Total body potassium in relation to thyroid hormones and hyperthyroidism

C. J. EDMONDS AND T. SMITH
Endocrinology Research Group, Divisions of Clinical Sciences and Radioisotopes, Clinical Research Centre, Harrow, Middlesex, U.K.

(Received 21 March/8 October 1980; accepted 13 October 1980)

Summary

1. Body weight and total body potassium were measured in 23 hyperthyroid patients before and at various stages during treatment and in 19 athyreotic patients who were being treated with high-dose L-thyroxine.

2. In the hyperthyroid patients the total body potassium rose by $23 \pm 2.8\%$ (SEM) within a few weeks of restoring the blood thyroid hormone levels to normal. The body potassium values after treatment were close to that expected in these individuals if they were healthy indicating that a considerable loss of body potassium is usual in hyperthyroidism.

3. The gain of total body potassium in hyperthyroidism averaged $71 \pm 8$ mmol for each kg of body weight gained (compared with muscle potassium concentration of about 92 mmol/kg). In contrast, weight loss produced by dietary treatment of obesity caused very little change of body potassium (maximum averaged was $14 \pm 4$ mmol/kg wt. loss).

4. Among the patients with hyperthyroidism, the greatest muscular weakness was present in those with the greatest body potassium loss and these patients regained a large amount of potassium relative to weight on recovery.

5. Total body potassium changes were closely related to total plasma tri-iodothyronine concentrations but unrelated to the thyroxine levels.

Key words: hyperthyroidism, thyroxine, total body potassium, tri-iodothyronine.

Introduction

Several studies have shown that exchangeable potassium is reduced in hyperthyroid individuals (Aikawa, 1953; Munro, Renschler & Wilson, 1958; Staffurth, 1962). These investigations were, however, restricted because the only available technique for body potassium measurement was the $^{42}$K dilution method so that the number of follow-up measurements that could be made during treatment was limited. Moreover, at the time of those studies available assays for thyroid hormones were not satisfactory. Measurement of the natural form of radioactive potassium, $^{40}$K, makes it possible to follow changes in total body potassium without the need for administering radioactive isotopes. We have made serial measurements of total body potassium in patients with hyperthyroidism and compared the results with the clinical condition and hormonal status of the patient.

Methods

The studies were made on 23 hyperthyroid patients (18 females and five males) aged 32–61 years, and on 19 athyreotic patients (17 females and two males) aged 28–74 years. The diagnosis of hyperthyroidism was based on the clinical assessment and measurement of the thyroid hormone concentration in the blood. The athyreotic patients had been treated previously for thyroid cancer by surgery and sufficient $^{131}$I to destroy all normal thyroid and tumour tissue. This total destruction was confirmed by several thyroid-uptake measurements after a relatively large dose of 185 MBq of $^{131}$I (Edmonds, 1979). The patients had been taking 200–400 $\mu$g daily of...
L-thyroxine for some years. None of the patients in this study had cardiac or other significant disease or complications, or were receiving medication likely to upset fluid and electrolyte metabolism. Measurements were carried out when the patients attended the out-patient clinic as part of normal follow-up and their treatment was unaffected. The hyperthyroid patients were treated with antithyroid drugs and/or 131I and some were also given propranolol initially. The hyperthyroid patients were considered as one group. Three of them were, however, obese (body wt. over 15% above the expected for their age, sex and height) and these are considered independently in the results in Table 1. Six of the hyperthyroid patients received carbimazole (45–60 mg daily) for several weeks to produce rapid control of hyperthyroidism and were measured periodically; the results obtained from these individuals were used to determine the rate of increase of total body potassium.

Symptomatic assessment was based on the method of Wayne (1960). Muscular strength was assessed from the history and examination and strength classified into three grades without knowledge of the body potassium measurements. Grade 2 included those who had moderate to severe weakness sufficient to cause difficulty in performing such acts as arising from a sitting position, climbing stairs or getting out of a bath. Muscular weakness was obvious on examination particularly on straight leg raising, the leg being able to be lifted and held above the examination couch for a few seconds only. Grade 1 included the patients who had recognized some weakness but which was insufficient to impair their activities and examination showed no more than a minor degree of impairment of muscle power. Grade 0 included those who had no significant weakness. Patients, with their outer clothing removed, were weighed to the nearest 50 g on a chair-type weighing machine (Avery); an allowance of 0·3 kg was made for the clothing worn.

