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Potassium studies in chronic obstructive airways disease

P d'A SEMPLE, W S WATSON, R HUME, AND G R SUTHERLAND

From the Division of Medicine, Department of Clinical Physics and Bio-engineering, and Radiology Department, Southern General Hospital, Glasgow G51, UK

Semple, P d'A, Watson, W S, Hume, R, and Sutherland, G R (1978). *Thorax*, **33**, 734–739. **Potassium studies in chronic obstructive airways disease.** Seventeen male patients with chronic obstructive airways disease in remission were separated into two groups according to arterial carbon dioxide tensions. Hypercapnia was associated significantly with hypoxia and increased red cell volume whereas normocapnia was not. Normocapnic patients were significantly lighter than those with hypercapnia. Total body potassium (TBK) measured by the whole body monitor was significantly low in two of the patients studied ($P<0.005$). The mean value for TBK for the normocapnic group as a whole was significantly low ($P<0.005$), but the mean value for the hypercapnic group was not. Serum potassium and erythrocyte potassium concentrations were normal even when TBK was low, and diuretics had no apparent influence on these potassium values. Of four patients (two in the series and two others) who had TBK measured after a recent episode of cor pulmonale, three had significantly low values. The only previous studies using a whole body monitor to measure TBK in chronic obstructive airways disease found no such low values, though other workers estimating exchangeable potassium by isotope dilution techniques had found evidence of gross potassium depletion. It is concluded that low TBK does indeed occur in patients with chronic obstructive airways disease and that gross depletion is more likely to follow an episode of cor pulmonale.

Studies of body potassium measuring exchangeable potassium by an isotope dilution method after the administration of potassium-42 have shown that gross potassium depletion may occur in patients suffering from chronic airways obstruction (COAD) (Baum *et al*, 1959; Telfer *et al*, 1968; Schloerb *et al*, 1970; Campbell *et al*, 1975; Telfer *et al*, 1975).

Possible reasons for low potassium values include anorexia or poor diet, increased urinary loss due to hyperaldosteronism, hypoxia-induced "sick-cell syndrome" where intracellular sodium is higher and intracellular potassium lower than normal (*British Medical Journal*, 1977), and loss of tissue mass resulting from hypoxia in acute exacerbations (Campbell *et al*, 1975). Campbell *et al* (1975), however, did note that these potassium values remained low even when their patients had recovered from cor pulmonale for two to three months and had regained body weight.

In contrast to isotope dilution studies Howie and colleagues (1976) using a whole body monitor found normal values of total body potassium (TBK) in 12 patients who had previously had acute respiratory failure with cor pulmonale but who at time of study were in remission. This discrepancy was considered to be due either to exchangeable potassium being a smaller fraction of body potassium in patients with COAD than in normal subjects or due in part to insufficient equilibration time used in isotope dilution studies (Boddy *et al*, 1978).

We report a study carried out to reassess the state of TBK in patients with chronic obstructive airways disease using a whole body monitor and to determine any differences in TBK between patients with normal and those with high arterial carbon dioxide tensions.

Methods

PATIENTS

When the hospital ethical committee had approved the project informed written consent was obtained

from all patients. The 17 men with COAD were chest clinic attenders and were selected to give a wide distribution of body habitus from frankly underweight to obese. A modified Medical Research Council questionnaire on respiratory symptoms (1966) was applied, and in all cases grade 3 or 4 dyspnoea had been present for more than one year. All but one were past or present cigarette smokers, and only one was free from cough or sputum. Spirometry was performed (Vitalograph—sitting), the best of three attempts being selected. Forced expiratory volume in one second (FEV_1) was always less than 70% of predicted normal value, and forced expiratory volume/forced vital capacity ratio ($FEV_1/FVC\%$) was always less than 70% signifying airways obstruction (table 1). No patient had blood urea concentration greater than 10 mmol/l. All were in remission and without cardiac failure, and medicinal treatment was continued during the study. Patients were grouped according to arterial carbon dioxide tensions ($Paco_2$), those with a $Paco_2$ level greater than 5·8 kPa hereafter being referred to as the "hypercapnic group" and those with a level less than 5·8 kPa as the "normocapnic group."

A further two male patients (No 18 and 19) who had been admitted in respiratory failure and in severe cor pulmonale were similarly studied as soon as right heart failure had cleared.

