

Cardiovascular autonomic nerve function in patients with hypoxaemic chronic obstructive pulmonary disease

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ABSTRACT: Intraneural hypoxaemia is recognized as a pathogenic mechanism in diabetic neuropathy. A similar pathophysiological process may occur in chronic obstructive pulmonary disease (COPD). Autonomic neuropathy is not recognized in COPD. We compared 96 patients with hypoxaemic COPD to 22 age-matched control subjects to see whether autonomic dysfunction occurs in COPD and whether there was any correlation with the severity of hypoxaemia.

The cardiovascular autonomic tests consisted of heart rate responses (mainly parasympathetic function) to a Valsalva manoeuvre, deep breathing and postural change and blood pressure responses (mainly of sympathetic origin) to postural change and sustained handgrip. Early autonomic neuropathy is defined as one abnormal test and definite autonomic neuropathy as two abnormal tests according to the normal range. These autonomic tests were reproducible in our study population.

Although the symptoms and signs of autonomic neuropathy were rare, definite autonomic dysfunction was found in 35%, and early autonomic neuropathy in a further 47%, of patients whose arterial oxygen tension (P_{aO_2}) was <8 kPa (60 mmHg). Only 18% of the control group had evidence of an age-related early autonomic dysfunction. Parasympathetic autonomic dysfunction was significantly correlated with P_{aO_2} whilst the sympathetic tests were relatively normal. Correction of hypoxaemia for one hour or administration of ipratropium bromide or terbutaline had no effect on autonomic function.

Subclinical autonomic neuropathy is a feature of hypoxaemic COPD. Its importance in the disease process and its role in prognosis needs evaluation.

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Chronic hypoxaemia is a recognized cause of peripheral neuropathy [1]. APPENZELLER *et al.* [2] noted a symmetrical bilateral neuropathy in chronic obstructive pulmonary disease (COPD) patients with muscular wasting, and KINSMAN *et al.* [3] showed the high frequency of sensory disturbances in patients with COPD. Between 58-95% [1, 4] of people with severe COPD have electrophysiological evidence of peripheral nerve damage, often with few clinical signs.

The peripheral neuropathy of hypoxic COPD and diabetes mellitus have pathological [5, 6] and electrophysiological [7, 8] similarities. Thickening of the endoneurial capillary basement membrane and an altered microcirculation may account for the endoneurial hypoxaemia which can have a pathogenic role in the development of diabetic peripheral neuropathy [9]. Indeed, supplemental oxygen has reversed some of the electrophysiological abnormalities seen in experimental diabetes [10].

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A similar process may be pathogenic in diabetic autonomic neuropathy. The presence of diabetic autonomic neuropathy has a grave prognosis [11] with a high incidence of sudden death [12] occurring under conditions of hypoxia [13]. This may relate to a depressed ventilatory response to hypoxia secondary to a reduced carotid body sensitivity [14].

Although alpha-adrenergic and cholinergic hyper-responsiveness together with beta-adrenergic hypo-responsiveness have been reported in cystic fibrosis [15] and asthma [16, 17], autonomic nerve dysfunction has not been reported in COPD.

We hypothesized that patients with hypoxic COPD may have an unsuspected autonomic neuropathy and that this dysfunction may correlate to the severity of hypoxaemia. We therefore assessed cardiovascular-respiratory autonomic nerve function in patients with hypoxaemic COPD.

Experimental method and design

Subjects with COPD were recruited from the chest clinic. The control group consisted of people without any significant illness amongst hospital staff, patients' spouses and people awaiting routine minor surgical operations.

Patients with concomitant diseases such as diabetes mellitus, hypertension, cerebrovascular accidents, Shy-Drager syndrome, rheumatoid arthritis, hyponatraemia, carcinoma, renal failure and liver disease were excluded. Patients on medications likely to interfere with the tests, such as vasodilators, angiotensin converting enzyme inhibitors and anti-hypertensive agents were also excluded. Those patients on diuretics stopped taking them for three days before the test. Where possible inhaled β_2 -agonists and ipratropium bromide were not taken in the 6 h preceding the tests. In the few cases where the patients had used their inhalers, the tests were delayed for at least two hours after inhaler use. Theophyllines and oral β_2 -agonists were stopped for 24 h.

