Potassium metabolism in patients with rheumatoid arthritis

Effects of treatment with depot tetracosactrin, spironolactone, and oral supplements of potassium chloride

GEORGE NUKI, KEITH BODDY, ALASTAIR C. KENNEDY, PRISCILLA KING, ANNE M. DUNCAN, AND W. WATSON BUCHANAN

From the Centre for Rheumatic Diseases and University Department of Medicine, and Chemical Pathology, Royal Infirmary, Glasgow, and Scottish Universities Research and Reactor Centre, East Kilbride, Scotland

Nuki, G., Boddy, K., Kennedy, A. C., King, P., Duncan, A. M., and Buchanan, W. W. (1975). Annals of the Rheumatic Diseases, 34, 506–514. Potassium metabolism in patients with rheumatoid arthritis. Effects of treatment with depot tetracosactrin, spironolactone, and oral supplements of potassium chloride. (1) Plasma and urine electrolytes and whole body potassium have been measured before and after a 2-week administration of depot tetracosactrin 0.5 mg on alternate days to eight patients with rheumatoid arthritis (RA). The effects of adding supplements of potassium chloride (48 mmol/d) and spironolactone 200 mg daily have been investigated. (2) Acute changes in red blood cell water and potassium content, plasma electrolyte concentration, and plasma 11-hydroxycorticosteroid levels were measured for 48 hours after a single intramuscular injection of 0.5 mg depot tetracosactrin in six patients with RA. (3) The measured total body potassium was significantly less than that predicted from the height, weight, and age formula in patients with RA. (4) Treatment with depot tetracosactrin resulted in an acute fall in plasma and red cell potassium independent of external potassium loss. (5) Two weeks of treatment with depot tetracosactrin resulted in hypokalaemia and a rise in plasma sodium and bicarbonate. There were no associated electrocardiogram changes or a rise in blood pressure. (6) Neither oral potassium supplements nor spironolactone altered total body potassium. (7) The significance of the findings and the physiological mechanisms underlying them are discussed.

The relationship between plasma potassium and corticosteroid as well as corticotrophin therapy has been studied by many workers (Goodman and Gillman, 1970; Havard, 1970; Kyle, Canary, Werdin, and Clive, 1966; Ernest, 1967). Similarly, primary hyperaldosteronism has been investigated and characteristically shows low total exchangeable potassium values (Conn, Cohen, Rovner, and Nesbit, 1965) and reduced muscle biopsy potassium content (Conn and Lonis, 1956; Milne, Muehreke, and Aird, 1957).

Recently clinicopharmacological studies in patients with rheumatoid arthritis (RA) treated with depot tetracosactrin, a synthetic polypeptide containing the N-terminal 24 of the 39 amino acids found in naturally occurring corticotrophin absorbed onto a zinc phosphate complex (depot Synacthen—CIBA 42, 915 Ma) showed that significant hypokalaemia occurred with 0.5 mg on alternate days or with higher doses despite oral potassium supplements of 48 mmol/d (Nuki, Jasani, Downie, Whaley, Dick, Williamson, Paterson, Boyle, and Buchanan, 1970).

We report the results of measurements of total body potassium, red blood cell potassium, and plasma electrolytes in patients with RA before and after treatment with this preparation, and data on total body potassium and plasma electrolytes after the addition of spironolactone or potassium supplements.

Accepted for publication April 30, 1975.
Correspondence to: Dr. Alastair C. Kennedy, Centre for Rheumatic Diseases, 35 Baird Street, Glasgow G4 0EH.
Materials and methods

BALANCE STUDIES

Patients

Eight patients with 'definite' or 'classical' RA (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) participated (Table I). All were inpatients at the Centre for Rheumatic Diseases with active joint disease which had not responded adequately to hospitalization and optimum doses of nonsteroidal analgesic anti-inflammatory drugs.