TEST PROCEDURES

Patients were admitted to a metabolic investigation unit for three days. Height and weight were measured, and the latter was compared with that predicted for sex, height, and age (Society of Actuaries, Chicago, 1959). A chest radiograph was obtained and examined by a radiologist (GRS) who awarded an "emphysema score" (Sutherland *et al*, 1971). An arterial blood sample for blood gas estimation was taken on each of two consecutive days from the radial artery with the patient lying rested and breathing room air for 30 minutes. The average of the two results was used.

Red cell volume and plasma volume determination were performed by administering ^{51}Cr labelled red cells and ^{125}I labelled human serum

Table 1 *Laboratory results of patients with chronic obstructive airways disease grouped according to* $Paco_2$ *values*

Patient	*Age (years)*	*Height (metres)*	*Weight (kg)*	*FEV_1 (% predicted)*	*FEV_1/FVC (%)*	*Pao_2 (kPa)*	*$Paco_2$ (kPa)*	*Red cell volume (measured/predicted) %*	*Plasma volume (measured/predicted) %*
Hypercapnic ($Paco_2 > 5·8$ kPa)									
1	70	1·55	66·9	68·0	61·8	8·1	5·9	143	98·0
2	53	1·70	98·0	26·6	40·5	7·2	6·4	157	106·1
3	66	1·59	84·4	30·9	41·5	7·2	6·0	134	88·2
4	66	1·65	76·0	28·6	38·8	5·3	9·0	165	93·7
5	48	1·67	72·7	28·8	43·9	8·2	6·4	88	83·4
6	59	1·58	67·7	34·0	68·0	6·2	7·9	159	96·4
7	52	1·69	79·6	54·8	54·0	7·4	5·9	141	104·9
8	69	1·81	52·6	25·0	25·7	6·3	7·6	103	115·5
Mean	60·4	1·66	74·7	37·1	46·8	7·0	6·9	136	98·3
Standard deviation	8·5	0·083	13·4	15·6	13·7	0·99	1·15	27·5	10·3
Normocapnic ($Paco_2 < 5·8$ kPa)									
9	38	1·83	57·4	24·4	42·2	7·7	5·1	96	93·9
10	70	1·61	37·8	28·3	44·2	9·8	4·7	86	99·5
11	56	1·55	41·2	26·0	30·9	8·4	4·7	124	122·2
12	48	1·64	50·0	8·4	45·1	7·4	5·7	118	122·5
13	53	1·64	54·6	48·4	40·0	7·5	5·3	118	89·4
14	52	1·69	46·3	29·7	47·6	8·2	5·3	107	104·8
15	56	1·64	42·2	20·0	33·7	9·8	5·1	110	78·3
16	61	1·64	54·4	22·6	48·7	8·0	5·2	120	107·6
17	57	1·73	80·0	66·7	51·9	9·6	5·3	105	91·6
Mean	54·6	1·66	51·5	30·5	42·7	8·49	5·15	111·6	101·1
Standard deviation	8·8	0·08	12·6	17·1	6·9	0·99	0·31	13·3	14·8
Significance of difference between the means	NS	NS	$P < 0·01$	NS	NS	$P < 0·01$	$P < 0·01$	$P < 0·05$	NS

FEV_1=Forced expiratory volume in 1 s; FVC=Forced vital capacity; Pao_2 and $Paco_2$=Partial pressure in arterial blood of oxygen and carbon dioxide; NS=Not significant.

albumin and measuring the radioactivity in samples 10, 20, and 30 minutes after injection. Predicted normal values were calculated using the equation developed by Nadler *et al* (1962) and modified by Hume and Goldberg (1964).

TBK values were obtained by measuring the naturally occurring radionuclide potassium-40 using a shielded room whole body monitor described by Runcie and Hilditch (1974). The results obtained were compared with predicted values calculated using height, weight, and age (Boddy *et al*, 1972). On the same day red cell potassium was deduced from a modification of the method of Hald (1946) and serum potassium was also measured.

Differences between groups were tested with Student's *t* test.

Results

There was no significant difference in age, height, or spirometric readings between the two groups of subjects separated according to $Paco_2$ values (table 1). The hypercapnic group of eight patients was significantly heavier and had a lower arterial oxygen tension and higher red cell volume expressed as a percentage of predicted normal. Considering the 17 patients individually there was a significant inverse relationship between level of Pao_2 and red cell volume ($P<0.05$) and a significant direct relationship between level of $Paco_2$ and red cell volume ($P<0.05$).

