HYPOKALAEMIC PARALYSIS DUE TO CARBENOXOLONE

by

JOHN RANKIN, M.B., B.Ch., House Officer

and

MICHAEL E. SCOTT, M.D., M.R.C.P., M.R.C.P.I.,
Consultant Physician (Cardiology), Craigavon Hospital, Craigavon, Northern Ireland

INTRODUCTION

HYPOKALAEMIA is known to occur in patients receiving long-term carbenoxolone therapy. (Brown et al., 1972). Though the loss of potassium with normal dosage rarely produces symptoms, several case reports of patients with muscle paresis and myopathy have appeared. (Mohamed et al., 1966; Forshaw, 1969; Swallow, 1969; Mitchell, 1971). We report a case of unusual severity.

CASE REPORT

A 48 year old man was admitted with a four-day history of muscle cramps and paralysis. Two months previously the patient had been treated in another hospital for haematemesis arising from a lesser-curve gastric ulcer. At that time the serum potassium was 3.44 m.Eq/1. He received 6 units of whole blood. Five days later carbenoxolone sodium 150 mg daily was commenced. No other drugs were prescribed. He took carbenoxolone for 28 days, and 7 days after discontinuing the drug he was reviewed at the first hospital. He reported no symptoms but had gained 10.1 Kg in five weeks. Later that day he developed cramps in his thighs and experienced difficulty in walking owing to weakness in his back and legs. The weakness got worse over the four days preceding admission to this hospital, until he could not lift his head from the pillow.

On examination there was complete paralysis of the extensors of the left wrist, severe weakness of the left biceps, triceps and deltoid muscles and marked winging of the left scapula. The right arm and both legs were less severely affected but there was almost complete paralysis of the sternomastoid and trapezius muscles. Ocular movements, speech and swallowing were normal. The tendon reflexes were absent in the left arm but present in the other limbs. The plantar responses were flexor. There was no muscle wasting but stretching of both quadriceps groups caused pain. Sensation was normal. The blood pressure was 160/100 mm.Hg: there was no oedema.

Investigations on admission were as follows: The serum electrolytes (m.Eq/l) were: sodium 149, potassium 2.19, chloride 91, CO₂ < 40, Astrup: pH 7.55, PCO₂ 53, base excess > +20, plasma bicarbonate 46. The Hb was 11.4 gm%, white cells 7,000/c.mm., and the serum proteins 6.85 gm%. Serum calcium was 8.5 mg%, and phosphorus 2.05 mg%. The serum creatine phosphokinase was 1,100 units/ml (normal 0-50 units/ml). The urine was alkaline and slightly smoky in appearance. There was a trace of albuminuria and microscopical examination
showed some red cells and a few organisms. No porphyrins were detected. Spectroscopic examination for myoglobin was not performed. The cardiogram showed marked hypokalaemic changes with ST segment depression, massive U waves and frequent ventricular ectopic beats.

He received 250 m.Eq of potassium by intravenous infusion over 36 hours, by which time the serum potassium had risen to 2.63 m.Eq/l and the patient felt much stronger. Oral potassium, 160 m.Eq/day in tablet form was commenced. On the sixth day of treatment, when recovery of muscle power was almost complete, serum potassium was 3.5 m.Eq/l, CO₂, 39 m.Eq/l and serum creatine phosphokinase 670 units/ml. His potassium intake and blood levels are illustrated in the Figure.

At review two weeks later no paresis remained. The blood pressure was 140/80 mm.Hg and the patient had lost 5.4 Kg since discontinuing carbenoxolone. The serum electrolytes (m.Eq/l) were: sodium 144, potassium 4.65, chloride 103 and CO₂ 32.1. The cardiogram was normal. Potassium supplements were discontinued. Three months later the electrolytes were normal, serum creatine phosphokinase was 8 units/ml and the serum aldolase 1.4 units/ml. The serum calcium was 10.0 mg%, phosphorus 3.8 mg% and serum proteins 6.3 gm%.

**COMMENT**

The onset of paralysis after only 4 weeks treatment with Carbenoxolone is most unusual. Mitchell (1971) reported the onset of paralysis after five weeks treatment in a patient on a higher dosage (200 mg. daily). The severity of potassium depletion
in our patient was remarkable. Based on replacement requirements more than one third of total body exchangeable potassium had been lost i.e. 30-40 m.Eq/day for four weeks (Figure). This is comparable to the severity of potassium loss in the case of Mohamed et al. (1966). We cannot explain the long interval between cessation of treatment and the onset of weakness. Though Duo gastrone may remain in the stomach for several days, Biogastrone is absorbed rapidly. Delayed paralysis was not precipitated by the administration of a thiazide diuretic as in the case of Fyfe et al. (1969). Swallow (1969) described a patient with weakness of the neck muscles but we have not discovered another case with complete "head-drop".

Muscle pain is often a more prominent feature than in the present case and may be the dominant symptom (Morgan et al. 1966). Mohamed et al. (1966) demonstrated myositis in patients with muscle pain and weakness. In the case of Swallow (1969), the electromyogram was consistent with a myopathic lesion although the muscle pain and tenderness were absent. The very high levels of creatine phosphokinase suggest that myositis occurred in the present case.

Flaccid paralysis with profound hypokalaemia due to carbenoxolone therapy has been attributed to an aldosterone-like metabolic action of the drug (Baron and Naborro 1967). Much of this patient's substantial weight gain and rise in blood pressure during treatment must have been due to fluid retention, a conclusion supported by the rapid weight loss and the return to normal of the blood pressure after discontinuation of the drug. Retention of sodium and water is accompanied by an increased excretion of potassium. The alkalosis is thought to be due to a physiological attempt to conserve potassium ions by the excretion of ammonium ions.

The present case emphasises the need for careful monitoring of the weight, blood pressure and serum potassium of all patients receiving Carbenoxolone. In view of the potentially lethal effects of severe hypokalaemia it would seem prudent to administer potassium 40 m.Eq daily to such patients.

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Requests for reprints to:
Dr. Michael E. Scott, M.D., M.R.C.P.,
Consultant Physician (Cardiology),
Craigavon Area Hospital,
Craigavon, Co. Armagh, N. Ireland.