Total body potassium was measured with a liquid scintillator whole-body counter (Smith & Cronquist, 1977) and a counting period of 1000 s. Calibration was based on the established 42K technique (Smith, Hesp & Mackenzie, 1979) and each patient’s calibration factor (counts s⁻¹ g⁻¹ of potassium) was determined by using the parameter (wt. x height⁻¹)¹. Standard errors of individual total body potassium estimates, including calibration and counting statistical errors, ranged from 2·8 to 4·5% for males and from 3·3 to 6·2% for females. After body potassium measurement blood was taken for measurement of the thyroid hormones: thyroxine (T₄) and tri-iodothyronine (T₃) being determined by radio-immunoassay. The normal ranges for these hormones were T₄ 60–150 nmol/l and T₃ 1·2–2·8 nmol/l.

The expected normal values of total body potassium were calculated from the patient’s body weight, height, age and sex by using regression equations derived for normal subjects by Boddy, King, Hume & Weyers (1972). These equations have been shown to be valid for use with the whole-body counter used in the present study (Smith et al., 1979). Results are given as means ± SEM.

Results

Hyperthyroid patients

Changes of body weight and total body potassium. When the hyperthyroid patients first presented their total body potassium was on average lower than expected from their age, sex, height and their body weight at that time. The observed total body potassium was 2298 ± 119 mmol compared with the expected value of 2545 ± 113 mmol. The deficit of total body potassium at 247 ± 65 mmol was highly significant (P < 0·0005, Student’s paired t-test). In Fig. 1, we have compared the total body potassium measured when the patients first presented with those measured when they had fully recovered. Full recovery was assumed to have occurred once the patient had remained clinically euthyroid with normal blood hormone values for at least 5 months. In all patients a rise of body potassium was found to take place on recovery although there was considerable variability. The average gain of potassium was 489 ± 51 mmol amounting to 22·8 ± 2·8% rise from the initial level. The greatest gain was 1146 mmol (corresponding to a rise of nearly 50%) that was observed in a patient who estimated that he had lost about 18 kg of body weight during his illness.

The amount of body potassium regained correlated well with the amount of body weight gain that occurred with recovery (Fig. 2). Moreover the values of total body potassium after full recovery (2787 ± 124 mmol) agreed well with those expected for the patients on the basis of their weight (recovered), height, age and sex (2690 ± 123 mmol). The latter value is greater than the expected value estimated when the patients first presented as body weight had also increased with recovery. The reversal of the body weight loss with recovery could only be approximately assessed as we had only the patients'
Body potassium and thyroid

313

FIG. 1. Change of total body potassium on complete recovery to euthyroidism. The recovered values were measurements obtained after normal blood hormone values had been established for at least 5 months. Even so the agreement between their estimate of their premorbid weight (67 ± 2·4 kg) and that which we obtained at the 5 month recovery measurement (68 ± 2·3 kg) was good. We concluded therefore that the gain of total body potassium with recovery and the increase of body weight reflected closely the loss of total body potassium and body weight that occurred as hyperthyroidism developed.

One patient gained a small amount of weight (about 2 kg) during the period of developing hyperthyroidism. Subsequently, when he became euthyroid, his weight rose by a further 5 kg and, in addition, the total body potassium recovered from 4172 mmol when he was hyperthyroid to 4593 mmol when he had fully recovered. In this individual, therefore, although he had not lost weight with the development of hyperthyroidism, he must have had an appreciable reduction of body potassium.

For each individual we calculated the change of total body potassium in relation to weight change, expressing this as mmol of potassium per kg of weight change (Table 1). If we assume, and evidence has been noted above in support of the assumption, that the loss of body potassium and body weight occurring when the patient was hyperthyroid was similar to that gained during recovery, then our present measurements can be compared with those obtained from obese, euthyroid patients losing weight because of dietary restriction. We have previously reported (Edmonds, Jasani & Smith, 1975) changes in total body potassium observed during dietary treatment of patients who were obese but otherwise healthy. These patients were treated only by dietary restriction, 12 of them for an initial period of 6 weeks in hospital on a diet of energy value 1·26 MJ daily. Five of the 12 had measurements at intervals for the subsequent 40 weeks while on a more liberal diet of 3·5–5 MJ daily. The comparison shows that the potassium loss per kg of weight loss was considerably greater in the hyperthyroid individuals (Table 1). It seems very unlikely that this difference was simply due to the obese individuals having a greater potential energy store in fat. For three of our hyperthyroid patients were appreciably obese before their illness began and yet these too lost body potassium (Table 1). The concentration of potassium lost was on average greater in the obese hyperthyroid than in the remaining hyperthyroid patients but the difference was not statistically significant.

