology, diagnosis, clinical features, medical treatment and surgical therapy, arranged in a way that provides ready access to conventional stroke syndromes. The print format is double column and clearly legible, and the sections to which access is required, either for reference purposes or to answer specific queries, are readily found by means of a comprehensive index present in each volume. The work is essentially a North American, or rather United States overview of the subject, since of the 68 authors, all are American, except for seven Canadian contributors, one of whom is the leading editor, three Japanese contributors, and one author each from France, Italy, Denmark and Australia. This in no way detracts from the value of the book which rightly stands as a tribute to present-day North American neurology.

All aspects of cerebrovascular disease are systematically reviewed. Some degree of repetition is inevitable in a multi-author volume of this size, but it is unobtrusive, and each chapter stands on its own. In volume I, introductory chapters on stroke epidemiology in North America and Europe are followed by chapters dealing with specific topics of current interest in stroke pathophysiology. These include atherogenesis, rheology and the cerebral microcirculation, with a helpful chapter on brain oedema as well as a review of the now somewhat outdated value of CSF changes in stroke patients. Modern diagnostic procedures are well covered with chapters on CT scanning, NMR imaging, digital venous angiography and Doppler ultrasound as well as cerebral angiography. The clinical manifestations of stroke and intracerebral haemorrhage are also thoroughly reviewed. Volume 2 covers intracranial aneurysms, vascular malformations, cerebral venous disease and spinal cord infarction. Valuable chapters on neurological syndromes following cardiac arrest, cardiogenic stroke, specific arteriopathies, haematological disorders associated with stroke, andBinswanger's subacute arteriosclerotic encephalopathy, are followed by a final section which deals with stroke therapy. This section, the most difficult to present in a balanced fashion, receives sound treatment from its contributors, and left me with the impression that the prognosis for the book, as well as for cerebrovascular disease, is favourable.

The editors have accomplished their aim, and in doing so produced a valuable comprehensive work on the current state of knowledge of cerebrovascular disease. Their book is not only well conceived and erudite, but conveys, in eminently readable form, balanced views that encompass aspects of controversial management such as transient ischaemic attacks, without overburdening the reader with tiresome bewildering detail. Views are succinctly offered, and if the reader wishes to pursue a topic, the list of references offered by the various contributors are authoritative and up to date. The only criticism I have is the extremely high price of the book, which at £135 means that it is unlikely to find its way onto the desks of many neurologists this side of the Atlantic, which is a great pity.

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