Nephroquiz
(Section Editor: M. G. Zeier)

Recurrent paroxysms of metabolic acidosis in a haemodialysis patient

Case

A 56-year-old haemodialysis patient was observed to have a substantial metabolic acidosis prior to a routine haemodialysis treatment. She had developed chronic renal failure and become dialysis-dependent 10 years earlier. A renal transplant had failed; she had peripheral vascular disease, and had decreased cardiac function because of a suspected cardiomyopathy. Otherwise, she was stable.

The patient voiced no complaints. However, her pH was 7.146, PaO$_2$ 124 mmHg, PaCO$_2$ 27 mmHg, and HCO$_3$ 9 mmol/l. The serum Na$^+$ was normal and the serum Cl$^-$ was elevated, commensurate with the HCO$_3^-$ decrease indicating that the anion gap was unchanged. She was haemodialyzed for 5 h against a 35 mmol/l HCO$_3^-$-containing dialysate without incident. At the end of the treatment, the pH was 7.41, PaO$_2$ 120 mmHg, PaCO$_2$ 34 mmHg, and the HCO$_3^-$ was 22 mmol/l. We were puzzled as to what was going on. Thereafter, her acid–base status was variable. The values remained normal until one month later, when she entered the dialysis unit with a pH of 7.07, with accompanying PaCO$_2$ 20 mmHg and HCO$_3^-$ of 5 mmol/l. Again, the Cl$^-$ was elevated while the anion gap remained unchanged. Again, a high HCO$_3^-$ dialysate rectified the situation. We remained perplexed. On other occasions, the hyperchloraemic metabolic acidosis was not as severe. Detailed questioning of the patient revealed nothing out of the ordinary. On another occasion, about six months after the episodes had begun, she again came in with a pH of 7.08, PaCO$_2$ 27 mmHg, and HCO$_3^-$ 6 mmol/l. We remained puzzled while she appeared no more the worse for wear. The episodes continued for several more weeks until we finally asked her to bring in any or all items she might be ingesting.

Perhaps you are cleverer than we were and can make the diagnosis without inspecting the items the patient brought with her?

The patient was taking a traditional German cough medicine Salmix®. Each lozenge contains 30 mg Stoechospermum atropurpureum, also known as Glycyrrhiza glabra, and 20 mg NH$_4$Cl (Figure 1). As the name implies, the compound contains glycyrrhizinic acid; however, lico-rice poisoning did not appear to be the problem here. The manufacturer claims the material is indicated for the treatment of cough and catarrh. She admitted to consuming 100 g of lozenges during each interdialytic interval, easily enough to explain the profound metabolic acidosis in the face of no renal function. We thought that this bizarre poisoning with over-the-counter (OTC) preparations might be a European phenomenon and were therefore interested in the report by Wong et al. [1]. These investigators described a patient with normal renal function, who entered the hospital with a pH of 7.19, PaO$_2$ 115, PaCO$_2$ 32 (both mmHg) and HCO$_3^-$ 12 mmol/l. That patient had a slightly elevated anion gap and a serum K of 2.7 mmol/l. The authors reported on phensedyl, a proprietary cough remedy available without prescription in Hong Kong. The material contains various ingredients; including NH$_4$Cl. NH$_4$Cl is a common component of many antitussives. For example, 5 ml of Benylin Expectorant®, a common cough remedy marketed in North America, contains 135 mg NH$_4$Cl in 5 ml of the compound. Megarbane et al. [2] reported on NH$_4$Cl poisoning in an elderly patient who was prescribed the material by her physician. The patient recovered from hyperchloraemic metabolic acidosis despite an admission pH of 6.9. The reasons for this therapeutic misadventure were not stated.

One of the authors (Luft) organized and participated in an investigation of Na$^+$/H$^+$ exchange in human lymphocytes and platelets in chronic and subacute metabolic acidosis [3]. The subjects ingested 15 g NH$_4$Cl for five days. Their pH decreased from 7.40 to 7.26. Cl$^-$ increased from 103 to 116 mmol/l, HCO$_3^-$ decreased from 27 to 13 mmol/l. Body weight fell 2 kg, while plasma renin activity and plasma aldosterone increased substantially. Urinary K$^+$ losses were increased. Na$^+$/H$^+$ exchange in lymphocytes was stimulated. Luft remembers feeling awful during the experiments. He recalls that his father, a German Himalayan climber from the 1930s, related that NH$_4$Cl was used as a strategy above 6000 m to combat respiratory alkalosis and high altitude sickness [4]. The strategy was a failure. This report is the first to our knowledge of NH$_4$Cl poisoning in a dialysis patient. Clearly, her lack of renal function made the clinical picture more dramatic and that much more puzzling.

Diagnosis: Metabolic acidosis from NH$_4$Cl poisoning through an OTC cough medicine.
Conflict of interest statement. The authors deny any conflicts of interest. They do not hold stock in the company which manufactures of Salmix®.

References


Fig. 1. Salmix® package and lozenges are shown. Each lozenge contains 20 mg NH₄Cl. About 500 of these lozenges in each interdialytic period would amount to 10 g NH₄Cl.