The rate at which the weight was lost did not appear to be responsible for the difference between the effects of hyperthyroidism and dietary weight loss (Table 1). The rate was greatest in the obese patients during severe dietary restriction although loss of body fluid at this stage exaggerates the apparent tissue wasting. But even during the longer period of less severe restriction, the rate of weight loss was not
TABLE 1. Change of total body potassium related to body weight change in hyperthyroid patients and obese individuals undergoing dietary weight reduction

Results are means ± SEM. Euthyroid-obese on diet: *1-26 MJ/day for 6 weeks and 3-5-5 MJ/day for 40 weeks: data from Edmonds, Jasani & Smith (1975).

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>Initial weight (kg)</th>
<th>Estimated rate of wt. loss (kg/week)</th>
<th>Potassium change (mmol/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroid</td>
<td>20</td>
<td>65</td>
<td>0.44 ± 0.04</td>
<td>69 ± 9</td>
</tr>
<tr>
<td>Hyperthyroid-obese</td>
<td>3</td>
<td>83</td>
<td>0.55 ± 0.18</td>
<td>87 ± 7</td>
</tr>
<tr>
<td>*Euthyroid-obese on diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-26 MJ/day</td>
<td>12</td>
<td>93</td>
<td>1.4 ± 0.05</td>
<td>14 ± 4</td>
</tr>
<tr>
<td>(88-121)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5-5 MJ/day</td>
<td>5</td>
<td>88</td>
<td>0.38 ± 0.06</td>
<td>&lt;2</td>
</tr>
<tr>
<td>(81-93)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE 2. Recovery of body weight and total body potassium in six hyperthyroid patients rendered euthyroid by high-dose carbimazole treatment

Results are means ± SEM. *Comparisons of values at 10 and 28 weeks: body wt. significantly greater at 28 weeks (P < 0.01: Student's paired t-test); total body potassium, not significantly different.

<table>
<thead>
<tr>
<th>Week</th>
<th>Body wt. (kg)</th>
<th>Total body potassium (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>58.2 ± 5.5</td>
<td>2278 ± 237</td>
</tr>
<tr>
<td>10</td>
<td>62.2 ± 5.7</td>
<td>2716 ± 297</td>
</tr>
<tr>
<td>28</td>
<td>65.0 ± 6.1*</td>
<td>2789 ± 325*</td>
</tr>
</tbody>
</table>

significantly different from that of the hyperthyroid patients. Estimates of the rate of weight loss in the hyperthyroid patients was based on their history and must therefore be treated with some caution; however, one patient, a 47-year-old engineer, had kept a record of his declining weight and this showed a fairly steady loss at an average rate of 0.56 kg/week. He had a substantial reduction of total body potassium with a ratio of 76 mmol of potassium/kg of weight loss.

Rate of recovery of body weight and total body potassium in six carbimazole treated patients.

These patients were treated with full doses of carbimazole so that hyperthyroidism was rapidly controlled; total body potassium and other measurements were carried out at about 10 weeks and at about 26 weeks after treatment was commenced (Table 2). Blood T3 concentration was within or very close to the normal range at the time of the 10 week measurement. The values obtained at the 28 week measurement were taken as the fully recovered values for body weight and body potassium since the patients had, by then, been euthyroid for several months and the values agreed reasonably well with those expected for normal euthyroid individuals of similar height, age and sex. On this basis, total body potassium was found to be fully restored by about 10 weeks after the initiation of treatment although body weight had not fully recovered (Table 2). When, in these patients, the increase of body potassium was expressed in relation to the increase of body weight, the potassium gain per kg of weight gain was found to be considerably higher during the first 10 weeks of recovery (122 ± 32 mmol/kg) than subsequently (25 ± 28 mmol/kg). All but one of these patients had marked muscular weakness initially that had recovered by the time of the measurement at 10 weeks. Although the mean value of potassium gain per kg during the first 10 weeks is appreciably higher than that usually assigned to skeletal muscle, about 92 mmol/kg (Widdowson & Dickerson, 1964), the difference is not statistically significant.

