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Total body and exchangeable potassium in chronic airways obstruction: a controversial area?

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Boddy, K., Davies, D. L., Howie, A. D., Monir Madkour, M., Mahaffy, Maureen E., and Pack, A. I. (1978). *Thorax*, **33**, 62–66. **Total body and exchangeable potassium in chronic airways obstruction: a controversial area?** Potassium deficiency is an important complication in the treatment of heart disease. However, there is a serious dichotomy in the literature. Severe potassium depletion has been reported in this condition when exchangeable potassium was measured whereas normal levels or marginal depletion were found in measurements of total body potassium. To clarify this situation, simultaneous measurements of total body potassium by whole-body counting, and of exchangeable potassium by isotope dilution using ^{43}K, were made in 10 male subjects with established airways obstruction. Sequential determinations showed that exchangeable potassium increased up to 68 hours after administration, and values obtained at only 24 hours would have been a substantial underestimate. In this group of subjects neither total body nor exchangeable potassium at 48 hours was significantly different from the expected normal value.

We have previously reported (Howie *et al.*, 1976) normal values of total body potassium (TBK) in a group of patients with chronic cor pulmonale, contrasting with earlier studies in which exchangeable body potassium (K_e) showed gross potassium depletion (Baum *et al.*, 1959; Bauer *et al.*, 1966; Telfer *et al.*, 1968, 1975; Schloerb *et al.*, 1970; Campbell *et al.*, 1975). It was pointed out (Howie *et al.*, 1976) that the apparent conflict in these findings was reconcilable if equilibration between the administered radioactive potassium and native potassium was delayed or if K_e was an unusually small fraction of TBK in this condition. This explanation has been investigated by measuring K_e and TBK simultaneously.

Material and methods

Ten male subjects were included in the study, each having established airways obstruction, judged from spirometric testing, and chronic bronchitis according to the Medical Research Council questionnaire of respiratory symptoms. Relevant physical and clinical details are summarised in Table 1. All patients had previously had at least one episode of acute respiratory failure complicated by raised jugular venous pressure and peripheral oedema, but at the time of the study they were in a chronic compensated state of their respiratory disease and free from oedema. No subject had a blood urea greater than 10 mmol/l (60 mg/100 ml). Drug therapy was discontinued 72 hours before the study, at which time all patients were active, ambulant, and taking their usual unrestricted diet and fluid intake.

Blood for blood gas estimation was obtained from an indwelling cannula inserted into the brachial artery. Each patient was rested in the sitting position for at least 15 minutes. Two arterial samples were taken at 30-minute intervals to ensure that stable results were obtained. The blood gases were analysed using an Instrumentation Laboratory blood gas analyser (Model 313).

Total body potassium was measured using the MERLIN mobile whole-body counter (Boddy, 1967) to detect the 1·46 MeV gamma rays from the naturally occurring radionuclide ^{40}K, which is a constant fraction of TBK. The counter uses a NaI detector, 29·2 cm diameter and 10·2 cm thick, housed in a lead shadow-shield. The patient, lying

Table 1 *Clinical features of patients included in study*

Patient	*Age (years)*	*Height (cm)*	*Weight (kg)*	*Drug therapy*[1]	*Duration of diuretic therapy (years)*	*FVC (litres)*	*FEV_1 (litres)*
1	76	167·6	73·9	Frusemide, 40 mg daily Slow K, 600 mg tid Salbutamol, 4 mg tid	3	1·78	0·56
2	60	162·6	50·3	Frusemide, 40 mg daily Slow K, 600 mg bd	5	1·52	0·46
3	63	162·6	60·3	Nil		1·85	0·92
4	70	170·2	85·7	Nil		2·74	1·52
5	47	175·0	77·7	Nil		2·94	1·81
6	76	161·3	44·0	Frusemide, 40 mg daily Slow K, 600 mg tid Salbutamol inhaler	1	1·65	0·89
7	67	165·1	65·8	Frusemide, 40 mg daily Slow K, 600 mg bd Salbutamol inhaler	7	2·13	0·89
8	68	165·1	65·8	Frusemide, 40 mg daily Slow K, 600 mg bd Salbutamol, 4 mg qid Digoxin	3	1·85	0·71
9	71	168·0	56·8	Frusemide, 40 mg daily Slow K, 600 mg tid	4	1·22	0·50
10	53	165·0	82·7	Frusemide, 80 mg daily Slow K, 600 mg tid Salbutamol inhaler	2	3·04	1·53

[1]All drug therapy discontinued 72 hours before study

on a motorised couch, passes beneath the detector in the supine and then the prone position. For an average male, the method has a standard error of less than 4%. The procedure has been described in detail previously (Boddy *et al.*, 1971). The measured TBK in each subject was compared with the expected normal values and range estimated from height and age and from height, weight, and age (Boddy *et al.*, 1972).

