STUDIES IN PARKINSONISM: VIII[1]

Arterial Blood Gas Analysis: Some Aspects of Its Relationship to the Clinical Manifestations

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IT is well known that in Parkinsonian states a wide variety of clinical manifestations may appear as a consequence of the neurologic dysfunction. Consequently, in the Research Laboratory of the Department of Neurology and Psychiatry, Northwestern University Medical School, the more conventional approaches to the study of this disorder have been replaced by careful analyses of the basic physiologic distortions, which lend themselves to accurate measurement. The methodology, results and correlative evaluation of some of these studies have been described in previous reports (3, 4, 5, 10, 12, 17, 18). The purpose of the present communication is to outline the importance of certain biochemical determinations in arterial blood (oxygen saturation and carbon dioxide content) when correlated with the severity of the clinical manifestations.

In Parkinson's disease, the occurrence of symptoms in the extremities due to increased muscle tone and tremor has engaged the attention of many clinicians and investigators. Less frequently, attention has been paid to disturbances produced by the impaired function of other important muscle groups. We are only now becoming increasingly aware of the significance and extent of involvement of the respiratory muscles in this disorder. Although Maty, quoted by Parkinson (15) in his original treatise, described that one of his patients "fetched the breath rather hard," dyspnea as a symptom in Parkinson's disease became fully recognized only in the past decade. In 1958, Nugent and his coworkers (14) studied the pneumodynamics of those patients who were also suffering from dyspnea and found no intrinsic pulmonary, cardiac or systemic disease to explain the respiratory distress. These investigators related the symptom to alterations of neuromuscular function and to non-respiratory factors, such as increased energy expenditure. Arterial blood gas determinations were not performed in this study. We considered it important, therefore, to inquire how extensive a role the respiratory alterations played in the Parkinsonian syndrome. Were these severe enough to impair the ability of the lungs to oxygenate the venous blood? To this purpose, studies in the composition of the blood gases were performed by our group in patients with Parkinson's disease, showing a wide range in the severity and characteristics of the pathological manifestations. In this investigation, attempts were made to answer the following questions: 1) Do these patients exhibit characteristic changes in the blood gas contents? 2) Can such changes account for the onset of dyspnea? 3) What is the relationship of these changes to the other signs and symptoms of the disease process? This report is primarily concerned with some aspects of the latter part of of the investigation.

Material

Eighteen male patients with the clinical syndrome of Parkinsonism, and without a history or clinical evidence of cardiac or primary lung disease, were examined. They ranged in age from 36 years, 6 months, to 73 years, 6 months, with a mean age of 56 years, 4 months. Although some of the patients probably had the changes

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consequent to loss of elasticity of the lungs with advancing age, none showing clinical signs of advanced pulmonary emphysema were included in this series. Subjects with clinical manifestations of systemic disease other than Parkinsonism were also excluded. All patients were off anti-Parkinsonian medication for at least the 24-hour period preceding the examination. Ten patients had dyspnea on exertion and, of these, four had dyspnea at rest.

Methods

After completion of a detailed medical history, all patients were examined clinically. Information from the medical history was used to determine the presence of respiratory discomfort and its characteristics. Numerical expressions in regard to this symptom were avoided since dyspnea in this study was considered in the strictest clinical sense of the word, a sensation, and, therefore, not susceptible of precise measurement. Thus, patients were classified only as to the presence or absence of dyspnea at rest and on exertion.

The clinical examination of muscle tone was carried out, taking into consideration the following: (a) the posture of the extremities, trunk and head in walking and at rest; (b) the resistance of the extremities and head to passive movements; and (c) by observation of the degree of pendulousness of the upper and lower limbs. In the clinical evaluation of tremor only its amplitude was used as a measure of severity.

The examiner determined subjectively the degree of rigidity or tremor according to the following scale:

0 . . . . . within normal limits
1 . . . . . mild
2 . . . . . moderate
3 . . . . . severe.

In instances of unequal involvement of the extremities or when the manifestations were apparent in one side of the body, only the most affected area was rated numerically.

For the gas analysis, the arterial blood was drawn by percutaneous puncture of the brachial artery. After the puncture was performed, the needle was left in the artery and the patient permitted to rest in bed for 20 minutes in the semi-recumbent position, since the minute volume of respiration is usually stabilized within that time (16). This precaution became necessary since some of the patients showed a tendency to hyperventilate during the puncture procedure. The blood was allowed to flow anaerobically into a glass syringe, previously rinsed with heparin solution. The oxygen content and capacity and the carbon dioxide content of the blood sample were measured by the method of Van Slyke. The percentage of oxygen saturation was calculated from the oxygen content and capacity with the necessary corrections for dissolved oxygen. Normal values of oxygen saturation and of carbon dioxide content were derived from the data suggested by the National Research Council of the National Academy of Sciences (8). Patients were then categorized as being either normal or abnormal in terms of the CO_2 content and O_2 saturations of their arterial blood.

