Persistent and symptomatic post-transplant hyperparathyroidism: a dramatic response to cinacalcet

Sir,

We read with interest the articles by Kruse et al. [1] and Serra et al. [2], which demonstrated the beneficial effect of cinacalcet HCl in the treatment of persistent hyperparathyroidism following renal transplantation. We would like to report our own experience of one selected case of post-transplant hyperparathyroid bone disease, which highlights not only normalization of laboratory-measured parameters but also a dramatic response in symptomatology.

A 79-year-old lady with stable graft function (serum creatinine 96 µmol/l) 13 years post-transplant on cyclosporin monotherapy developed widespread bone pain and myalgia requiring opiate analgesia and eventual hospitalization. Investigations revealed the following: plasma intact parathyroid hormone (PTH) 2690 pg/ml, alkaline phosphatase (ALP) 689 U/l, calcium 2.07 mmol/l and phosphate 0.98 mmol/l. X-ray of her hands showed evidence of early hyperparathyroid bone disease.

Her hyperparathyroidism was refractory to vitamin D therapy and, due to multiple comorbidities, she was deemed unfit for parathyroidectomy. She was, therefore, treated with cinacalcet at a starting dose of 30 mg daily, reducing to alternate day dosing following the development of hypercalcemia. PTH fell to 470 pg/ml after 2 weeks of therapy, this response being sustained over almost 4 months (237 pg/ml at 15 weeks). ALP fell to 342 U/l and calcium and phosphate levels remain within normal limits at 15 week follow-up. Most importantly, her severe bone pain and myalgia have improved dramatically allowing withdrawal of opiate analgesia, significantly improving her quality of life. There has been no change in graft function, blood pressure control or other medication during this time and she has suffered no side effect attributable to cinacalcet.

This patient demonstrates a dramatic and sustained response to cinacalcet, characterized by a 91% fall in PTH (Serra et al. [2] observed an 18% reduction) and resolution of symptomatic hyperparathyroidism, previously effected only in renal transplant patients by parathyroidectomy. We would, therefore, advocate a role for cinacalcet in transplant recipients with symptomatic persistent hyperparathyroidism who are not suitable for parathyroidectomy.

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Estimation of glomerular filtration rate in patients with normal serum creatinine undergoing primary PCI: is it really normal?

Sir,

Kidney disease and cardiovascular disease seem to be lethally synergistic and both approach a level of epidemic, particularly in the elderly. The 2002 DOQI (Dialysis Outcomes Quality Initiative) states that individuals with a reduced glomerular filtration rate (GFR) are at greater risk for cardiovascular disease (CVD) and cardiac deaths [1]. The ability to identify chronic renal insufficiency may allow early implementation of treatments that could arrest or delay the progression of renal damage, enable effective treatment of its complications and reduce the risk of drug-induced nephrotoxicity. Contrast nephropathy is a potentially serious complication of diagnostic angiography and percutaneous coronary intervention (PCI) [2]. Unfortunately, the cardiovascular risk increases in a concentration range of serum creatinine where this parameter is very insensitive to changes in GFR. The current Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines advocate creatinine-based equations for estimating the GFR to identify patients with potential kidney disease and to classify them into different stages on the basis of these values [1].