Study protocol

Electrolyte levels were studied for 30 days. After a 4-day base-line period each patient was given intramuscular depot tetracosactrin 0·5 mg on alternate days from day 5 to day 29. Three patients (Cases 6, 7, and 8) were given oral spironolactone (Aldactone A, Searle) 50 mg t.i.d. from day 18 to day 30 of the study, while the other five (Cases 1–5) were given oral potassium chloride supplements (Slow K, CIBA), 2 tabs t.i.d. = 48 mmol/d over the same period.

Patients were weighed daily between 9:00 and 11:00 a.m. and were not confined to bed after resting recumbent blood pressure had been recorded each morning. They were instructed how to collect 24-hour urine specimens (8.00 a.m.–8.00 a.m.) in labelled plastic containers without preservative, and collections were continued throughout the 30 days of the study.

Diet

Patients were allowed a diet with alternative choices, carefully weighed and calculated to contain nominally 65 mmol potassium/d and approximately 100–200 mmol sodium/d using the tables of McCance and Widdowson (1960). All food eaten was meticulously recorded and any food rejects were made up at the end of each day with food or fruit juice containing equivalent amounts of potassium. Certain items such as coffee, known to be very variable in potassium content, were excluded from the diet and no added salt was permitted, but water intake was not restricted.

Sodium and potassium analyses were carried out by direct flame photometry on eight homogenized specimen diets after extraction with boiling deionized water and filtration. This method has been shown to give optimum electrolyte extraction when compared with wet ashing procedures (R. Rae and J. Shakeshaft, personal communication, 1971). The mean (± SEM) dietary potassium was 51·2 ± 1·8 mmol/d (range 47–57) and mean sodium was 174·6 ± 13·9 mmol/d (range 138–173).

Electrolyte estimations

Venous blood samples were taken from an uncuffed arm into heparinized tubes at 8:00 a.m. each morning for estimation of plasma sodium, potassium, chloride, and CO₂ content. Plasma electrolytes were estimated by the standard Technicon Autoanlyser systems. Urine sodium and potassium were measured by flame photometry (Instrumentation Laboratories Inc., Flame Photometer).

Total body potassium

Total body potassium was measured in each subject by use of the MERLIN mobile whole-body radioactivity counter (Boddy, 1967). The counting rate from the naturally occurring radioisotope K⁺, which is a constant fraction of the total body potassium, was expressed as mmol potassium using the calibration equation derived previously (Boddy, King, Tothill, and Strong, 1971). Predicted values for the normal body potassium of each subject were derived from (1) the height and age, and (2) from the height, weight, and age of the subject (Boddy, King, Hume, and Weyers, 1972).

Electrocardiograms

Standard 12-lead ECGs were performed on each patient on days 4, 17, and 28 with a Transrite III machine (Cambridge Instruments Ltd.). Heart rate, Q-T interval, and Q-Tc were calculated with a Freibrite ECGT rule (Catalog No. 79–1, The Birtcher Corporation).

Red blood cell studies

A separate group of six patients with classical RA were studied. None was receiving corticosteroid or diuretic drug therapy, and nonsteroidal anti-inflammatory drugs were discontinued during the 48 hours of study. Venous blood was taken from an uncuffed arm into two heparinized and one sequestrinated tube before, and at 30 minutes, at 4, 8, 24, and 48 hours after a single intramuscular injection of 0·5 mg depot tetracosactrin. Plasma potassium and whole blood potassium were estimated by direct flame