Serum potassium values were always normal, and there was no difference between the two groups in serum or erythrocyte potassium. Two patients (2 and 8) in the hypercapnic group (table 2) had significantly low values of TBK (TBK 79·1% and 77·8% of predicted normal; $P<0.005$) as had the two additional cor pulmonale patients (18 and 19) (table 3). The mean value of TBK in the normocapnic group was significantly lower than normal, though that for the hypercapnic group was not. The difference between the mean values of TBK in the two groups (90·2% and

Table 2 *Potassium studies including total body potassium of patients with chronic obstructive airways disease grouped according to* $Paco_2$ *values*

Patient	*Serum potassium (mmol/l)*	*Erythrocyte potassium (mmol/l)*	*TBK (mmol/l)*	*TBK (predicted)*	*TBK (measured/predicted) %*	*Emphysema score**	*Diuretic*
Hypercapnic							
1	4·8	105·2	2680	2450	109·4	16	—
2	3·6	102·4	3095	3913	79·1†	23	Frusemide 40 mg, Slow-K
3	3·9	96·8	3125	2926	106·8	23	—
4	3·8	105·9	2847	3056	93·2	24	Frusemide 40 mg, Slow-K
5	4·2	89·4	2849	3261	87·3	23	Frusemide 40 mg, spironolactone 100 mg
6	4·2	106·8	3036	2639	115·0	ND	Frusemide 40 mg
7	3·3	102·6	3183	3483	91·4	ND	—
8	4·6	114·6	2350	3020	77·8†	26	—
Mean	4·05	103·0	2896	3094	95·0	22·5	
Standard deviation	0·50	7·4	279	464	14·0	3·4	
Normocapnic							
9	3·9	102·0	3235	3583	90·3	21	—
10	5·3	111·9	1926	1959	98·3	25	Amiloride 5 mg, hydrochlorthiazide 50 mg
11	4·1	101·7	2023	2012	100·2	22	—
12	4·3	96·6	2386	2616	91·2	23	—
13	5·1	104·9	2309	2665	86·6	19	—
14	3·8	97·0	2304	2675	86·1	26	—
15	5·0	107·0	1910	2325	82·2	25	—
16	4·4	105·6	2120	2552	83·1	ND	Bendrofluazide 2·5 mg with k
17	3·8	104·0	3452	3668	94·1	18	—
Mean	4·41	103·4	2408	2672	90·2‡	22·4	
Standard deviation	0·58	4·8	560	602	6·4	2·9	
Significance of difference between the means	NS	NS	$P<0.05$	NS	NS	NS	

*0=Emphysema absent; 32=Most extreme score (Sutherland *et al*, 1971).
†Significantly low ($P<0.005$).
‡Significantly low ($P<0.005$).
TBK=Total body potassium; ND=Not done; NS=Not significant.

Table 3 *Various laboratory results including total body potassium values in two patients recently recovered from severe cor pulmonale*

Patient	*Age (years)*	*Height (metres)*	*Weight (kg)*	*FEV_1 (% pred)*	*Pao_2 (kPa)*	*$Paco_2$ (kPa)*	*Red cell volume* $\frac{(measured}{predicted)}$ %	*Plasma volume* $\frac{(measured}{predicted)}$ %
18	42	1·65	55·8	12·3	4·7	6·7	144	83
19	78	1·59	99·7	15·0	5·7	11·9	167	119

Patient	*Serum potassium (mmol/l)*	*Erythrocyte potassium (mmol/l)*	*TBK (mmol)*	*TBK (predicted)*	*TBK* $\frac{(measured}{predicted)}$ %	*Diuretic*
18	4·9	96·8	2026	2880	70·3%*	Frusemide 40 mg, Slow-K
19	5·1	101·0	2376	3297	72·5%*	Frusemide 40 mg, Slow-K

*$P < 0·005$.
FEV_1=Forced expiratory volume in 1 s; Pao_2 and $Paco_2$=Partial pressure in arterial blood of oxygen and carbon dioxide; TBK=total body potassium.