Muscular weakness and total body potassium. It has been previously reported (Ramsay, 1966) that muscular weakness recovers within 2–3 months of commencing effective therapy and, as noted above in our patients, muscular power recovered and restoration of total body potassium occurred within this time. This suggested that the loss of body potassium might be an important factor in production of muscular weakness. The relationship between the degree of weakness and loss of body potassium (taken as equivalent to the gain of potassium on recovery) was therefore examined. With total body potassium before treatment expressed as a proportion of the final recovered value, the increase of potassium loss associated with increasing weakness was evident. Thus patients with no muscular weakness (grade 0) had a body potassium content averaging 89 ± 1.8% (n = 11) of the recovered
Body potassium and thyroid

value. The corresponding values for grades 1 and 2 were 80 ± 2·6% (n = 4) and 76 ± 2·5% (n = 8) respectively, significantly (P < 0·01) lower than for grade 0. When the potassium loss was related to body weight loss, whereas grades 0 and 1 were in similar proportion (44 ± 8·2 and 45 ± 9·1 mmol/kg respectively), grade 2 showed at 90 ± 11 mmol/kg, a significantly (P < 0·005) higher proportion of potassium loss.

Comparison of hyperthyroid patients with athyreotic patients treated with L-thyroxine

Relationship of total body potassium loss to the blood levels of T₄ and T₃. The object of this comparison was to determine whether elevation of plasma T₄ or T₃ or both was associated with the change of body potassium. The 19 athyreotic individuals who had been treated some years before by surgery and ¹³¹I comprised a group of patients who had elevated plasma T₄ levels yet normal T₃ levels. They had been taking L-thyroxine orally for several years at a rather higher dose than is customary for routine replacement to ensure full thyrotrophic hormone (TSH) suppression (Edmonds, 1979). All these patients were considered euthyroid on clinical assessment (Wayne scale) but had abnormally high concentrations of T₄ in the blood although T₃ remained within the normal range (2·1 ± 0·1 nmol/l). The T₃ in these patients is derived from conversion of T₄ into T₃ in the peripheral tissues (Bernal & Refetoff, 1977). The body weight of the patients averaged 64·2 ± 3·4 kg, which was close to that expected, 64·7 ± 1·7 kg (difference N.S., Student’s paired t-test) on the basis of the age, sex and height (Society of Actuaries Tables, 1959). Moreover their total body potassium values were also not significantly different (Student’s paired t-test) from those expected from their age, sex, weight and height, averaging 2511 ± 141 mmol compared with the expected 2412 ± 115 mmol. The individual values together with those from the recovered hyperthyroid patients are shown in Fig. 3, which indicates the range of T₄ measurements. These results clearly show that no significant correlation between the blood level of T₄ and total body potassium was demonstrable (r = 0·14, N.S.). Thus there was no indication that body weight or body potassium of these patients was influenced by the excess of T₄.

The data for examining the effect of T₃ were obtained from the hyperthyroid patients at presentation and from all the patients who subsequently, during treatment, showed relatively stable serum T₃ concentrations (that is, not varying by more than ±10%) over at least 3 months of observation. As in some of the hyperthyroid patients treated with ¹³¹I, recovery was slow, T₃ concentrations remained moderately elevated for some time. The plasma T₄ level was also usually elevated to some extent in these patients but, as shown above, variations in plasma T₄ did not affect the total body
Fig. 4. Plasma level of T₃ in relation to total body potassium, presented as in Fig. 3. The expected total body potassium of each patient was estimated on the basis of age, sex, height and body weight, the latter being the patient’s weight when fully recovered. The data of the figure were obtained from hyperthyroid patients (○) before treatment and during treatment, provided their condition was stable, and from athyreotic patients taking L-thyroxine (●). The interrupted lines indicate the 95% confidence limits.

Discussion

The present findings confirm previous reports based on measurement of exchangeable potassium, showing that hyperthyroid patients gain a considerable amount of body potassium when they are treated. We have shown that this increase in body potassium is a correction of the loss that occurred during the development of hyperthyroidism. The loss of body potassium varied between patients presumably reflecting the severity of the disease, its duration and possibly differences in dietary intake. Whereas the loss of body weight in the hyperthyroid patients was associated with considerable potassium loss, a similar weight loss due to dietary restriction in obese patients caused little reduction in body potassium. That this difference was not simply due to the large fat store in the obese was shown by our results in several, initially obese, hyperthyroid patients who had also considerable reduction of body potassium.