Table I Details of patients with rheumatoid arthritis under study

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Lean body mass* (kg)</th>
<th>TBK measured (mmol)</th>
<th>TBK (1) (mmol)</th>
<th>TBK (2) (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>F</td>
<td>154·9</td>
<td>50·4</td>
<td>36·3</td>
<td>2263</td>
<td>2049</td>
<td>2102</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>M</td>
<td>167·6</td>
<td>52·8</td>
<td>44·7</td>
<td>2455</td>
<td>2706</td>
<td>3026</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>F</td>
<td>170·2</td>
<td>56·1</td>
<td>44·5</td>
<td>2340</td>
<td>2706</td>
<td>2818</td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>F</td>
<td>158·8</td>
<td>59·3</td>
<td>40·7</td>
<td>2076</td>
<td>2248</td>
<td>2220</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>F</td>
<td>168·9</td>
<td>66·5</td>
<td>47·0</td>
<td>2579</td>
<td>2560</td>
<td>25422</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>F</td>
<td>151·1</td>
<td>39·4</td>
<td>31·5</td>
<td>1434</td>
<td>1831</td>
<td>1997</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>F</td>
<td>152·4</td>
<td>61·2</td>
<td>38·5</td>
<td>1982</td>
<td>2010</td>
<td>1895</td>
</tr>
<tr>
<td>8</td>
<td>53</td>
<td>F</td>
<td>161·3</td>
<td>91·7</td>
<td>51·3</td>
<td>2439</td>
<td>2765</td>
<td>2286</td>
</tr>
</tbody>
</table>

* Lean body mass calculated from Hume and Weyers's (1971) formula.
TBK (total body potassium) (1) estimated from patient's height, weight, and age.
TBK (2) estimated from patient's height and age.
photometry (EEL Flame Photometer) after diluting whole blood samples 1:10 to haemolyse, and bringing the whole blood sodium concentration to approximately 140 mmol. Haematocrit (PCV, packed cell volume) was measured on the sequestirated sample using a standard microhaematocrit method. Red blood cell potassium concentration (RBCK) was calculated according to the indirect method of Boyd (1970).

\[
RBCK = \frac{WBK - (100 - PCV \times PK)}{100} \times \frac{PCV}{PK}
\]

where \(WBK\) = whole blood potassium (mmol/l), \(PK\) = plasma potassium (mmol/l).

No correction was made for trapped plasma. Red blood cell water was measured by drying aliquots of packed red cells to constant weight. In our laboratory the reproducibility of this method between duplicate samples has been found to be ±5 mmol/l and the normal range (mean ± 2 SD) in patients with RA not receiving diuretic or corticosteroid therapy is 86-97 mmol/l. Red blood cell water content was estimated by heating aliquots of packed red cells in a low temperature oven (90°C) to constant weight. Red blood cell water content was expressed as g water/g dry weight.

Results

ELECTROLYTES

The mean (SEM) of the daily plasma sodium, potassium, CO₂ concentrations, and urine volume, potassium, sodium, and weight for the first 18 days of the study are shown in Fig. 1. After starting treatment with depot tetracosactrin 0-5 mg on alternate days there was a significant fall in plasma potassium (t = 6.36; \(P < 0.001\)) and a significant rise in plasma sodium and CO₂ (Fig. 1). Plasma chloride levels did not change. There was a mean weight rise of 2 kg despite marked increases in urine volume. A significant fall in urine sodium excretion immediately after starting depot tetracosactrin was followed by the characteristic 'escape phenomenon' (Mattingly, 1968) 4 to 5 days later. There was a significant increase in mean urine potassium excretion on the day of each injection with a decrease on the intervening days.

TOTAL BODY POTASSIUM (TBK)

TBK expressed in mmol/kg body weight and mmol/kg lean body mass is shown in Table I, together with values predicted from the patient's height, weight, and age (Boddy and others, 1972). The pretreatment measured values are lower than those predicted with a mean difference of 163 mmol K (11%). The changes in TBK after 2 weeks of therapy with depot tetracosactrin 0-5 mg on alternate days are shown in Table II. There was no significant change (\(P > 0.05\)) in the measured TBK.

