Hypokalaemic Alkalosis Following the Abuse of Purgatives

CASE REPORT

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SUMMARY

The case of a 25-year-old woman addicted to the secretive chronic abuse of purgatives is described. She developed a weight loss, thirst, an increase in skin pigmentation, hypotension, muscular weakness, amenorrhoea and oedema of the face and legs. Biochemically hypokalaemia, hypochloraemia, metabolic alkalosis and a raised secretion of renin and aldosterone were found. In spite of low total body potassium the urinary loss over a 24-hour period was higher than expected. In addition, azotaemia, hypovolaemia, increased uric acid and inability to secrete ammonia after loading with ammonium chloride were demonstrated. A renal biopsy exhibited arteriolar thickening and hyperplasia of the juxtaglomerular apparatus. The disturbed carbohydrate metabolism reverted back to normal after replacement of the depleted body potassium.


A 25-year-old woman was admitted to this hospital complaining of swelling of the eyes and legs, and amenorrhoea. She had lost 14 kg in weight during the previous 3 years. A year before admission she noticed marked oedema of the eyes and legs during the day. She complained of tiredness and increased thirst. Menarche had occurred at the age of 12 years, and regular menstrual periods followed until 2 years before admission when oligomenorrhoea developed. Sequens tablets (mestranol 80 µg and chlormadinone acetate 2 mg) were then prescribed and used until 6 months before admission. When they were discontinued, amenorrhoea had been noted.

On examination the patient was of slender build, weighed 50 kg and was 169 cm tall. There was considerable pigmentation of the skin, but not of the mucous membranes. In addition to the 1+ peripheral oedema, bilateral swelling of the parotid glands was present. The blood pressure was 100/70 mmHg in the right arm; temperature was 37°C; pulse 80/minute with a regular rhythm and the respiration rate was 16/minute.

The urine was yellow in colour, pH 6, and showed a 1+ proteinuria. No microscopic abnormalities were noted. Maximum urine concentration was to SG 1,018; creatinine clearance 66.2 ml/min (1310 ml). The IVP, renal scintogram and renogram were normal. Blood electrolytes were as follows: sodium 137, potassium 2.8, chloride 95.7, and bicarbonate 23.7 mEq/litre; blood urea 64 mg/100 ml, uric acid 7.7 mg/100 ml and, creatinine 1.5 mg/100 ml. The following were all found to be normal: serum calcium, phosphorus, liver functions (protein electrophoresis), ECG and blood count. The cholesterol was 352 mg/100 ml.

A diagnosis of glomerulonephritis of the salt-losing variety was made, and the patient treated with Navidrex K (0.25 mg cyclopenthiazide with 600 mg KCl) and Kalisol (7.5 g KCl).

After discharge from hospital, the patient was seen at the Outpatient Department. The swelling of the face and legs persisted to a lesser degree than before treatment. On direct questioning, the patient admitted that 3 years previously, owing to troublesome constipation following an appendectomy, she commenced taking Brooklax (phenolphthalein) for a period of 6 months. She had also taken Carter's Pink Pills (containing podophyllum and aloin) and cascara. She denied having taken these drugs since then. A faecal specimen contained no phenolphthalein. A diagnosis of renal disease due to purgatives was now considered. At this stage the blood urea was 77 mg/100 ml, creatinine 1.1 mg/100 ml, uric acid 7.0 mg/100 ml and the urine and blood electrolytes were normal. After 4 months at the Outpatient Department contact with the patient was temporarily lost.

RE-ADMISSION

Two years later the patient still complained of oedema of the face and legs, as well as amenorrhoea. In addition, severe tiredness and muscular weakness (at times even a paresis with achroparaesthesia) which occasionally coincided with cramps and muscular spasms, especially of the hands and facial muscles, were noted. Her weight had remained constant during the previous 5 months and she still adamantly denied the further use of purgatives or diuretics, other than those prescribed to control the oedema. These had been used irregularly at variable intervals. On specific inquiry she revealed that polyuria and nocturia, 3 - 4 times, accompanied severe thirst.