All tests were performed under quiet, controlled conditions [18], after an informed consent had been given and the patients clinical history (including smoking history), symptoms and signs assessed.

Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were recorded on a Vitalograph Compact spirometer. Urea and electrolytes, random blood glucose and liver function tests (Technicon SMAC analyser) were measured to exclude other diseases.

Arterial blood gases were taken at rest after the autonomic tests and measured within 5 min using a Corning 170 pH/blood gas analyser.

Autonomic nerve function was assessed by the method described by EWING and CLARKE [19].

Heart rate response to Valsalva

After a three minute rest in a sitting position, the patient performed a Valsalva manoeuvre. After a moderate inspiration, the patient blew into a mouthpiece attached to a sphygmomanometer and maintained a pressure of 40 mmHg for 15 s. The patient then breathed normally for one minute. During the test, the heart rate was recorded as the inverse of the R-R interval. The Valsalva ratio was calculated as the maximum heart rate recorded during the Valsalva divided by the slowest rate recorded on release of the Valsalva. It was important to ensure that a maximal inspiration was not taken, as this might lower the Valsalva ratio [20]. An average of three readings was recorded. A value <1.11 is abnormal.

Heart rate response to deep breathing

With the patient in a sitting position the heart rate was recorded during six deep breaths in and out over

a one minute period. Heart rate is maximal during inspiration (I) and minimal on expiration (E). The I-E difference is the average of the maximum differences in heart rate during each breath. Patients with an autonomic neuropathy lose this variability. A heart rate difference of <11 beats \cdot min $^{-1}$ is abnormal.

Heart rate and blood pressure response to standing

After lying supine for 3 min and allowing systolic blood pressure to settle at a stable level the patient was asked to rise rapidly, without help, from the supine to an upright standing position. The heart rate response was recorded and the systolic blood pressure taken at 10-15 s after attaining the upright position. A systolic fall >30 mmHg is abnormal.

In a normal response the heart rate is maximal at the 15th beat and slowest around the 30th beat. The 30:15 ratio is the longest R-R interval around beat 30 divided by the shortest around beat 15. Patients with autonomic neuropathy have a heart rate which continues to rise throughout this observed time. The average of two recordings was taken. A value <1.01 is abnormal.

Diastolic blood pressure response to handgrip

The seated patient was asked to maximally grip a handgrip dynamometer. The greatest of two grips is designated the maximum voluntary contraction (MVC). The patient is allowed to recover over 3 min by which time the diastolic blood pressure should be stable, as shown by three consecutive similar readings which are then averaged. The patients then sustained a handgrip at one third of MVC for up to 5 min or as long as they could manage. The maximum diastolic pressure reached was measured and the increase from the pre-grip level recorded. A rise of <10 mmHg is abnormal.

The heart rate responses primarily tested the parasympathetic system and the blood pressure changes assessed sympathetic function.

On the basis of these tests, patients were categorized into having an early autonomic neuropathy if one parasympathetic test was abnormal, a definite autonomic neuropathy if two tests were abnormal and a combined autonomic neuropathy if there were abnormal parasympathetic and sympathetic tests.

The correlation between autonomic function and arterial oxygen tension, arterial carbon dioxide tension, cigarette consumption and spirometry was assessed.

The following groups of patients were also compared: a) controls; b) patients with COPD with arterial oxygen tension (P_{aO_2}) >8 kPa (60 mmHg); c) severely hypoxaemic COPD with P_{aO_2} <8 kPa (60 mmHg) but without hypercapnia; d) patients with hypercapnia, arterial carbon dioxide tension (P_{aCO_2}) >6 kPa (45 mmHg) and severe hypoxaemia with a P_{aO_2} <7.3 kPa (55 mmHg).

In 20 patients the tests were repeated at an interval of one day to three months to test for reproducibility. The patients were clinically stable with no recent acute

exacerbation. Medication was the same at the two visits and, where possible, the tests were performed at the same time of day.

Ten patients who had gone without bronchodilators for at least 12 h were tested before and 30 min after receiving 5 mg terbutaline *via* a nebulizer. A different group of ten patients received 500 µg ipratropium bromide.

In twenty patients with severe hypoxaemia the tests were performed before and on 2 l·min⁻¹ oxygen for at least one hour to see if short-term correction of hypoxaemia improved autonomic function.