If it is assumed that the potassium concentration in the tissues of normal and hyperthyroid individuals was similar, then as the average amount of potassium lost was 71 mmol/kg of weight loss in our 23 hyperthyroid patients, and as the potassium concentration in skeletal muscle is about 92 mmol/kg (Widdowson & Dickerson, 1964), then on average nearly 80% of the body weight reduction in the hyperthyroid patients was due to loss of lean tissue. The rest of the weight loss was probably from reduction of body fluid (Savoie & Jungers, 1965) and fat.

The assumption that the potassium concentration in lean tissues was unaltered may not be entirely justified for all patients. There is evidence from muscle biopsy and from body composition studies that a few hyperthyroid patients had appreciable reduction of intracellular potassium.
Body potassium and thyroid

(Satoyoshi, Murakami, Kowa, Kinoshita, Noguchi, Hoshini, Nishiyama & Ho, 1963; Savoie & Jungers, 1965). Some of our patients, particularly those with severe muscle weakness, showed a markedly high gain of potassium in relation to weight gain during the early recovery period with a potassium concentration per kg regained exceeding that in skeletal muscle. Some hyperthyroid patients may have an intracellular potassium depletion as well as loss of lean tissue, but our data do not provide unequivocal evidence for this.

Nearly 70% of the total body potassium of normal man is located in muscle (Black, 1972; Pierson, Lin & Phillips, 1974) and probably therefore the reduction of body potassium largely reflected loss of muscle potassium. Reduced muscle bulk is often clinically evident and muscle weakness is a frequent symptom. It occurred in some degree in about half of our hyperthyroid patients and was moderately severe in eight of the 23. Muscular weakness was not found in any of the thyroxine treated patients. Ramsay (1966) observed that recovery of muscle strength took place within 2 months of beginning effective treatment and our findings were similar: this period coincided with the recovery of body potassium. A more recent study by Wiles, Young, Jones & Edwards (1979) showed that, in four of five hyperthyroid patients with measurable muscle weakness, the turnover rate of ATP was faster than normal. Thus energy provision was unlikely to be a limiting factor and they concluded that muscle-fibre wasting together with increased relaxation rate was probably responsible for the weakness. Our findings are consistent with this view as the greater loss of body potassium in the weaker patients probably largely reflects a greater loss of muscle mass. However, as discussed above, intracellular potassium depletion was possibly also present and this could contribute to the change in muscle relaxation time.

Our studies indicate that T₄ alone has no effect on total body potassium. The reduction of total body potassium appeared, however, to be linearly related to the blood T₃ level over a wide range, findings which agree with the view that T₃ is responsible for the characteristic effects of thyroid hormones at cellular level. They are also consistent with the intracellular distribution of the hormones. Thus specific intracellular receptors for T₃ are present in a variety of cell types and, although both T₃ and T₄ bind to these receptors, in the case of muscle considerable T₃ but very little T₄ is located intracellularly (Nicoloff, 1978). The considerable effect of hyperthyroidism on body potassium presumably reflects some specific effect(s) of T₃ on muscle metabolism. In contrast, weight loss induced by moderate dietary restriction produces very little change in body potassium. It is probably significant in this respect that during treatment of obesity by dietary restriction, blood T₃ levels fall (Cavalieri & Rapoport, 1977) whereas administration of T₃ to preserve the blood levels results in excessive protein catabolism (Gardner, Kaplan, Stanley & Utiger, 1979). Storage fat appears to be much less influenced by T₃ than are the lean tissues, probably indicating that there is no direct effect on fat cells. On this hypothesis, it would be predicted that, provided food intake is adequate, fat storage mass could increase in hyperthyroidism yet total body potassium be reduced. The observations on one of our patients who gained weight supported this view.

Acknowledgments

We gratefully acknowledge the Clinical Chemistry and Radioisotopes Laboratory of Northwick Park hospital for the hormone assays and Miss Jennifer Mackenzie for technical assistance.

References


Munro, D.S., Renschler, H. & Wilson, G.M. (1958) Exchangeable potassium and sodium in hyperthyroidism and hypothyroidism. Metabolism, 7, 124–133.