Exchangeable body potassium was measured by the general method of Davies and Robertson (1973) except that ^{43}K alone was administered. Samples were taken at 20, 44, and 68 hours after the oral administration of 40 μCi of ^{43}K. Three separate 'spot' urine samples were taken after each equilibration period, which was preceded by a 12-hour overnight fast. The potassium content of the samples was measured using a Technicon Mark III flame photometer. Potassium-43 was measured in duplicated 10-ml aliquots using a Packard 5330 automatic gamma spectrometer.

Results

Blood gas and plasma electrolyte measurements are summarised in Table 2, showing hypoxaemia in all subjects ($Pao_2 < 10{\cdot}3$ kPa). The arterial carbon dioxide tension ($Paco_2$) was frequently increased, but in all patients the plasma potassium was within normal limits.

Table 2 *Measurements of arterial blood gases and electrolytes*

Patient	*pH*	*PaO_2 (kPa)*	*$PaCO_2$ (kPa)*	*Plasma electrolytes (mmoles/l)*				
				K	*Na*	*Cl*	*HCO_3*	*Urea*
1	7·42	9·40	4·54	4·0	139	104	27	7·2
2	7·43	5·08	6·61	3·9	138	98	28	6·2
3	7·43	9·79	5·21	4·4	136	101	27	5·3
4	7·46	8·51	4·40	3·8	135	97	29	5·6
5	7·41	9·88	5·51	3·4	136	97	27	4·7
6	7·43	8·78	4·88	4·0	138	102	29	6·7
7	7·42	9·92	5·61	4·2	137	101	26	7·0
8	7·40	10·32	5·19	4·1	138	103	25	7·4
9	7·35	9·24	6·82	4·2	139	99	31	8·1
10	7·44	9·58	5·64	3·8	136	100	23	5·2

Conversion: SI to traditional units—Potassium: 1 mmol/l ≈ 1 mEq/l. Sodium: 1 mmol/l ≈ 1 mEq/l. Chlorine: 1 mmol/l ≈ 1 mEq/l. Bicarbonate: 1 mmol/l ≈ 1 mEq/l. Urea: 1 mmol/l ≈ 6 mg/100 ml.

The observed and expected normal values of TBK are given in Table 3. The measured TBK was not significantly different from the expected normal values based on height, weight, and age, with the exception of subject 5, whose measured value was significantly greater than that expected ($P < 0{\cdot}05$). In comparison with the expected values based on height and age, the measured value of TBK in subject 5 was again significantly greater ($P < 0{\cdot}01$), and in subjects 6 and 9 they were significantly lower ($P < 0{\cdot}05$). In the group as a whole, the measured TBK was not significantly different

Table 3 *Measured and predicted values of K_e and TBK*

Patient	K_e (mmol) measured			K_e estimated		TBK (mmol)	TBK estimated	
	20 h	44 h	68 h	Moore	Skrabal	Measured	Ht, Wt, Age	Ht, Age
1	2452	2614	2693	2733	2666	2726	2982	2841
2	1632	1983	2120	2702	2212	2450	2435	2731
3	2662	2864	2943	2363	2406	3110	2637	2701
4	2994	3352	3411	3054	3063	3604	3430	3036
5	3317	3774	3954	3421	3254	4206	3683[1]	3517[1]
6	1216	1512	1528	1920	1849	1774	2043	2506[1]
7	2355	2569	2679	2513	2536	3008	2808	2795
8	2718	2843	2912	2513	2524	3105	2795	2785
9	1615	1841	1936	2268	2341	2123	2647	2910[1]
10	2834	3297	3419	3573	3112	3579	3402	2932
Mean	2379·5	2664·9	2759·5	2706·0	2596·3	2965·5	2886·2	2875·4
SD	679·9	719·4	742·2	514·9	439·4	737·1	500·5	267·8
SE	215·0	227·5	234·7	162·8	138·9	233·1	158·3	84·7

[1]Measured TBK significantly different from predicted value.

from the expected values ($P>0.10$, Wilcoxon's signed ranks test).

As shown in the Figure, K_e increased progressively in all subjects up to 68 hours post-administration. The values obtained (Table 3) at 20 hours were significantly lower ($P<0.002$) than those at 44 hours, which in turn were significantly lower ($P<0.002$) than those at 68 hours (Wilcoxon's signed ranks test). The respective mean values (±SE) were 2380±215 mmol K, 2665± 228 mmol K, and 2760±235 mmol K. In all subjects, exchangeable potassium at 68 hours was 92·9±1·3% (mean±SE) of TBK, 101·2±5·1% of the expected normal values using the equations of Moore *et al.* (1963) and 104·8±4·5% using the data of Skrabel *et al.* (1973).