The aim of our study was to establish the prevalence of kidney dysfunction in patients with normal serum creatinine
using estimated GFR according to the simplified MDRD [1] and Cockcroft–Gault [3] formulae in a cohort of 1413 consecutive patients undergoing primary PCI due to ischaemic heart disease (988 males, 425 females). Normal serum creatinine (<1.5 mg/dl in males and <1.2 mg/dl in females) was observed in 1337 (95%) patients (943 males, 394 females). The mean GFR was 73.02 ± 21.96 ml/min (Cockcroft–Gault formula) and 90.37 ± 25.11 ml/min (MDRD). According to the Cockcroft–Gault formula, stage 2 chronic kidney disease (CKD), i.e. GFR 60–89 ml/min, was found in 627 patients (49.29%) and stage 3 CKD, i.e. GFR 30–59 ml/min, in 391 (30.74%) patients with normal serum creatinine. According to the MDRD formula, stage 2 CKD was found in 639 patients (50.78%) and stage 3 in 94 (7.49%) patients with normal serum creatinine. Patients with hypertension (n = 749), hyperlipidaemia (n = 417), smokers (n = 207) and those with a positive family history of ischaemic heart disease (n = 219) tended to have lower GFR, but not elevated serum creatinine. Patients with diabetes (n = 299) have a lower GFR measured using the Cockcroft–Gault formula (64.05 ± 23.68 vs 69.99 ± 22.93 ml/min, P < 0.05), but not with the MDRD (82.76 ± 28.66 vs 85.65 ± 24.92, P = 0.20) despite comparable values of serum creatinine (1.07 ± 0.45 vs 1.06 ± 0.35 mg/dl, P = 0.66). Normal serum creatinine was found in 394 females (92.7%). According to the Cockcroft–Gault formula, stage 2 CKD was found in 165 (40.74%) and stage 3 in 195 (48.15%) females with normal serum creatinine. According to the MDRD formula, stage 2 CKD was found in 249 (63.20%) and stage 3 in 65 (16.50%) females with normal serum creatinine. Normal serum creatinine was found in 943 males (95.45%). According to the Cockcroft–Gault formula, stage 2 CKD was found in 661 (49.73%) and stage 3 in 196 (20.96%) males with normal serum creatinine. According to the MDRD formula, stage 2 CKD was found in 431 (42.63%) and stage 3 CKD was found in 29 (3.08%) males with normal serum creatinine. Females were significantly older (63.84 ± 11.08 vs 57.39 ± 11.47 years, P < 0.01) with significantly lower GFR estimated using the Cockcroft–Gault formula (60.59 ± 17.27 vs 78.21 ± 21.63 ml/min, P < 0.001), MDRD (78.29 ± 19.91 vs 95.36 ± 23.55 ml/min, P < 0.001), lower serum creatinine (0.85 ± 0.14 vs 1.03 ± 0.19 mg/dl, P < 0.01) despite similar body mass index (28.08 ± 4.75 vs 28.29 ± 4.07 kg/m²).

Interventional cardiologists are being asked to perform PCI on increasing numbers of patients with significant co-morbidities such as CKD. Patients with CKD have an enhanced mortality after an acute coronary syndrome and after PCI with or without stenting [4]. Since a marked reduction in GFR can be present before it is reflected as elevated serum creatinine, it is recommended that the chemical laboratory reports not only the serum creatinine concentration, but also the estimated GFR [5]. Surprisingly, in our study, we found a high prevalence of CKD, on the basis of estimated GFR, in patients with coronary artery disease and normal serum creatinine undergoing primary PCI. CKD is an under-recognized co-morbidity in patients with coronary artery disease and is associated with higher mortality risk. A recent study by Reddan et al. [6] published in the October issue of this journal prompted us to estimate GFR using two formulae: the simplified MDRD formula and the Cockcroft–Gault formula in a cohort of 1413 patients undergoing primary PCI. We found that in 1337 patients, creatinine was normal. In the SYMPHONY and 2nd SYMPHONY trials, patients with creatinine were also excluded [6]. We found a slightly higher percentage of patients with a creatine clearance <90 ml/min according to the modified MDRD formula—55.57 vs 50.10% in the study of Reddan et al. [6]. In addition, when the Cockcroft–Gault formula was used, the percentage of CKD in studied patients reached 80.03%. We found this prevalence of CKD enormously high.

The K/DOQI guidelines recommend estimating GFR in patients who are at risk for kidney disease using the MDRD study formulae. Within the 5th and 95th percentile for age, both formulae provide similar measurements, which were consistent with age-specific historic inulin clearance values [5]. The Cockcroft–Gault equation provided higher estimates at younger ages, and lower estimates at older ages (e.g. >70 years) than those obtained with the simplified MDRD formula [5]. It may at least partly explain our results. However, the accuracy of the MDRD formula in patient populations outside of the USA is also unclear [7]; therefore, we used both methods to estimate the GFR in our patients. On the basis of our results, we should stress that the prevalence of CKD and the impact of CKD on mortality and morbidity in patients with coronary artery disease undergoing primary percutaneous transluminal coronary angioplasty is probably underappreciated. It is reported that this population is not treated aggressively or with evidence-based therapies as frequently as those with normal GFR [6]. Renal dysfunction is thus a novel risk factor which must be incorporated into currently used algorithms to assess risk factor profiles. We also have to bear in mind that the risk of contrast nephropathy with worse outcomes is enhanced in these patients. A lower GFR in women, due to older age and lower body weight, explains why females are more prone to contrast nephropathy. Formulaic estimates of clearances can provide better information than serum creatinine alone.