ADDITION OF ORAL POTASSIUM SUPPLEMENTS

Mean values for plasma sodium, potassium, and CO₂ for the five patients who received oral supplements of potassium chloride are shown in Fig. 2, together with mean daily weight, urine volume, urinary sodium and potassium. The fall in plasma potassium induced by therapy with depot tetracosactrin was initially reversed after adding oral potassium supplements, the rise in plasma potassium being accompanied by a fall in plasma sodium and CO₂. However, at the end of the investigation the plasma potassium remained low at 3.1 mmol/l (Fig. 2). Mean urine potassium excretion rose from 46 mmol/24 h to 83 mmol/24 h after adding potassium supplements. There was no significant change in measured TBK (\(P > 0.05\)), as shown in Table II.

The mean daily urine volume increased from 1627 ml to 1908 ml and this was associated with a mean increase in urine sodium excretion of 54.2 mmol/24 h and mean weight gain of 1.3 kg/patient over 13 days.

ADDITION OF SPIRONOLACTONE

Mean daily plasma sodium, potassium, and CO₂ concentration for the three patients who received supplements of spironolactone are shown in Fig. 3, together with mean daily weight, urine volume, urinary sodium and potassium excretion. The addition of spironolactone 150 mg/d did not reverse the fall in plasma potassium induced by depot tetracosactrin, mean plasma potassium level being 2.9 mmol/l for
Table II  Total body potassium in patients with rheumatoid arthritis before, during, and after treatment with depot tetracosactrin

<table>
<thead>
<tr>
<th>Case no.</th>
<th>On Slow K</th>
<th>A. Pretreatment (mmol)</th>
<th>B. After first 2 weeks of treatment (mmol)</th>
<th>C. After second 2 weeks of treatment (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2263</td>
<td>2176</td>
<td>2242</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2340</td>
<td>2347</td>
<td>2368</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2076</td>
<td>2071</td>
<td>2245</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2578</td>
<td>2375</td>
<td>2670</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1434</td>
<td>1442</td>
<td>1447</td>
<td></td>
</tr>
</tbody>
</table>

Comparing group A with B: $t = 1.37$ NS
B with C: $t = 2.06$ NS
A with C: $t = 1.67$ NS

<table>
<thead>
<tr>
<th>Case no.</th>
<th>On spironolactone</th>
<th>A. Pretreatment (mmol)</th>
<th>B. After first 2 weeks of treatment (mmol)</th>
<th>C. After second 2 weeks of treatment (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2455</td>
<td>2493</td>
<td>2416</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1982</td>
<td>1907</td>
<td>1964</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2439</td>
<td>2415</td>
<td>2173</td>
<td></td>
</tr>
</tbody>
</table>

Comparing group A with B: $t = 0.51$ NS
B with C: $t = 1.0$ NS
A with C: $t = 1.36$ NS

FIG. 2  Mean daily plasma and urine electrolytes, urine volume, and weight in 5 RA patients before and during treatment with depot tetracosactrin 0.5 mg on alternate days, and during the addition of oral supplements of potassium chloride (48 mEq/d)

FIG. 3  Mean daily plasma and urine electrolytes, urine volume, and weight in 3 RA patients before and during treatment with depot tetracosactrin 0.5 mg on alternate days and during the addition of spironolactone 150 mg/d
Table III  Blood pressure and ECG conductivity before and after treatment with depot tetracosactrin and after addition of oral potassium (48 mmol/d or spironolactone (150 mg/d)

<table>
<thead>
<tr>
<th>ECG ((QT/QTc) x 100)</th>
<th>Blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case no.</td>
<td>Control</td>
</tr>
<tr>
<td>1</td>
<td>102</td>
</tr>
<tr>
<td>2</td>
<td>108</td>
</tr>
<tr>
<td>3</td>
<td>106</td>
</tr>
<tr>
<td>4</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>114</td>
</tr>
<tr>
<td>7</td>
<td>106</td>
</tr>
<tr>
<td>8</td>
<td>109</td>
</tr>
<tr>
<td>Mean</td>
<td>101-6</td>
</tr>
<tr>
<td>Mean±SEM</td>
<td>104-6(±2-3)</td>
</tr>
</tbody>
</table>

the 13 days of therapy. During this time plasma sodium and CO2 remained slightly raised at mean levels of 145 and 27-1 mmol/l, respectively, but plasma chloride was not altered. Urine potassium excretion remained unchanged but there was an increase in mean urine sodium excretion of 76-9 mmol/24h and mean urine volume increased from 1579 to 2181 ml/24 h over the treatment period. This was associated with a mean weight loss of 0·8 kg/patient over 13 days. (There was no significant change in TBK: P > 0·05; Table II.)