Examination

On re-examination the patient was thin and despondent. Nevertheless, she was alert in answering all questions and co-operated adequately. Her weight was 41 kg and blood pressure in the right arm 80/50 mmHg. The only difference
in the physical examination from that previously recorded was diminution of tendon reflexes and a decrease in the size of the parotid glands. Trousseau and Chvostek signs were absent and no fasciculation or muscular tremor were noticed.

The colour of the urine was yellow, pH 8, and no biochemical or microscopic abnormalities were detected. A blood count showed a haemoglobin level of 14.8 g/100 ml (100%) and a white cell count of 7 800/mm², of which 59% were polymorphs and 41% lymphocytes. The haematocrit was 41%, reticulocytes 1% and the platelet count was normal. Total serum proteins were 6.3 g/100 ml (albumin 3.6 g and globulins 2.7 g; α₁, α₂, β and γ globulins showed normal distribution with electrophoresis and no abnormal bands could be found). Serum bilirubin and alkaline phosphatase were normal. Blood urea was, however, still elevated (95 mg/100 ml) and the blood creatinine was 1.9 mg/100 ml with a uric acid of 14.5 mg/100 ml. At this stage the maximum urine concentration attained an SG of 1.010 and the creatinine clearance was 44.2 ml/min (1 600 ml). Blood electrolytes were: sodium 113.0, potassium 1.8, chloride 83.0 and bicarbonate more than 40 mEq/litre; blood calcium 10.1, phosphorus 2.1 and magnesium 2.6 mg/100 ml. In a 24-hour specimen, with a volume of 1 675 ml, the following were found: sodium 104 mEq/litre, potassium 59.6 mEq/litre, and chloride 60.5 mEq/24 hours. The phosphate was 65 mM/24 hours, and the ammonia 1.2 g/24 hours; the alpha amino acids totalled 140.7 mg/24 hours, and chromatographically the presence of glycine, glutamine, alanine, histidine, thyroxine and valine were demonstrated. Osmolality of the urine after 5 units of pitressin increased from 360 mOsm/kg to 470 mOsm/kg. Plasma cortisol was 32.5 μg/100 ml and the 17-ketosteroids and 17-ketogenic steroids were 6.2 mg and 5.6 mg/day respectively. FSH was positive at 48 units (1 250 ml/day). The ACTH stimulation test of adrenal function was normal. Sputum sodium was 13.2 and potassium 29.6 mEq/litre.

An Astrup determination confirmed the existence of a metabolic alkalosis (pH 7.53; actual pCO₂ was 46.0 mmHg, base excess +13.5 mEq/litre, standard bicarbonate 36.0, mEq/litre, and actual bicarbonate 37.4 mEq/litre). Determination of the total body potassium by means of ⁴⁰K in the whole body counter (standard chair type with a single crystal and a NAI(Tl) scintillator) showed a reduced value of 32.4 mEq/kg, compared with a control value of 43.8 mEq/kg. Thus a biochemical state of hypokalaemic alkalosis was present.

The results of an oral glucose tolerance curve done with 50 g of glucose are shown in Table I (determination done on plasma according to the ferricyanide method of Hoffman, and the insulin according to the method of Hales and Randle).

<table>
<thead>
<tr>
<th>Time</th>
<th>Blood glucose (mg/100 ml)</th>
<th>Urine (Tes-Tape)</th>
<th>Serum insulin (μU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>103</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>1/2 hour</td>
<td>228</td>
<td>0</td>
<td>195</td>
</tr>
<tr>
<td>1 hour</td>
<td>235</td>
<td>0</td>
<td>181</td>
</tr>
<tr>
<td>1 1/2 hours</td>
<td>167</td>
<td>0</td>
<td>177</td>
</tr>
<tr>
<td>2 hours</td>
<td>100</td>
<td>0</td>
<td>153</td>
</tr>
<tr>
<td>2 1/2 hours</td>
<td>80</td>
<td>0</td>
<td>88</td>
</tr>
</tbody>
</table>

The thyroxin (Biorad column method) was 7.8 μg/100 ml and the cholesterol 437 mg/100 ml. Electrocardiographic changes consistent with hypokalaemia were found (QT time 0.36 sec; QTc 0.36; T-waves depressed merging with the U-waves). X-rays of the chest showed normal lung fields with a noticeably small heart (Fig. 1). An infusion IVP showed only delayed excretion of dye.