The study was approved by the Sheffield Health Authority Ethical Committee.

Table 1. — Repeatability of the autonomic tests in 20 patients (n=20) (mean (SEM))

	Day 1	Day 2	Coefficient of repeatability	
Pao ₂ kPa	7.7 (0.2)	7.9 (0.3)		
Paco ₂ kPa	6.2 (0.2)	6.1 (0.3)		
Valsalva ratio	1.19 (0.04)	1.21 (0.05)	0.05	
I-E difference	8.9 (1.1)	9.9 (1.1)	3.1	
30:15 ratio	1.04 (0.01)	1.05 (0.01)	0.02	
Postural BP fall mmHg	13.9 (2.0)	14.7 (1.8)	5.8	
Handgrip BP rise mmHg	17.3 (1.4)	16.4 (1.3)	3.1	

Pao₂, Paco₂: arterial oxygen and carbon dioxide tension, respectively, I-E: inspiration-expiration; BP: blood pressure.

Statistical analysis

Results are given as means with standard error of the means (SEM) in brackets. The reproducibility experiment was assessed using the method described by BLAND and ALTMAN [21] to give a coefficient of repeatability. This involves plotting the differences between the two readings against the mean of the two readings, providing the size of the difference is not proportional to the mean, then the coefficient of repeatability is two standard deviations of the differences. This gives a value of repeatability which will include results from 95% of the patients. The COPD groups were compared by analysis of variance (ANOVA), then all different pairs of results were compared by Scheffes test. Correlation data was assessed by the Spearman rank method. The chronic bronchitis group were compared to the emphysema group by the Mann Whitney test for two independent samples. The effects of oxygen, terbutaline and ipratropiumbromide were assessed by a Student's paired t-test.

Results

The autonomic tests used were repeatable in our population of patients with COPD (table 1).

Parasympathetic autonomic dysfunction is common amongst patients with hypoxaemia, the abnormality being greatest amongst those patients with both hypoxaemia and hypercapnia (table 2 and figs 1-4).

Table 2. — Cardiovascular autonomic function results in control subjects and in groups of patients with varying severities of hypoxaemic COPD, mean (SEM)

Groups	Controls	Moderately hypoxic COPD	Severely hypoxic COPD	Hypercapnic COPD
n	22	36	30	30
Age	64.5 (1.7)	65.2 (1.3)	65.6 (1.3)	66.0 (1.1)
Pao ₂ kPa	11.1 (0.1)	9.2 (0.2)	7.5 (0.1)	6.5 (0.1)
Paco ₂ kPa	5.2 (0.1)	5.3 (0.1)	5.7 (0.2)	7.0 (0.2)
FEV ₁ l	2.82 (0.16)	1.41 (0.13)**	0.91 (0.07)***	0.73 (0.06)***
FVC l	3.89 (0.16)	2.79 (0.15)*	2.22 (0.12)**	2.04 (0.14)**
Cigarettes pack-yrs	8.4 (2.0)	38.3 (8.0)***	29.5 (2.5)**	30.4 (4.8)**
Heart rate response to:				
Valsalva ratio	1.48 (0.04)	1.27 (0.03)**	1.19 (0.02)***	1.14 (0.2)***
I-E difference	15.5 (1.6)	11.3 (1.1)	10.5 (1.0)*	8.2 (0.7)**
Standing 30:15 ratio	1.13 (0.02)	1.07 (0.01)**	1.05 (0.01)***	1.04 (0.01)***
Blood pressure change:				
On standing mmHg	6.2 (0.8)	10.9 (1.7)	10.8 (1.5)	14.2 (1.5)*
Handgrip mmHg	20.4 (1.3)	17.9 (1.1)	16.4 (0.7)	16.9 (1.0)
Neuropathy status [†] :				
No autonomic neuropathy	18 22	18 27	9 17	2 10
Early autonomic neuropathy	4 0	15 5	13 8	15 8
Definite autonomic neuropathy	0 0	3 4	8 5	13 12

[†]: neuropathy status as defined by EWING & CLARK [19] and O'BRIEN *et al.* [22] respectively. *: p<0.05; **: p<0.01; ***: p<0.001 compared to the control group. FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; COPD: chronic obstructive pulmonary disease. For further definitions see legend to table 1.