Blood Pressure and ECG

Table III shows blood pressure and ECG conductivity (QT/QTc x 100) for each patient before and after 13 days of therapy with depot tetracosactrin and after the addition of oral supplements of potassium chloride or spironolactone. Neither blood pressure nor QT interval were significantly increased. Gross ECG signs associated with hypokalaemia were not detected and the QT interval was only prolonged beyond the normal range (QTc ±10%) in one patient (Case 6) in whom it appeared to be unaffected by the therapy and independent of potassium status.

Red Blood Cell Studies

Mean (± SEM) plasma 11-hydroxycorticosteroids (11-OHCS), sodium, and potassium, red cell water, and potassium and packed cell volume at 0, 0·5, 4, 8, 24, and 48 hours after a single intramuscular injection of 0·5 mg depot tetracosactrin are shown in Fig. 4. The plasma 11-OHCS 'profile' after a single intramuscular injection of 0·5 mg depot tetracosactrin was similar to that previously described (Nelson, Neill, Montgomery, MacKay, Sheridan, and Weaver, 1968; El Shaboury, 1968; Nuki and others, 1970). Plasma 11-OHCS levels rose significantly at 30 minutes, were maximal after 8 hours and still significantly raised after 24 but not after 48 hours.

Plasma sodium fell transiently 4 and 8 hours after depot tetracosactrin while significant falls in plasma potassium occurred after 24 hours and were maintained at 48 hours. Red blood cell potassium showed a significant fall as early as 30 minutes after injection. Minimal values occurred after 24 hours and red blood cell potassium was still depressed after 48 hours. There was a mean rise in red blood cell water content and a fall in PCV from 4 to 48 hours after injection but these changes were not statistically significant.
Discussion

These studies confirm our previous findings (Nuki and others, 1970) that significant falls in plasma potassium occur after short courses of intramuscular depot tetracosactrin 0.5 mg on alternate days. This fall can be seen as early as 24 hours after an injection, becomes maximal after a week of therapy, and appears to be preceded by a fall in red blood cell potassium concentration. These changes occur before any significant urinary loss of potassium has taken place and support the view that hypokalaemia induced by corticosteroids results at least in part from cellular electrolyte shifts (Roberts and Randall, 1955; Bagshawe, Curtis, and Garnett, 1965a). However, the suggestion that the fall in plasma potassium results from movement of potassium ions from the extracellular to the intracellular space (Bagshawe, Curtis and Garnett, 1965b) is not borne out by our data on red blood cell potassium (RBCK) concentration. The interpretation of the red blood cell studies is, however, subject to certain reservations. The use of an indirect method of measurement of RBCK concentration and the omission of any correction for trapped plasma are likely to reduce the accuracy of RBCK water and electrolyte estimations (Bellin, Knight, Munro-Faure, and Anderson, 1966), although the trapping error is likely to be small in the case of potassium, a predominantly intracellular cation. Notwithstanding these strictures, it seems that the acute changes in RBCK and plasma potassium together with the changes in plasma sodium are better explained by an initial expansion of both extra and intracellular fluid spaces than by a shift of potassium ions into the intracellular compartment. The study further shows that after starting treatment with depot tetracosactrin there was a transient reduction in urine volume despite overall weight gain. The ‘escape’ from the sodium retaining effect of adrenocortical stimulation is thought to result from a reduction in functional proximal tubular sodium reabsorption induced by expansion of the extracellular fluid which is independent of glomerular filtration rate and mineralocorticoid activity (Rovner, Conn, Knopf, Cohen, and Hsueh, 1965; Davis, Johnston, Howards, and Wright, 1967). Glucocorticoids are, however, well known to increase glomerular filtration rate directly (Dingham, Finkenstaedt, Laidlaw, Renold, Jenkins, Merrill, and Thorn, 1958) and to increase water diuresis (Raisz, McNeely, Saxon, and Rosenbaum, 1957) by an action on the diluting segment of the nephron (Beck and McGarry, 1962). Studying the effects of cortisone and ACTH in patients with RA, Sprague, Power, Mason, Albert, Mathieson, Hench, Kendall, Slocomb, and Polley (1950) found that hypokalaemia and extracellular retention of salt and water were accompanied by depletion of intracellular potassium as a consequence of protein catabolism. This group also suggested that there was no effect on water turnover; however, polydipsia as well as polyuria can be produced experimentally in animals (Scoggins, Coughlan, Denton, Farr, McDougall, Oddie, and Schulkes, 1974), possibly as a result of a primary increase in thirst induced by osmolar imbalance (Green, Saunders, Van Arman, Calvin, and Sturtevant, 1952) as well as direct effects on the kidney. Urine potassium loss continued, however, even when protein catabolism was inhibited by testosterone.