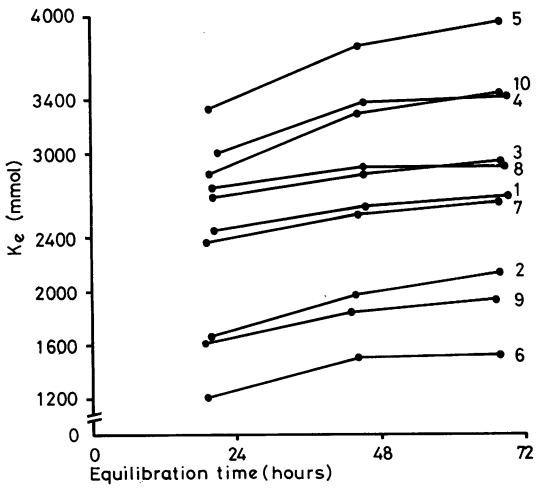

Figure *Exchangeable potassium values are shown for each patient (identified by case number) as measured at various equilibration times. Equilibration is not complete even at 48 hours post-administration, and values obtained after only 24 hours substantially underestimate K_e.*

Discussion

The present study confirms our previous findings (Howie *et al.*, 1976) of normal TBK in a group of subjects with cor pulmonale and, in addition, the value of K_e at 68 hours was not significantly different from the expected normal values (Moore *et al.*, 1963; Skrabel *et al.*, 1973). In no subject was the measured TBK significantly less than both predicted normal values (Boddy *et al.*, 1972). However, in two subjects (6 and 9) the measured value was less than that estimated from height and age only. This could be explained by the comparatively low body weight relative to the height of these subjects, and the measured K_e was also low. If body potassium was low in these two subjects, it might be due indeterminately to the disease or to causes such as loss of lean tissue (bearing in mind their age) or dietary deficiency. Nevertheless, in the group as a whole we did not find evidence of potassium deficiency.

It was clear from the sequential measurements of K_e that equilibration of the administered radionuclide and native potassium was incomplete at 20 hours, and misleadingly low values for K_e would be obtained (86% of the value at 68 hours) after this period. This finding confirms that of Telfer and colleagues (1975), who found significantly higher values (an increase of 20%) at 48 hours than at 24 hours in similar patients, and suggests that apparent deficiencies of potassium derived from 24-hour values of K_e (Baum *et al.*, 1959; Bauer *et al.*, 1966; Telfer *et al.*, 1968; Campbell *et al.*, 1975) require cautious interpretation. In the present study, the values at 68 hours were consistently higher than at 44 hours post-

adminstration but the mean value was only 3–4% greater.

There remains an unexplained discrepancy between the gross potassium depletion reported (Schloerb *et al.*, 1970; Telfer *et al.*, 1975) at 48 hours after administration of ^{42}K and our previous (Howie *et al.*, 1976) and present findings. However, it is interesting to note in the study of Telfer *et al.* (1975) that both the value of K_e at 48 hours per litre of intracellular water and the volume of intracellular water were normal. Since the greater part of body potassium (about 98%) is intracellular, these observations seem to imply that K_e should also have been normal. In addition, total body water, which usually correlates closely with the lean body mass and TBK, was normal, and the patients were said to be free from oedema. We have re-examined the data for the individual patients of Telfer *et al.* (1975) and, for comparison, expressed the 24-hour values of K_e as a percentage of that predicted using the relationships of Skrabel *et al.* (1973). In six patients the measured values were extraordinarily low (less than 56%, mean 48·7±2·3%), and the values for sodium and bromine, in some cases, also appeared anomalous. The discrepancy in the findings might be attributable partly to the more complex multinuclide method used by Telfer *et al.* (1975) compared with the one we adopted or it might be due to differences in clinical circumstances, including medication.

In the study of Schloerb *et al.* (1970), in three of the four patients with chronic respiratory failure, in whom K_e was measured at 42 to 48 hours post-administration, the K_e per litre of intracellular water was the same as the mean±1 SD found in healthy controls by Telfer and colleagues (1975). Furthermore, these authors (Schloerb *et al.*, 1970) used unspecified relationships of Moore *et al.* (1963), but, using the equation $K_e = 1383 + 2623$ Wt for males from 31–60 years and $K_e = 723 \pm 27{\cdot}2$ Wt for males from 61–90 years taken from the same source (Moore *et al.*, 1963), we obtained different values for predicted K_e from those quoted. In this case the predicted mean (±1 SD) for the four patients of 2893±361 mmol was not significantly different ($P > 0{\cdot}05$) from the mean measured K_e of 2451±803 mmol (paired Student's *t* test).

It is possible that we have misunderstood or misinterpreted the published data relating to potassium status in chronic respiratory disease and based on exchangeable body measurements. Nevertheless, our findings clearly showed that a 24-hour period of equilibration is inadequate in this condition, and our direct measurements of total body potassium fail to confirm the significant depletions of potassium reported by other workers.

The present findings may be relevant to a recent review (British Medical Journal, 1977), which concluded that potassium depletion was associated with heart failure but cited only evidence based on measurements of K_e. In contrast, our previous direct determination of total body potassium (Lawson *et al.*, 1976) and those of others (Davidson *et al.*, 1976; Delwaide, 1973) indicated that potassium deficiency was not a major problem in this condition. Further investigations are proceeding.

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