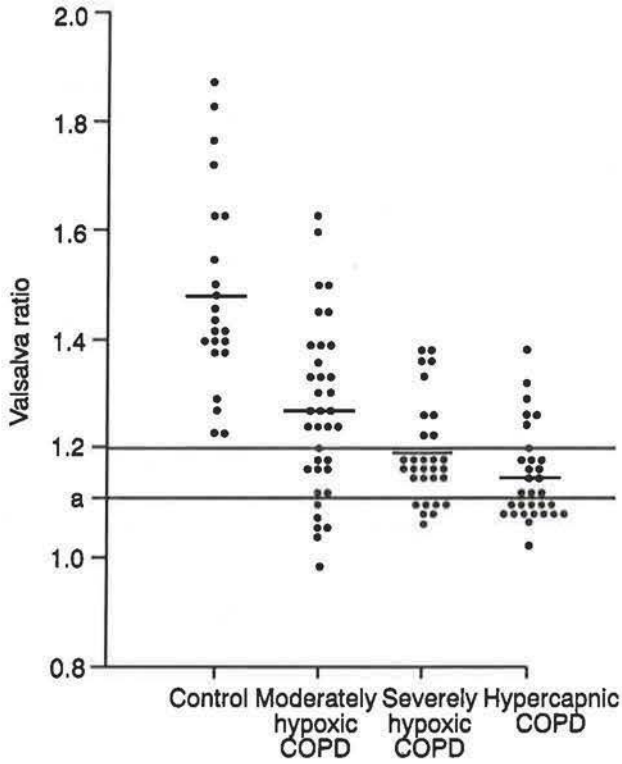


Fig. 1. - The Valsalva ratio in normal controls (n=22) and patients with moderate hypoxemia (n=36), severe hypoxaemia (n=30) and severe hypoxaemia and hypercapnia (n=30). Values above 1.2 are normal and those below line "a" (1.1) are abnormal. Solid bar indicates the group mean. COPD: chronic obstructive pulmonary disease.

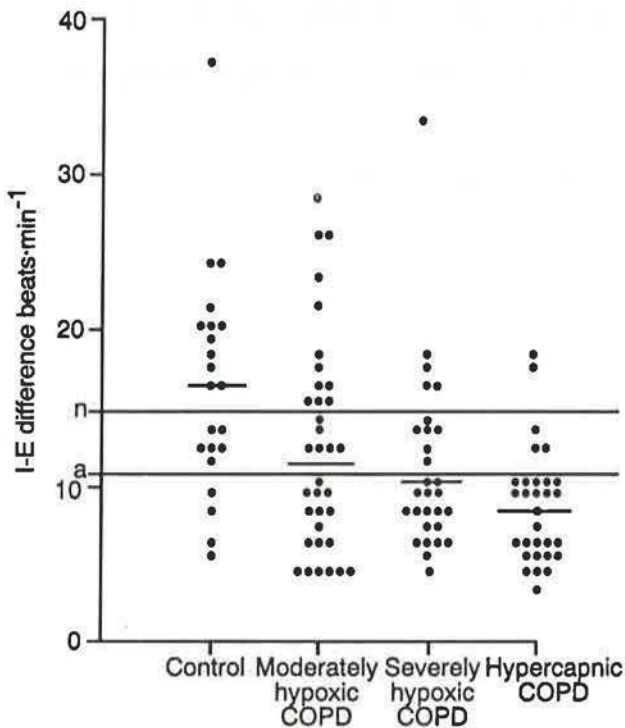


Fig. 2. - The inspiration-expiration heart rate difference (I-E) in normal controls and patients with moderate hypoxaemia, severe hypoxaemia and severe hypoxaemia and hypercapnia (numbers as in Fig. 1). Values above line "n" (14) are normal and those below line "a" (11) are abnormal. Solid bar indicates the group mean.