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Prevention of clot formation during haemodialysis using the direct thrombin inhibitor melagatan in patients with chronic uraemia

Sir, We have read the editorial comment by MJ Flanigan [1] on our recent study ‘Prevention of clot formation during haemodialysis using the direct thrombin inhibitor melagatan in patients with chronic uraemia’. We appreciate the comments, and agree with Dr Flanigan that the incriminate use of any anticoagulant also carries a risk for bleeding which can be serious. It is also true that the side-effects of post dialysis residual anticoagulant activity may not always be appreciated by patients or health care staff. However, we feel that the statement >90% of routine haemodialysis can be achieved without anticoagulation does not reflect the current practice in the majority of dialysis centres. Although it is well established that haemodialysis treatment can be performed without anticoagulation in selected cases with increased risk for bleeding, this procedure is often laborious and is not generally practised. The almost universal use of anticoagulation in clinical practice should reflect the need for anticoagulation in routine haemodialysis.

Heparins are cheap but have potentially serious side-effects as reviewed in our paper. We therefore feel that the search for means to achieve both safe and predictable anticoagulation for haemodialysis must continue. We have explored the use of a new drug and a novel mode of administration and the future application of these principles must, of course be, evaluated as reviewed in our paper. We therefore feel that the search for a new drug and a novel mode of administration and the future application of these principles must, of course be, evaluated from all aspects, including the risk for bleeding in farther studies.

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An accident with Tenckhoff catheter placement: urinary bladder perforation

Sir, Continuous ambulatory peritoneal dialysis (CAPD) is the usual method of maintenance therapy for patients with end-stage renal failure. Tenckhoff catheter placement is well established to facilitate CAPD treatment. The most serious complications of these catheters are infectious; others are mechanical and technical, some related to insertion of the catheter.

Perforation of the urinary bladder is a very rare complication, which has been reported in only 13 cases [1-7]. Another case of the iatrogenic placement of a Tenckhoff catheter in the urinary bladder is reported, a mistake which was probably triggered by urinary retention secondary to a neurogenic bladder.

Case. A 55-five year-old man with end-stage renal failure secondary to hypertensive nephropathy started treatment with maintenance haemodialysis 3 years ago. Five months after beginning treatment, he suffered from intracerebral haemorrhage and underwent neurosurgical treatment. After that disability with left hemiparesis remaining, the patient had difficulties with speech and occasionally symptoms of neurogenic bladder. Because of continuous problems with vascular access, the patient rejected construction of a new fistula and was switched to CAPD.

Before CAPD catheter placement, the patient was instructed to defecate and to void his bladder completely. Catheter insertion (Tenchhoff Swan-neck double-cuff pigtail-right) was performed under general anaesthesia to allow placement of the catheter tip in the right pelvis by the standard blind implantation procedure. His immediate post-operative progress was normal. With an abdominal plain radiograph, the position of the catheter in the pelvis was demonstrated; sonography showed the tip of the catheter in the pelvis. Between instillations of the dialysate on the next day, the patient complained of abdominal discomfort and urinary urgency. With the subsequent increase in input volume of dialysate, there was a marked increase in urinary volume. Urinary analysis was positive for glucose. Cystoscopy revealed the tip of the catheter in the urinary bladder. Six weeks after removal of the catheter, a second catheter was placed through a separate left supraumbilical incision. After that, CAPD was commenced successfully.

Comment. Complications of CAPD using the Tenckhoff catheter may be classified as infectious or mechanical [3]. Mechanical complications are mostly catheter related and include obstruction of the flow, leakage of the peritoneal fluid, ventral and inguinal hernias, catheter malposition or malfunction, and intra-abdominal organ injury [2,3]. Most mechanical complications occur during the first month after catheter placement [4]. Accidental placement of the peritoneal catheter in the urinary bladder is a very rare complication.

In our case, there were two very important factors. The first was our mistake; we expected a patient with a neurogenic bladder to empty his bladder. This could have been avoided with placement of a urinary catheter before surgery. The second was a misleading interpretation of the catheter position by radiography and sonography.

Our case shows that urinary catheterization before surgery must be performed in all cases where patient cooperation cannot be ensured.

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