A renal arteriogram done by the Seldinger technique demonstrated a normal vascular pattern in both kidneys and adrenals. Retrograde pyelography and cystoscopy were normal. Vaginal smears suggested adequate oestrogen secretion. An open kidney biopsy was then performed and the appearance of both kidneys and adrenals was considered to be normal.

Professor I. W. Simpson of the Pathology Department, University of Pretoria, reported that 'the surgical biopsy specimens from the kidneys show the presence of a focal chronic pyelonephritis. In the area of pyelonephritis there

Fig. 1. X-ray of the chest taken during the second admission.
is marked glomerular and tubular atrophy with interstitial fibrosis and chronic inflammatory cell infiltration.

The glomeruli outside the pyelonephritis areas appear normal but there is marked hyperplasia of the juxtaglomerular apparatus. The mean cell count in the hyperplastic juxtaglomerular and lacis cells is 32 and the mean cell count of the macula densa is 13. The juxtaglomerular complexes measure 75 - 100 micrometers in diameter.

The smaller arteries and arterioles show marked medial thickening with mild intimal hyperplasia.

The proximal tubules show coarse vacuolation which is consistent with hypokalaemia (Figs. 2 and 3).

Renin (Boucher method) and aldosterone estimations (method of Fraser and Jones) were determined after 1 litre of Macrodex was administered within 51 minutes. The values are listed in Table II. The patient was supine and the blood pressure remained constant.

The angiotensin infusion test (done with 4 ng/kg/minute given within 5 minutes) resulted in an increase in the diastolic pressure of less than 10 mmHg.

Professor O. Wrong, Department of Medicine, Royal Postgraduate Medical School, who saw the patient at this stage, suggested that the ability of the kidneys to secrete ammonia should be measured after ingestion of ammonium chloride (Table III).

### TABLE II. RENIN AND ALDOSTERONE VALUES AFTER THE INFUSION OF 1 LITRE MACRODEX

<table>
<thead>
<tr>
<th>Time</th>
<th>Renin (ng/100 ml)</th>
<th>Blood volume (litres)</th>
<th>Haematocrit</th>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>pH</th>
<th>Serum aldosterone (ng/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0800</td>
<td>5 200</td>
<td>2,2</td>
<td>41</td>
<td>14,3</td>
<td>51</td>
<td>24</td>
<td>6,9</td>
<td>54</td>
</tr>
<tr>
<td>0830</td>
<td>5 700</td>
<td>—</td>
<td>—</td>
<td>3,3</td>
<td>21</td>
<td>20</td>
<td>6,7</td>
<td>—</td>
</tr>
<tr>
<td>0900</td>
<td>5 200</td>
<td>3,42</td>
<td>26,5</td>
<td>&lt; 0,83</td>
<td>33</td>
<td>4</td>
<td>5,65</td>
<td>47</td>
</tr>
<tr>
<td>0930</td>
<td>1 080</td>
<td>—</td>
<td>&lt; 0,83</td>
<td>16</td>
<td>6</td>
<td>5,45</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>1200</td>
<td>6 240</td>
<td>3,13</td>
<td>28,0</td>
<td>&lt; 0,83</td>
<td>10</td>
<td>2</td>
<td>5,8</td>
<td>34</td>
</tr>
</tbody>
</table>

Normal values:
- Renin: up to 600 ng/100 ml.
- Aldosterone: 5 - 17 mg/100 ml (mean 8,0).

Renin (Boucher method) and aldosterone estimations (method of Fraser and Jones) were determined after 1 litre of Macrodex was administered within 51 minutes. The values are listed in Table II. The patient was supine and the blood pressure remained constant.

The angiotensin infusion test (done with 4 ng/kg/minute given within 5 minutes) resulted in an increase in the diastolic pressure of less than 10 mmHg.