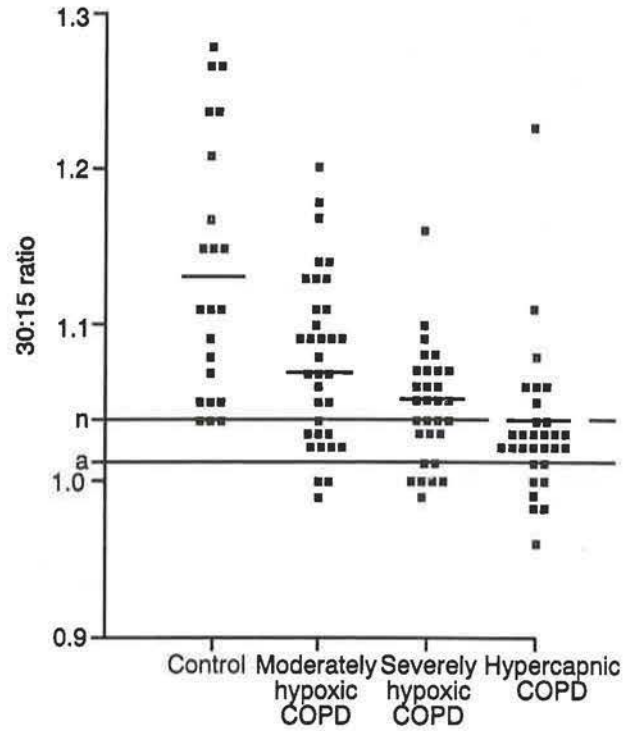


Fig. 3. - The 30:15 ratio in normal controls and patients with moderate hypoxaemia, severe hypoxaemia and severe hypoxaemia and hypercapnia (numbers as in Fig. 1). Values above line "n" (1.04) are normal and those below line "a" (1.01) are abnormal. Solid bar indicates the group mean.

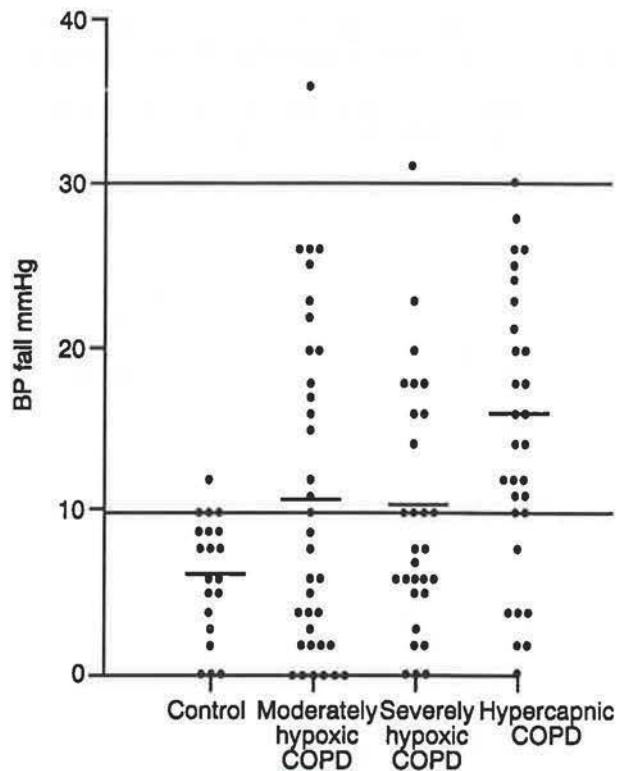


Fig. 4. - Systolic blood pressure (BP) fall on standing in normal controls and patients with moderate hypoxaemia, severe hypoxaemia and severe hypoxaemia and hypercapnia (numbers as in Fig. 1). Values above 30 mmHg are abnormal and those below 10 mmHg are normal. Solid bar indicates the group mean.

Analysis of the groups showed a highly significant difference between groups for Valsalva and heart rate response to standing ($p < 0.001$), all groups being different from the control. For I-E heart rate difference, the moderately hypoxic group was not different from the control but the other groups were ($p < 0.01$). For systolic blood pressure response to standing, only the hypercapnic group was significantly different to the control ($p < 0.05$). There was no difference between groups for blood pressure response to handgrip. In terms of FEV₁ the hypercapnic and the severely hypoxic group were homogeneous, all other groups were significantly different from each other ($p < 0.05$). All COPD groups were homogeneous and smoked significantly more cigarettes than did the control group.