In 6 patients, quantitative determinations of muscle tone and tremor were available. These were obtained by previously described electronic techniques. Tone was quantitated in terms of megadyne-cm of torque, by the method of Brumlik and Boshes (4). On the basis of pre-determined normative data, all values above 4.0 megadyne-cm were considered abnormal (4). The parameters of tremor considered in relation to the blood gas values were: harmonic wave-forms, spindle formation, amplitude regularity, frequency regularity and actual frequency. These were obtained utilizing the electronic equipment and methodology described by Wachs and Boshes (17, 18).

The relationships of arterial blood gas composition with data derived from the history, clinical evaluation, and objective measurements were investigated statistically. Since most of the data were expressed in terms of rank order, non-parametric methods were employed. Chi-square tests of homogeneity were performed to determine whether or not the blood gas state and selected factors from the history and clinical examination were mutually independent. The Spearman Rank-Order Correlation Technique was applied to the evaluation of the relationships between blood gas values and electronic measurements. In both instances the .05 level of confidence was selected.

TABLE I

Clinical Status									Arterial Blood Gas Analysis	
						Rigidity			Oxygen saturation (normal ≧ 96%) (borderline = 93.5—96%)	Carbon dioxide content (normal range 44.6—50.2 vol. %)
Patient	Age	Duration of illness (years)	Dyspnea on exertion	Dyspnea at rest	Predominant side involved*	Extremities	Trunk	Tremor		
D. B.	56–1	25	+	—	B	1	1	1	97.2	43.9
M. M.	58–8	8	+	—	Rl	3	3	3	86.0	43.9
L. P.	54–0	5	+	+	Rl	3	2	1	97.2	55.7
J. W.	48–5	6	+	—	Rl	3	2	1	98.9	44.5
H. W.	73–6	3	+	—	Rl	1	2	2	93.1	50.1
T. H.	46–5	3	—	—	L	0	0	2	94.5	48.0
J. M.	62–9	10	—	—	Lr	1	1	2	97.0	42.6
R. A.	35–6	7	—	—	Lr	3	3	0	96.7	49.8
N. K.	56–1	4	+	—	Rl	2	2	2	89.0	46.2
R. D.	43–11	16	+	—	Rl	3	1	2	95.5	42.1
H. R.	68–2	9	—	—	B	1	1	1	94.4	56.3
J. L.	64–4	6	—	—	B	2	3	1	95.7	51.7
J. F.	59–4	19	+	+	Lr	2	2	2	92.8	46.4
E. P.	56–10	5	—	—	Rl	2	2	1	92.1	50.0
J. J.	58–8	12	—	—	L	0	0	1	88.2	40.7
J. S.	54–6	10	+	+	B	3	3	3	92.2	52.2
J. E.	54–8	5	—	—	B	1	1	1	94.3	45.8
E. F.	65–0	5	+	+	Rl	2	2	2	94.5	51.4

*Key: B - Bilateral; Rl - Bilateral, greater on right; Lr - Bilateral, greater on left; L - Unilateral, left; R — Unilateral, right.

TABLE II

ELECTRONIC MEASUREMENTS AND BLOOD GAS VALUES

Arterial Blood		Muscle Tone	Tremor						
CO_2 content (vol. %)	O_2 saturation (%)	Torque megadyne-cm.	Frequency (cps)	Frequency regularity (%)	Amplitude regularity (%)	Amplitude periodicity (%)	Harmonics (%)	Spindles (%)	Abrupt wave-form change (%)
50.0	92.1	2.70	8.2	7	0	0	0	0	0
50.1	93.1	5.75	7.1	40	6	26	15	6	8
51.7	95.7	3.50	6.4	47	17	0	0	25	0
46.4	92.8	7.05	6.0	71	29	0	39	39	0
43.9	97.2	8.45	5.6	73	65	0	7	18	0
43.9	86.0	4.85	4.2	100	89	0	56	22	0

Results

The data obtained from the history, clinical examination and arterial blood gas analysis are summarized in Table I. The analysis of this data shows that in no instance is the obtained value of the chi-square statistic great enough to reject the hypothesis of independence ($p > .05$). Nevertheless, certain observations are of interest. It is apparent that in the group whose illness is of longer duration, there is a higher proportion of patients with decreased oxygen saturation. However, the lack of correlation between age and hypoxemia supports the concept that the observed abnormalities are not only a function of the aging process. Of 4 patients with dyspnea at rest, none showed a reduction of the carbon dioxide content whereas 43% of the group not showing dyspnea at rest had a decreased CO_2 content of their arterial blood.

The data derived from electronic measurements are given in Table II. Although not statistically significant, perhaps due to the limited number of patients, there are suggestions of a direct relationship between the frequency of tremor and the carbon dioxide content of arterial blood. Also, there are evidences of an inverse relationship between the CO_2 content and the frequency regularity and and amplitude regularity of the Parkinsonian tremor. Further investigations are necessary to elucidate the meaning of these observations.