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Fig. 2. Renal biopsy specimen showing hyperplasia of the juxtaglomerular apparatus (H. and E. × 550).
TABLE III. EXCRETION OF AMMONIA AFTER AMMONIUM CHLORIDE INGESTION

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>NH (mEq/L)</th>
<th>Total acid (mEq/ specimen)</th>
<th>Volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal value (immediately before 4.1 g NH₄Cl)</td>
<td>6.5</td>
<td>0.208</td>
<td>6.2</td>
<td>0.93</td>
</tr>
<tr>
<td>1 hour after NH₄Cl</td>
<td>5.5</td>
<td>0.379</td>
<td>7.8</td>
<td>0.83</td>
</tr>
<tr>
<td>2 hours after NH₄Cl</td>
<td>5.8</td>
<td>0.538</td>
<td>8.4</td>
<td>1.19</td>
</tr>
<tr>
<td>3 hours after NH₄Cl</td>
<td>5.8</td>
<td>0.56</td>
<td>6.7</td>
<td>1.06</td>
</tr>
<tr>
<td>4 hours after NH₄Cl</td>
<td>5.0</td>
<td>0.64</td>
<td>8.0</td>
<td>1.04</td>
</tr>
<tr>
<td>5 hours after NH₄Cl</td>
<td>5.0</td>
<td>0.55</td>
<td>7.8</td>
<td>0.98</td>
</tr>
</tbody>
</table>

TABLE IV. SODIUM AND POTASSIUM BALANCE STUDIES*

<table>
<thead>
<tr>
<th>Intake</th>
<th>Output</th>
<th>Retention</th>
<th>Serum electrolytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Food, fluid and K⁺ supplements)</td>
<td>(Urine: 1 290 ml/24 h; faeces: 450 g/24 h)</td>
<td>(mEq/24 h)</td>
<td>(mEq/100 ml)</td>
</tr>
<tr>
<td>Na⁺ 64</td>
<td>Na⁺ 32.5</td>
<td>K⁺ 38.7</td>
<td>Na⁺ 27.5</td>
</tr>
<tr>
<td>Mean 137</td>
<td>Mean 1.9</td>
<td>range 134 - 140</td>
<td>range 1.8 - 2.0</td>
</tr>
</tbody>
</table>

* Average values over period of 5 days.
Body weight and blood pressure remained constant.
Patient moved about freely.

Fig. 3. Renal biopsy specimen showing arteriole with medial thickening and mild intimal hyperplasia (H. and E. × 550).
TABLE V. BALANCE STUDIES DONE WITH "K"

<table>
<thead>
<tr>
<th>% Body load</th>
<th>Time after ingestion</th>
<th>% Secreted</th>
<th>Total</th>
<th>Faeces</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>5 min</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>61,9</td>
<td>24 hours</td>
<td>10,2</td>
<td>10,2</td>
<td>5,0</td>
<td>5,0</td>
<td>77,1</td>
</tr>
<tr>
<td>58,7</td>
<td>48 hours</td>
<td>9,0</td>
<td>19,2</td>
<td>3,1</td>
<td>8,1</td>
<td>86,0</td>
</tr>
<tr>
<td>2nd test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>5 min</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>89,9</td>
<td>24 hours</td>
<td>8,42</td>
<td>8,42</td>
<td>2,73</td>
<td>2,73</td>
<td>100</td>
</tr>
</tbody>
</table>

Potassium Balance Studies

In the meantime a special watch was kept on the patient for full 24-hour periods. This was done to carry out potassium balance studies and to ascertain whether the patient vomited, or whether there was any intake of purgatives or diuretics. No irregularities were noted, and the result of these balance studies are reflected in Table IV.

The suspicion that this patient was losing potassium elsewhere was confirmed with the aid of balance studies done in the whole body counter after administering "K" (Table V). The first test totalled only 86% recovery of "K" while the second test gave a 100% recovery with the patient under strict observation.

Due to the probable unreliability of the patient no further balance studies were attempted.

In the differential diagnosis the syndrome of Conn, Cushing, Addison and Bartter were considered. However, on the grounds of the clinical picture and biochemical findings the chronic abuse of purgatives appeared to be a more acceptable proposition.