Table 3. — O'Brien *et al.* [22] lower 95% confidence level for age

Age yrs	55	60	65	70	75
Valsalva ratio	1.17	1.15	1.13	1.11	1.09
Deep breath	6	5	5	4	3
Standing ratio	1.06	1.04	1.03	1.02	1.00

Table 4. — Spearman rank correlation coefficients (significant at $p < 0.01$)

	Valsalva ratio	I-E difference	30:15 ratio	BP fall mmHg
Age	NS	NS	NS	NS
Pao ₂ kPa	0.66**	0.38**	0.51**	-0.27
Paco ₂ kPa	0.26	NS	NS	NS
FEV ₁ l	0.56**	0.32	0.51**	-0.26
Cigarettes pack-yrs	-0.41**	-0.31	-0.37*	0.32*

*: $p < 0.001$; **: $p < 0.0001$; NS: not significant. For further definitions see legends to tables 1 and 2.

Using the criteria set down by EWING and CLARKE [19] the hypercapnic group ($n=30$) contained 15 patients with early and 13 with definite autonomic neuropathy, only two people were normal. The severely hypoxic group ($n=30$) contained 9 normal, 13 early and 8 definite neuropathies. In comparison the control group had only 4 early autonomic neuropathies, in this and the moderately hypoxaemic groups most abnormalities occurred in the heart rate response to deep breathing. Using the age related ranges of O'BRIEN *et al.* [22] (table 3) with the criteria of EWING and CLARKE [19] all the people categorized as having an early autonomic neuropathy due to an abnormality in I-E difference are recategorized as being normal (table 2). The diastolic blood pressure response to a sustained handgrip was either normal or occasionally borderline and never frankly abnormal. However, it was significantly lower in those with a subclinical autonomic neuropathy.

Although several patients gave a history of occasional dizziness on standing, only three had a significant postural systolic blood pressure fall of 30 mmHg. With the exception of impotence, which may be multifactorial in a chronically ill group of this age, no patient had other symptoms or signs of autonomic dysfunction.

Analysing the group as a whole, there are many statistically significant correlations (table 4).

The parasympathetic tests were highly correlated to the arterial oxygen tension and to FEV₁. The correlation with smoking was weak. There was no good correlation between postural blood pressure fall and diastolic blood pressure rise during handgrip and any other parameter.

Short-term correction of hypoxaemia with supplemental oxygen had no significant effect on autonomic nerve function (table 5). Likewise, nebulized terbutaline and ipratropium did not significantly alter the autonomic results (table 5).

Table 5. — The effects of 2 l·min⁻¹ of oxygen, nebulized terbutaline or atrovent on cardiovascular autonomic function, mean (SEM)

	Oxygen 2 l·min ⁻¹		Terbutaline 5 mg nebulized		Atrovent 500 µg nebulized	
	Before	After	Before	After	Before	After
n	20	20	10	10	10	10
Pao ₂ kPa	7.5 (0.3)	10.6 (0.4)***	-	-	-	-
Paco ₂ kPa	6.2 (0.3)	6.5 (0.3)	-	-	-	-
FEV ₁ l			2.92 (0.30)	3.43 (0.36)*	1.73 (0.41)	1.92 (0.44)
Pulse rate	85.9 (3.3)	82.1 (2.9)	89.2 (4.8)	89.2 (5.1)	81.5 (4.3)	81.2 (5.5)
Valsalva ratio	1.23 (0.04)	1.24 (0.04)	1.51 (0.12)	1.50 (0.13)	1.49 (0.09)	1.53 (0.10)
I-E difference	11.2 (1.35)	11.1 (1.1)	17.4 (2.9)	19.5 (3.3)	20.8 (4.6)	20.5 ()
30:15 ratio	1.05 (0.01)	1.05 (0.01)	1.10 (0.02)	1.11 (0.03)	1.10 ()	1.11 ()
Postural drop mmHg	12.4 (1.3)	13.7 (1.5)	5.5 (1.9)	4.6 (1.5)	8.8 ()	9.2 ()

*: $p < 0.05$ (Student's t-test paired); ***: $p < 0.001$ comparing before and after therapy result. For definitions see legends to tables 1 and 2.

Discussion

Our study demonstrates the presence of a previously unsuspected subclinical autonomic neuropathy in patients with hypoxaemic COPD. The degree of dysfunction correlates most closely to the level of hypoxaemia during stable convalescence. Although the correlation with $Paco_2$ is poor, patients with hypercapnia have the worst autonomic dysfunction. Within the group of patients tested there was no correlation with age, possibly because those patients who survived to the greatest age had less severe chest disease.

