Phosphate binders and timing of levothyroxine administration

Sir,

Recently, we diagnosed hypothyroidism in one of our haemodialysis patients, a 62-year-old woman with chronic tubulointerstitial nephritis. She had severe symptoms and her TSH was 297 mU/l (reference range 0.30–4.20 mU/l). Levothyroxine was prescribed and administered with breakfast as well as with amlodipine 5 mg, enalapril 5 mg, esomeprazole 20 mg, paracetamol 1000 mg, sevelamer 3200 mg and vitamins B. The dose was gradually increased to 150 μg daily. After 3 months of treatment, the clinical response was still unsatisfactory and TSH was 297 mU/l. Then, the patient was instructed to take levothyroxine at night, at least 4 h after any other medication. Three weeks later, she felt much better and her TSH was 19 mU/l. Levothyroxine treatment was continued according to this schedule at the dose of 175 μg daily. Nine months later, routine testing again revealed a high TSH level (76 mU/l). This was right after a hospital stay due to arteriovenous (A-V) fistula problems during which levothyroxine was given with the morning medications. After switching back to levothyroxine administration at night, the TSH level rapidly normalized.

Most likely, the absorption of levothyroxine was disturbed by a simultaneously administered medication. It is well known that many substances interfere with the absorption of levothyroxine, e.g. the phosphate binders aluminium hydroxide [1] and calcium carbonate [2]. Since phosphate binders have certain characteristics in common, such as positive charge, we assumed that sevelamer was the culprit. This assumption was supported by the Swedish Pharmacopoeia [FASS (www.fass.se)], according to which hypothyroidism has been reported in patients who ingested sevelamer and levothyroxine at the same time (reports not found by a MEDLINE search with the keywords sevelamer and levothyroxine). Moreover, sevelamer binds bile acids. Other bile acid sequestrants have been reported to disturb the absorption of levothyroxine [3].

Calcium preparations are widely used as phosphate binders in uraemic patients. However, the fact that calcium interferes with the absorption of the frequently-prescribed levothyroxine does not seem to have caught the attention of the nephrological community. This may be explained by the paucity of reports, the first prospective study being published only 7 years ago [2]. In addition, adjustments of the levothyroxine dose in response to routine TSH analyses probably prevents severe clinical consequences in most cases.

In conclusion, the present case supports the notion that sevelamer binds levothyroxine in the intestinal tract. If this hypothesis proves to be correct, we now know of three phosphate binders that interfere with the absorption of levothyroxine. This raises the question whether the same applies to all phosphate binders, including lanthanum carbonate. It seems prudent to administer phosphate binders and levothyroxine with an interval of several hours.

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Sheathless or ‘over-the wire’ technique for tunnelled cuffed catheter insertion

Sir,

We read with great interest the article by Polaković et al. [1] regarding the insertion of tunnelled cuffed catheters without using a peel-away sheath. This technical note is very helpful, as increasing numbers of nephrologists are performing these procedures.
procedures. We have switched over to this sheathless or ‘over the wire’ technique for the past 3 years now [2]. It certainly reduces the amount of blood loss and possibly also decreases the risk of air embolism [3]. The advantage of avoiding the sheath is primarily to reduce the venotomy size, thus allowing the catheter to fit snugly, preventing oozing around the venotomy site. We have been using this technique not only for new insertions, but also for replacements. The technique works equally well with both split and stepped catheter tips. In case of split catheter tip, the wire is woven through the venous tip, then brought out through the side hole of the venous lumen. The wire is then passed into the tip of the arterial end and pulled out through the arterial hub. Moreover, with the availability of tunnelled catheters with a ‘stiffener’ or stylet makes using this technique simple, even for a novice. The sheathless technique can be difficult in patients who have multiple previous catheters or scarring and hence we recommend having a valve-sheath handy in case of an emergency.

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Sodium citrate anticoagulation during sustained low efficiency dialysis (SLED) in patients with acute renal failure and severely impaired liver function

Sir,

Due to severe side effects, sodium citrate anticoagulation has been avoided in patients with severely impaired liver function undergoing renal replacement therapy [1]. Based on a previously published protocol, seven patients with acute renal failure (diagnosed according to accepted guidelines) and severely impaired liver function (mean Child–Pugh score: 10.5 ± 0.5) received a total of 10 sustained low efficiency dialysis (SLED) treatments using the Genius dialysis system [2–4]. For this study, a high-flux membrane (FX 50, Fresenius Medical Care, Bad Homburg, Germany) was used. The dialysate contained 1.0 mmol/L calcium, 30 mmol/L bicarbonate and 135 mmol/L (n = 9) or 138 mmol/L (n = 1) sodium. Three percent sodium citrate (110.9 mmol/L; Fresenius Medical Care, Bad Homburg, Germany) was infused pre-filter at a rate to maintain the post-filter ionized calcium levels between 0.6 and 0.7 mmol/L. There was no routine calcium supplementation at the venous line (supplemental Figure 1). Mean patient age was 61.7 ± 4.8 years. APACHE II and SOFA score were 34.6 ± 3.4 and 16.4 ± 0.8, respectively. Laboratory values are given in Table 1. All patients were on daily dialysis before initiation of SLED therapy with sodium citrate anticoagulation. The rationale for sodium citrate anticoagulation was repeated filter clotting (filter lifetime <2h) under heparin-free or low-dose heparin therapy. Mean dialysis time with sodium citrate anticoagulation was 17.3 ± 4.1 h. There was a mean of 0.043 ± 0.017 clotting events per h, translating to a mean (theoretical) filter lifetime of 23.3 h. No major bleeding episodes related to the dialysis therapy were observed. Total calcium, ionized calcium, calcium gap (total calcium – ionized calcium), electrolytes and base excess (as well as other parameters of acid–base balance) were maintained at stable levels during therapy and thereafter (Table 1 and supplemental Figure 2). This was also applicable in repeated SLED treatments using sodium citrate anticoagulation in the same patient. There were no significant hypotensive episodes during SLED therapy and norepinephrine dosage was significantly reduced during therapy (P < 0.04; Table 1). Our observation is in contrast with previous publications, where sodium citrate anticoagulation in patients with impaired liver function led to severe disturbances of electrolytes, acid–base haemostasis or even death [1]. The main difference between our protocol and conventional protocols is the lower sodium citrate infusion rate with higher targeted post-filter ionized calcium levels and the absence of routine calcium supplementation at the venous line. The risk of accumulating calcium-citrate complexes is further reduced by elimination of citrate complexes by high-flux dialysis [2,5]. This protocol offers the unique opportunity for sodium citrate anticoagulation in patients with even pronounced impairment of liver function. However, in the absence of serum citrate measurements and clearance determinations, accumulation of citrate complexes with longer duration of treatment or repeated treatments cannot be entirely excluded.

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