The alkalosis that follows ACTH or corticosteroid administration is believed to be mainly a consequence of hydrogen ion exchange after depletion of intracellular potassium and renal tubular reabsorption of bicarbonate in exchange for potassium (Roberts and Randall, 1955). It has been shown, however, that this alkalosis can occur without potassium depletion (Sprague and others, 1950; Moore, Boling, Ditmore, Sicular, Teterick, Ellison, Hoye, and Ball, 1955; Bagshawe and others, 1965a).

It is of interest that measurements of whole body potassium in the eight patients with RA before starting treatment with depot tetracosactrin were significantly lower than those predicted from estimates of height, weight, and age. One reason why total body potassium in patients having RA with marked wasting of muscles might be less than that predicted from height, weight, and age is that lean body mass does not in fact have a constant composition or potassium content. Cadaveric measurements have shown that skeletal muscle contains significantly more potassium per gram of tissue than bone, skin, tendon, or fat (Forbes and Hursh, 1963), and total body potassium has been found to be reduced in patients with neuromuscular disorders and muscle wasting (Bladh, Cassen, and Lederer, 1963; Kossmann, Peterson, and Andrews, 1965; Delwaide, 1973). Conversely, ‘ultra fit’ athletes have a higher total body potassium than would be predicted (Boddy, Hume, King, Weyers, and Rowan, 1974), suggesting that differences between measured and predicted total body potassium may be associated with the degree of development of the skeletal musculature. In RA patients the situation may resemble that found in malnourished infants where reduction in total body potassium is also associated with expansion of the extracellular fluid space (Alleyne 1968). The physiological significance of low total potassium in RA patients is uncertain, but certainly seems to demand further study.

As in previous short-term studies, significant rises in blood pressure were not observed with depot tetracosactrin 0.5 mg on alternate days, although hypertension is a significant side effect of long-term therapy with depot tetracosactrin (G. Nuki, A. C. Kennedy, and W. W. Buchanan, unpublished, 1974) and ACTH (Savage, Copeman, Chapman, Wells, and Treadwell, 1962).
Hypokalaemia occurring after tetracosactrin therapy was not associated with ECG abnormalities in this study, although such changes have been noted in other patients (Nuki and others, 1970). Despite scrupulous double checking of daily diets, the measured potassium content of the 8 sample diets analysed was consistently less than that calculated from tables (McCance and Widdowson, 1960) with 95% confidence limits of ± 10.2 mmol potassium.