The autonomic tests involving prolonged expiration and regular deep breathing did not prove too difficult for our patients with COPD, as was confirmed by their reproducibility.

However, determining which patients have evidence of an autonomic neuropathy is more difficult. The EWING and CLARKE [19] normal ranges and criteria refer to a younger age group than is seen in patients with COPD. The normal decline in autonomic function with age means that such criteria should be used with caution [22-24]. Comparison to our age-matched control group confirms the marked differences in parasympathetic function seen in our COPD patients. Although the control group is not large enough to define an accurate normal range for people over the age of 60 yrs, it would appear that the EWING and CLARKE [19] range for Valsalva response and 30:15 ratio are acceptable. However, the I-E heart rate difference is much lower in both controls and patients than might be expected. These results are similar to those reported by O'BRIEN *et al.* [22] (table 3). The tests of O'BRIEN *et al.* are slightly different in their analysis and are performed supine. Our breathless COPD patients could not tolerate this position, with consequent poor compliance and reproducibility. For this reason we preferred the sitting upright Ewing and Clarke tests. Using the O'Brien normal range, all of our control group and many of the least affected COPD patients would appear to have normal autonomic function for their age (table 2). However, this latter group contain some patients whose I-E difference is much lower than that seen in the controls, some of these patients might now be categorized as being normal, when indeed they may have an early subclinical autonomic neuropathy.

Although we cannot define the absolute numbers, depending upon which criteria are used, autonomic neuropathy would appear to occur in 40% (O'BRIEN *et al.* [22]) to 82% (EWING and CLARKE [19]) of patients whose Pao_2 was less than 8 kPa. Likewise, between 67-93% of hypercapnic patients qualifying for long-term oxygen therapy, have evidence of a cardiovascular autonomic neuropathy.

The poor correlation between autonomic dysfunction as determined by autonomic function tests and clinical symptoms is well recognized in all diseases which produce an autonomic neuropathy [25].

It was reassuring to see that terbutaline and ipratropium therapy had no significant effect on the

autonomic function tests. The lack of correlation between autonomic function and previous long-term bronchodilator therapy suggests that these drugs may not have a chronic adverse effect on autonomic function. Even so, drug ingestion was standardized and where possible avoided on the day of investigation to avoid introducing confounding variables.

The use of diuretics is more difficult to control. The majority of patients were not on diuretics. Pilot studies suggested that in clinically stable euvoletic patients, diuretic usage had little effect on the autonomic tests. Even so, we decided to stop them for three days without any deleterious effects on patient health. Indeed, GENOVELY and PFEIFER [18] showed that intravenous frusemide sufficient to produce a diuresis of 1.6 l had no effect on R-R variation.

The high metabolic activity of nerves makes them extremely susceptible to hypoxaemia and could cause a reversible impairment in electrophysiological function. The evidence that short-term correction of hypoxaemia does not alter autonomic function suggests that our results are not due to a reversible impairment of nerves working in a hypoxic environment. Patients well-established on long-term oxygen therapy (LTOT) have results consistent with their Pao_2 on air rather than the values on oxygen. However, it is possible that LTOT, through long-term correction of hypoxaemia, may have reduced the rate of autonomic function decline rather than reversing the developed neuropathy.

Although cigarette smoking may be an important aetiological factor in the development of COPD related peripheral neuropathy [26], our study shows only a weak correlation between cigarette consumption and autonomic dysfunction. The association is much weaker than that between hypoxaemia and dysfunction. Some heavy smokers who were normoxic had relatively normal autonomic function, while some severely hypoxaemic nonsmokers had abnormal function.

The correlation between airway function as measured by FEV_1 and autonomic function could be explained by the association between FEV_1 and Pao_2 in our group of patients.

Although increased intrathoracic pressures can affect cardiac function and arterial pressure [27] this is unlikely to be the explanation of our results. Increasing intra-thoracic pressure changes by breathing against a resistance does not alter cardiorespiratory reflexes and, likewise, patients with bronchial asthma have increased rather than decreased parasympathetic autonomic reflexes [17].