95·0%) was not significant. The degree of potassium depletion in these 17 stable COAD patients was not apparently related to diuretic treatment (table 2). There was no significant correlation between the severity of emphysema as measured by the emphysema score and the level of TBK, though the more severely depleted patients tended to have a higher emphysema score (table 3).

The validity of the equation for predicting normal TBK values (Boddy *et al*, 1972) was checked in the whole body monitor by measuring TBK in 18 normal male volunteers, and the mean measured values were within 99·8% of predicted normal (99·83±7·32).

Discussion

As potassium concentrations are much higher in cells than in extracellular fluid any loss of tissue mass is associated with a consequent drop in body potassium. Campbell *et al* (1975) noted that patients lost weight during exacerbations of cor pulmonale and that this weight loss was associated with a fall in exchangeable potassium, which rose again when weight was regained in remission though it remained lower than normal. Emphysematous patients also lose weight (Vandenbergh *et al*, 1967; Heard *et al*, 1969) though often retaining normal arterial blood gas tensions. Such a fall in tissue mass might be expected to be associated likewise with a drop in TBK. Hence the decision to compare two groups of patients; underweight emphysematous patients with relatively normal arterial blood gases and their overweight hypercapnic counterparts.

The 17 patients, all with stable COAD, had incapacitating dyspnoea. Both groups (table 1) were similar with respect to age, height, and spirometry, but the hypercapnic group had a lower mean Pao_2 value, were of heavier build, and had an abnormally high mean red cell volume as compared with the normocapnic group. We confirmed the finding of Hume (1968) that red cell mass does reliably relate to both Pao_2 and $Paco_2$ values.

The mean TBK level in the normocapnic group was significantly low, though no individual had a significantly low value. In the hypercapnic group three patients (2, 5, and 8) had low levels of TBK though the mean value for this group as a whole was not significantly low. Patient 2 had spent two weeks in hospital with severe cor pulmonale two months previously, had responded well to diuretics, and by the time of measurement was free of oedema. Patient 8, on the other hand, although treated at home four weeks previously for a severe exacerbation of dyspnoea associated with chest infection, had not had frank cor pulmonale in more than a year. In the case of patient 5, the TBK value was low, though not significantly, and he, like patient 2, had been in hospital four months previously with severe cor pulmonale. The remainder of the 17 patients had been free of cor pulmonale for more than one year.

In view of the finding of low TBK values in three hypercapnic patients, patients 18 and 19 were studied additionally some 10 days after they were admitted to hospital with severe cor pulmonale, which by this time had settled (table 3). Their very low values of TBK confirmed that potassium depletion can occur in patients recovering from cor pulmonale, as previously shown by Campbell *et al* (1975). Howie *et al* (1976) showed normal values of TBK in patients recovered from cor pulmonale but did not state for how long they had been in remission. In our series all the patients on diuretics (table 2) had in the past had manifest

cor pulmonale, but most did not have significantly low potassium values when measured.

Of the four patients (2, 8, 18, and 19) with significantly low TBK values three (2, 8, and 19) had higher than normal plasma volumes (tables 2 and 3), suggesting that in fact latent cardiac failure may have been present (Hume, 1968) giving rise, because of increased extracellular fluid, to falsely low values of TBK as a percentage of predicted. TBK values did not seem to correlate inversely with plasma volume in other patients, however, nor did they relate to diuretic treatment (table 2). It may be that in those patients recently recovered from severe cor pulmonale, gross diuresis as well as loss of tissue mass contributes to potassium depletion, though Dargie *et al* (1974) showed that frusemide without potassium supplements was not associated with a lowering of TBK.

Red cell potassium, usually well preserved and not a good indicator of intracellular potassium values in general, was normal in both groups and was not low in the subjects with significantly low TBK (table 2). This finding conforms with that of Boddy *et al* (1976), that in normal subjects red cell potassium values are not related to TBK values and our finding of normal serum potassium values even where TBK is severely depleted reinforces those of other workers (Schloerb *et al*, 1970).

This study confirms that TBK may in fact be low in COAD, that weight loss may be responsible, and that the diuretic phase of treated cor pulmonale may contribute. Further studies are required to determine whether the low values are associated with low intracellular potassium or with a larger than usual extracellular fluid compartment.

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Requests for reprints to: Dr P d'A Semple, Division of Medicine, Southern General Hospital, Glasgow G51.