Dear Sir,

The rhabdomyolysis is a clinical and laboratory syndrome resulting from skeletal muscle injury with release of muscle cell contents into the plasma. It can be induced by numerous factors [1]. Among these factors, numerous cases of rhabdomyolysis and myoglobinuria secondary to hypokalemia have been described [1–3], which are due to drug therapy (diuretics, carbenoxolone and amphotericin B) licorice ingestion (pseudohyperaldosteronism), primary hyperaldosteronism, gastrointestinal potassium losses (laxative abuse, malabsorption syndrome, etc.) renal tubular acidosis exercise in hot weather, prolonged nasogastric drainage and inadequate electrolyte replacement associated with total parenteral nutrition.

I have recently seen a case of severe hypokalemic rhabdomyolysis secondary to pseudohyperaldosteronism that appeared after the prolonged application of a lotion with 9-α-fluoroprednisolone (9-FP).

Case Report

J.P., a male 67-year-old patient was admitted to hospital for arterial hypertension and assumed hematuria. Due to a dermatitis affecting the scrotum and inguinal regions, he started using a lotion containing 9-FP 3 months before admission. One month later, hypertension was detected. He received about 350 mg of 9-FP monthly. For 12 days before admission he had been suffering from progressive muscle pain and severe generalized muscular weakness and dark brown urine. He had not taken any diuretics, carbenoxolone, laxatives or licorice. There was no history of vomiting or diarrhea.

On physical examination, the prominent findings were blood pressure 220/100 mm Hg, decreased muscular strength in all extremities, and depressed deep tendon reflexes. Laboratory data on admission showed hematocrit 38%, hemoglobin 13.1 g/dl, leukocyte count 7,900 with normal differential count, platelet count 290,000/mm3, hemolysis screening was negative. Serum sodium was 144 mmol/l, serum potassium 1.3 mmol/l, arterial blood pH 7.57 and carbon dioxide 40 mmol/l. Blood urea nitrogen, serum creatinine, serum total protein, glucose, total bilirubin, calcium, phosphorus, uric acid, alkaline phosphatase and aldolase were normal. The muscular enzymes were markedly elevated: the glutamic oxaloacetic transaminase was 300 mU/ml (normal < 40 mU/ml), lactic dehydrogenase was 897 mU/ml (normal < 240 mU/ml), creatinine phosphokinase was 3,200 mU/ml (normal < 50 mU/ml).
The urinalysis showed that the urine was dark brown with a specific gravity of 1.015. The sediment was normal, without any red blood cells. The orthotolidine test was strongly positive. Myoglobin was detected by absorption spectrophotometry. The urine gave plus test for protein. Urine cultures were negative. The ante meridiem plasma cortisol, urinary 17-ketosteroids and the urinary 17-hydroxycorticoids in 24 h were normal. Plasma renin activity under basal conditions was 0.2 ng/ml/h (normal 0.2–2.3 ng/ml h) and after stimulation with frusemide and 2 h of ambulation was supressed. Basal aldosterone was 61 pg/ml (normal 12–125 pg/ml), and after stimulation with frusemide and 2 h of ambulation the value was similar. Electrocardiogram, ophthalmoscopic examination, X-ray film of the chest and urography were normal. Electromyography disclosed muscle fibre lesions and a mild decrease of motor nerve conduction velocity. The lotion was stopped, and the blood pressure and serum potassium returned to normal within 12 days. The muscular pain and weakness and the dark brown urine equally disappeared. Muscular enzymes were normal in 21 days. Two months later, the serum potassium, blood pressure and muscular enzymes were normal. The ARP and aldosterone, under basal conditions and after stimulation with frusemide and 2 h of ambulation, were normal.

Discussion
The pseudohyperaldosteronism is a clinical picture characterized by hypertension, hypokalemia, depressed plasma renin activity and absence of aldosterone hyper-secretion. This syndrome may be caused by several enzymatic deficiencies, tumours producing mineralcorticoids, prolonged intake of licorice or carbenoxolone, and several cases have been described recently after prolonged application of nasal sprays [4], creams [5, 6] and lotions [7] containing 9-FP, a substance with an activity similar to aldosterone. Frank rhabdomyolysis with marked elevation of enzymes and myoglobinuria has been observed when serum potassium is below 2 mmol/l. Moderately severe hypokalemia causes [8] (A) abnormally low muscle blood flow with exercise (B), suppresed ability for glycogen synthesis and storage in muscle, and (C) deranged ion transport. If the muscles are excessively exercised, these metabolic and hemodynamic abnormalities can precipitate frank rhabdomyolysis.
In the present case, the use of a lotion containing 9-FP during 3 months due to a dermatitis affecting the scrotum and inguinal regions caused a picture of pseudohyperaldosteronism with severe hypokalemic and secondary rhabdomyolysis.
The more and more frequent publications of clinical cases where secondary effects due to the use of preparations of 9-FP are described advise to stop using it.

References