Discussion

In patients with chronic pulmonary disease and over-all hypoventilation, the composition of the arterial blood gases usually show well recognized characteristic alterations (1, 2, 6, 11, 13, 20). When dyspnea is present, the oxygen saturation is distinctly reduced and the carbon dioxide tension is moderately to markedly elevated (13). These changes, which contribute to the increase of ventilation, are closely related to the production of the respiratory discomfort. When the hypercapnia is pronounced, however, hypoxemia becomes the only or most important stimulus to ventilation (7, 9). In these circumstances, the severity of the dyspnea seems to parallel the reduction in oxygen saturation of the arterial blood (13).

In the Parkinsonian patient, the alterations in the blood gas values are entirely different. The reduction in oxygen saturation is slight when compared with the values observed in severe pulmonary disease. The carbon dioxide content of arterial blood is normal, slightly elevated or reduced. These changes are not related to the presence of respiratory discomfort, at rest or on exertion. The striking differences between the findings in diffuse pulmonary disease and those in Parkinsonism are probably related to the different pathologic physiology of the two processes. Nevertheless, it should be emphasized that in respiratory pathology, various clinical entities may produce similar physiologic disturbances and any one disease may result in widely different functional disturbances. Furthermore, pulmonary emphysema may show a pattern similar to the one we have observed in some Parkinsonian patients whenever a ventilation perfusion ratio inequality exists (19). Here, the oxygen saturation is reduced as a consequence of the inability of the alveoli with high ventilation perfusion ratios to compensate for those with low ratio. The carbon dioxide tension, on the other hand, is normal or even low because the alveoli with low ventilation perfusion ratio do not raise it excessively, whereas a high ventilation perfusion ratio can lower the carbon dioxide tension considerably.

Since we did not examine our patients for other important factors in the genesis of dyspnea, we lack the necessary data to elucidate its cause in Parkinsonism. The inability to correlate this symptom with deviations from the normal in the blood gas values indicates that other mechanisms (alterations in lactic acid metabolism, reflexes from proprioceptors, impaired heat dispersal, etc.) should be examined.

If we were able to say that all patients examined in our laboratory who had severe rigidity of their trunk or limbs also had demonstrable changes in the blood gas values, then the physiologic diagnosis of the respiratory disturbances would be simplified. The lack of correlation between the peripheral clinical signs and the composition of the blood gases indicates, however, that involvement of the mechanics of breathing may be more severe than

generally appreciated. Thus, restrictive ventilatory dysfunction may produce little apparent respiratory disability. The latter can be consistently recognized only if physiologic measurements are employed. Obviously, arterial blood gas analysis cannot be advocated as a regular procedure in patients with Parkinsonism. However, if disturbances of the cleansing function, frequent lower respiratory infections, or any other process capable of embarrassing further respiratory function appear, the diagnostic importance of this procedure should not be overlooked. As long as the percentage of oxygen saturation does not accurately portray the severity of impairment in oxygen transfer, all other pulmonary function tests become necessary to assess the extent of the pathologic involvement.

Summary and Conclusions

The oxygen saturation and carbon dioxide content of the arterial blood were investigated in 18 patients with Parkinson's disease and without a history or clinical evidence of cardiac or primary pulmonary disorders. In these same patients, clinical evaluation and measurement by electronic methods of the severity of their rigidity and tremor were performed.

The data thus obtained was statistically treated. The relationships of O_2 saturation and CO_2 content with clinical evaluation of symptoms were studied by means of chi-square tests of homogeneity. The Spearman rank-order technique was used to investigate the correlation between some of the electronic measurements and the blood gas data.

The results suggest the following conclusions:

1. The slight reduction in arterial oxygen saturation with normal, slightly elevated or reduced arterial carbon dioxide content which were observed is in striking contrast to the findings in patients with diffuse chronic pulmonary disease. This difference is probably related to the different pathologic physiology of these two processes.

2. The Parkinsonian dyspnea is not related exclusively to changes in the composition of the blood gases.

3. The lack of correlation between the peripheral clinical signs and the oxygen saturation indicates that involvement of respiratory muscles cannot be predicted entirely on the basis of clinical examination. Therefore, tests of pulmonary function are recommended in the Parkinsonian patients whenever it becomes necessary to know the true status of the respiratory mechanisms.

4. There are evidences of an inverse relationship between the carbon dioxide content of the arterial blood and the frequency regularity and amplitude regularity of the Parkinsonian tremor. Suggestions of a direct relationship between CO_2 content and actual frequency are also present. To determine the real significance of these observations, further investigations are necessary. Nevertheless, they raise what seem to be important questions in the understanding of the disturbed mechanisms which underlie the symptoms.

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