Diagnosis

On direct confrontation and later with the help of a psychiatrist, the patient eventually admitted to continuous use of purgatives. She had resorted to collecting her faeces in plastic bags while in hospital and had asked her friend during visiting hours to dispose of them. Both the ward sister and the special nurses who did the individual observations had at no time noticed any irregularity. The psychiatrist commented on an underlying depression and tendency to evasion.

Follow-up

After discharge, the patient was again seen at the Outpatient Department. Treatment consisted of a free diet and Zyloprim (100 mg allopurinol) 1 tablet t.d.s., Slow K (KCl 600 mg) 2 tablets t.d.s., Aldactone (25 mg spironolactone) 1 tablet q.i.d. She felt better and continued her occupation as a teacher. The biochemical picture at that stage showed blood urea 72, blood creatinine 1,4 and uric acid 8,5 mg/100 ml; serum sodium 4,3, chloride 94 and bicarbonate 24,0 mEq/litre. Blood pressure was 80/50 mmHg and her weight 42 kg. On subsequent visits the clinical picture remained unchanged, and the total body potassium and glucose tolerance curve reverted to normal. In spite of this the blood pressure, low weight, amenorrhoea and moderately raised blood urea persisted (Fig. 4). The histology of a second kidney biopsy taken 1 year later remained unchanged.

DISCUSSION

Metabolic changes due to potassium loss resulting from the abuse of purgatives was described in detail in 1953 by...
Schwartz and Relman. Since then numerous excellent articles on this subject have been published.

These patients usually have a striking number of characteristics in common, namely: they are predominantly women (often with a psychiatric disturbance) who are guilty of chronic secretive misuse of diuretics and purgatives. This is then followed by anorexia, hypokalaemia, dehydration, oedema and constipation, which leads to further abuse. As a result of a mounting hyponatraemia and hypovolaemia, increased secretion of renin and aldosterone follows. At this stage the classical picture of anorexia nervosa develops.

The signs and symptoms found in this patient are similar to those described in the literature on this subject (thirst, amenorrhoea, dark discolouration of the skin, small heart, abnormal carbohydrate metabolism, raised uric acid and oedema).

In spite of contrary reports, it would seem likely that the dehydration, hyponatraemia and raised secretion of renin and aldosterone could explain the clinical and biochemical findings adequately, with perhaps the exception of skin pigmentation, oedema, amenorrhoea and the size of the heart (possible brown atrophy).

It is interesting to note the pronounced arteriolar changes of the kidney vessels in these cases. Despite systematic hypotension, definite changes, namely the thickening of the arteriolar walls, develop. Research done on animals proved that with the administration of crude extracts of renin, the sustained vasoconstriction caused thickening of the arteriolar walls and a lack of sensitivity to exogenous angiotensin.

We wish to thank Dr W. H. F. Kenny, Superintendent of the H. F. Verwoerd Hospital, for permission to publish; Professor L. S. de Villiers for the biochemical determinations, Dr V. Hesse for the surgical biopsy of the kidney; Professor I. W. Simpson for the histology; Professor O. Wrong for his valuable suggestions; Professor B. J. Meyer for the renin determinations; Professor C. J. Jansen for the isotope studies; and Mr G. J. de Swardt for the photomicrographs.

REFERENCES


Book Reviews: Boekbesprekings

INCOME TAX


An interesting and concise work which differs from the conventional pattern in that the subject is approached from the viewpoint of the taxpayer. It includes an outline of the South African Income Tax system and aspects related thereto. Among others there are interesting chapters on the question of how tax evasion is detected by the Revenue authorities; Income Tax vis-à-vis Travelling and Entertainment Expenses; Income Tax as it affects Partnerships as well as specific Income Tax problems of Medical Practitioners.

P.V.

HINTS FOR HOUSEMEN


The first few chapters intended for housemen in the National Health Service have little application elsewhere. Three rather verbose sections on theatre lore and peri-operative management followed by sections on fluid and electrolyte balance which help to resuscitate the book.

A description of practical ward procedures is obviously no substitute for clinical demonstrations. The concluding chapter on legal aspects of housemanship and the appendices which are well compiled and most useful, help to make this book worth its cost.

W.F.L.