Although the fact that the Valsalva ratio, I-E difference and 30:15 ratio are abolished by atropine but unaffected by propranolol suggests that they are primarily parasympathetic reflexes, they are in practice extremely complex. The relatively simple I-E response involves many components. Inspiration expands the lungs; activating stretch receptors in the lung, chest wall, and heart chambers. These stimulate the afferent nerve, probably the vagus, which transmits the information to the brainstem (the nucleus solitarius) where it is processed, leading to a decrease in

parasympathetic tone and possibly a small increase in sympathetic tone via the efferent vagus and the cervicothoracic sympathetic nerves, respectively. The efferent impulses terminate at a motor end-plate on the end organ the heart, which responds with an increase in heart rate. Damage to any part of this reflex will cause a failure of conduction of stimulus to response. We now have to determine the site of dysfunction in these complex reflex arcs.

The high incidence of subclinical autonomic neuropathy in COPD patients may have important implications with regard to prognosis. Diabetics [12] and alcoholics [28] with autonomic neuropathy have a high mortality and incidence of sudden death occurring under conditions of stress and hypoxaemia [13]. Anecdotally, those COPD patients who had the worst autonomic nerve function have subsequently died. Furthermore, those patients with rapidly deteriorating lung function and severe disabilities have poor results. In contrast those patients with a long history of well compensated hypoxic COPD seem to have relatively preserved autonomic function.

In conclusion, people with COPD have a subclinical autonomic neuropathy which correlates with the severity of hypoxaemia. Its potential presence should be considered in chest patients presenting with autonomic type symptoms. Studies are needed to determine both its prognostic and aetiological relevance in COPD. Studies are also needed to see whether interventional therapy, such as long-term oxygen, can either reduce or even reverse this decline in autonomic function. The concept that inappropriate or defective responses to major events such as septicaemia or hypoxaemia might contribute to death in COPD patients with autonomic neuropathy warrants further investigation.

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Fonction nerveuse autonome cardiovasculaire chez les patients atteints d'une maladie pulmonaire obstructive chronique hypoxémique. A.G. Stewart, J.C. Waterhouse, P. Howard.

RÉSUMÉ: L'hypoxémie intraneurale est un mécanisme pathogénique reconnu dans la neuropathie diabétique. Un processus pathophysiologique similaire peut se produire dans la maladie pulmonaire obstructive chronique (BPCO). Une neuropathie autonome n'a pas été reconnue jusqu'ici dans les BPCO. Nous avons comparé 96 patients atteints de BPCO hypoxémique à 22 sujets contrôle pairés, pour déterminer si une dysfonction du système nerveux autonome se produit dans les BPCO et si elle est en corrélation avec la sévérité de l'hypoxémie. Les tests autonomes cardiovasculaires ont consisté en la mesure des réponses du rythme cardiaque (fonction principalement parasympathique), en une manoeuvre de Valsalva, en une respiration profonde, et en des modifications posturales, ainsi que, finalement, en l'étude des réponses de la pression artérielle (principalement d'origine

sympathique) aux modifications posturales et à un effort de serrement de main prolongé. La neuropathie autonome précoce est définie comme correspondant à un test anormal, tandis qu'une neuropathie autonome caractérisée correspond à deux tests anormaux selon les limites de normalité. Ces tests autonomes se sont avérés reproductibles dans la population étudiée. Quoique les symptômes et signes de neuropathie autonome ont été rares, l'on a trouvé une dysfonction autonome caractérisée dans 35 % et une neuropathie autonome débutante dans 47 autres % de patients dont la tension artérielle en oxygène (P_{aO_2}) était inférieure à 8 kPa (60 mmHg). Dix-huit % seulement du groupe contrôle avaient des signes d'une dysfonction autonome précoce en rapport avec l'âge. La dysfonction autonome para-sympathique est en corrélation significative avec la P_{aO_2} , alors que les tests sympathiques sont relativement normaux. La correction de l'hypoxémie pendant une heure, ou l'administration de bromide d'ipratropium ou de terbutaline, n'ont pas d'effet sur la fonction autonome.

Une neuropathie autonome subclinique est une caractéristique des BPCO hypoxémiques; son importance dans le processus pathologique et son rôle pronostique doivent encore être évalués.

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