The steroid hormone or hormones responsible for these fluid and electrolyte changes after treatment with depot tetracosactrin require some consideration. Tetracosactrin in doses as small as 3 µg/h has been shown to elicit a maximal rise in plasma 11-OHCS (Landon, James, Cryer, Wynn, and Frankland, 1964). Injection of 0.5 mg depot tetracosactrin results in a maximal rise in 11-OHCS which is similar to that induced by 40 units of ACTH gel (Nelson and others, 1968; El Shaboury, 1968) but the adrenocortical stimulation is more prolonged. Maximal stimulation of cortisol and corticosterone can be obtained with a dose of 1250 µg, but the threshold for stimulation of aldosterone is much higher (Fraser, Brown, Chinn, Lever, and Robertson, 1969). In pharmacological doses, however, aldosterone secretion is markedly increased (Arguelles, Chekkerdemian, Ricca, and Cardinali, 1964; Ganong, Biglieri, and Mulrow, 1966) but only transiently so (Tucci, Espiner, Jagger, Pauk, and Lauler, 1967; Newton and Laragh, 1968), the aldosterone secretion rate falling below control levels after 48 hours (Tucci and others, 1967). The mechanism for this fall is not clear. It may be associated with a fall in plasma renin activity (Newton and Laragh, 1968) but occurs in primary aldosteronism when the renin-angiotensin system is already maximally suppressed (Newton and Laragh, 1968). Benraad and Kloppenbourg (1970) have shown that it cannot be explained by sodium retention and the suggestion that it may be a specific consequence of increased levels of plasma cortisol (Newton and Laragh, 1968) is made unlikely by the observation that the biphasic aldosterone response to corticotrophin occurred in a patient with the adrenogenital syndrome (Bartter, Mills, Biglieri, and Delea, 1959) where no increase in cortisol occurred.

While it seems most likely that the fluid and electrolyte changes observed after a short course of depot tetracosactrin are induced by the relatively intense and prolonged stimulation of 11-OHCS which follows each injection (Besser, Butler, and Plumpton, 1967; Nelson and others, 1968; El Shaboury, 1968; Nuki and others, 1970) the possibility that significant aldosterone stimulation occurs after such an intermittent treatment regimen cannot be ruled out and warrants investigation. Long-term studies of potassium balance and whole body potassium, as well as of other elements of body composition, are in progress now to determine whether prolonged courses of treatment with tetracosactrin result in depletion of body potassium or these other elements in patients with RA.

We are grateful to Mr. R. Rae for analysis of diets, to Dr. J. J. Brown for helpful advice, and to the nursing staff of the Centre for Rheumatic Diseases for help in conducting these studies. G.N. held a CIBA Clinical Research Fellowship and A.C.K. is in receipt of an MRC Research grant. The interest and encouragement of Professor H. W. Wilson is greatly appreciated. The study was supported in part by a grant from the Hospital Endowments Research Trust, which is gratefully acknowledged.

References


BAGSHAW, K. D., CURTIS, J. R., AND GARNETT, E. S. (1965a) Lancet, 1, 18 (Effect of prolonged hydrocortisone administration on potassium metabolism)

——, ——— (1965b) ibid., 1, 342 (Hydrocortisone and plasma potassium)


Potassium metabolism in patients with rheumatoid arthritis


Ernest, I. (1967) Acta. Endocr. 54, 411 (Changes in body composition after therapeutically induced remission on 12 cases of Cushing's syndrome)


Milne, M. D., Muehrke, R. C., and Aird, I. (1957) Quart. J. Med., 26, 317 (Primary hyperaldosteronism)


Potassium metabolism in patients with rheumatoid arthritis. Effects of treatment with depot tetracosactrin, spironolactone, and oral supplements of potassium chloride.

G Nuki, K Boddy, A C Kennedy, P King, A M Duncan and W W Buchanan

Ann Rheum Dis 1975 34: 506-514
doi: 10.1136/ard.34.6.506

Updated information and services can be found at:
http://ard.bmj.com/content/34/6/506

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/