In conclusion, urinoma is an uncommon complication of idiopathic retroperitoneal fibrosis, which develops acutely into unusual back pain. Either CT or magnetic resonance imaging (MRI) should be considered to define the cause of vague, non-specific and severe back pain or flank pain.

Conflict of interest statement. None declared.

Department of Nephrology, College of Medicine, Korea University Ansan Hospital, Ansan City, Korea
E-mail: starch70@korea.ac.kr

Jin Joo Cha
Jung Yeon Heo
Gang Ji Ko
Dae Ryong Cha
Young Sun Kang

1. Patil KK, Wilcox DT, Samuel M *et al*. Management of urinary extravasation in 18 boys with posterior urethral valves. *J Urol* 2003; 169: 1508–1511; discussion 1511
2. Gayer G, Zissin R, Apter S *et al*. Urinomas caused by ureteral injuries: CT appearance. *Abdom Imaging* 2002; 27: 88–92
3. van Bommel EF, Siemes C, Hak LE *et al*. Long-term renal and patient outcome in idiopathic retroperitoneal fibrosis treated with prednisone. *Am J Kidney Dis* 2007; 49: 615–625
4. Vaglio A, Salvarani C, Buzio C. Retroperitoneal fibrosis. *Lancet* 2006; 367: 241–251
5. Nemec P, Rybnickova S, Fabian P *et al*. Idiopathic retroperitoneal fibrosis: an unusual cause of low back pain. *Clin Rheumatol* 2008; 27: 381–384
6. Kijima T, Okuno T, Sakai Y *et al*. A case of idiopathic retroperitoneal fibrosis accompanied by asynchronous bilateral urinoma. *Hinyokika Kiyo* 2006; 52: 211–214
7. Caruso Lombardi A, Rinaldi MF, Bartalena T *et al*. Urinary ascites due to retroperitoneal fibrosis: a case report. *Acta Radiol* 2007; 48: 119–121
8. Fry AC, Singh S, Gunda SS *et al*. Successful use of steroids and ureteric stents in 24 patients with idiopathic retroperitoneal fibrosis: a retrospective study. *Nephron Clin Pract* 2008; 108: c213–c220
9. Swartz RD, Lake AM, Roberts WW *et al*. Idiopathic retroperitoneal fibrosis: a role for mycophenolate mofetil. *Clin Nephrol* 2008; 69: 260–268

doi: 10.1093/ndtplus/sfp011

Long-term effects of calcium antagonists on augmentation index in hypertensive patients with chronic kidney diseases

Sir,

In 2004, the Japanese Society of Hypertension recommended calcium channel blockers (CCBs) as second line drugs, with the renin–angiotensin (Ang) system (RAS) inhibitor as the first choice, for the treatment of hypertension associated with chronic kidney disease (CKD). We reported that augmentation index (AI) is related to proteinuria in CKD patients, and that RAS inhibition preserves arterial compliance in CKD [1,2]. However, the effects of CCBs on arterial stiffness remain unclear among CKD patients.

A prospective comparative study was performed between 26 non-diabetic CKD patients treated with amlodipine and 27 patients on benidipine (supplemental methods). Patient backgrounds including the prescription of the RAS inhibitor did not differ between groups (supplemental table). Brachial blood pressure was controlled equally well in both groups for a year (supplemental figure). A year later, body weight (to 59 ± 11 kg, $P < 0.05$) and estimated glomerular filtration rate (eGFR) were decreased, and AI was increased without changes in proteinuria (Figure 1) in the amlodipine group. However, in the benidipine group, either eGFR, body weight or AI was not altered, but proteinuria was reduced.

In renal tissue, L-type calcium channels are only found in afferent arterioles, while N-type and T-type calcium channels are localized in both afferent and efferent arterioles [3]. Amlodipine blocks L-type and N-type calcium channels and dilates afferent arterioles much more than efferent arterioles. In contrast, benidipine that inhibits L-type and T-type calcium channels, dilates both afferent and efferent arterioles and reduces glomerular pressure. We have demonstrated that efferent arteriolar constriction is mediated by inositol trisphosphate-induced calcium mobilization and calcium entry through transient receptor potential (TRP) channels [4]. T-type CCBs inhibited AngII-induced calcium mobilization rather than calcium entry in efferent arterioles [3]. TRP channels possess molecular similarity with voltage-dependent calcium channels, but they lack the structure of voltage-sensor, gating independently of voltage. It is possible that some CCBs including benidipine inhibit calcium entry through TRP channels into efferent arteriole.

Increasing AI elevates central blood pressure, worsening glomerular hypertension, proteinuria, renal and cardiovascular prognosis [1,2]. Although we would not deny the other possibilities (supplemental discussion), benidipine could reduce oxidative stress on arterial wall by decreasing proteinuria. Albumin passed through slit diaphragm is absorbed by proximal tubular cells. Although a small amount of protein is cleaved by acidification [5], oxidative process is involved in dealing a large amount of protein, generating reactive oxygen species that appear to leak from the kidney. This escalation of AI should worsen glomerular hypertension further, forming a vicious circle of progressive kidney damage [1,2].

Our results provided the evidence that benidipine may be superior to amlodipine in renoprotection as the antihypertensive additional to the RAS inhibitor when similar blood pressure levels are attained. Furthermore, the present data suggest that the influence on AI differs among types of CCBs in patients with CKD.

Conflict of interest statement. None declared.

Supplementary data

Supplementary data is available online at http://ndtplus.oxfordjournals.org.

Department of Nephrology, Faculty of Medicine, Saitama Medical University, Iruma Saitama 350-0495, Japan
E-mail: iromichi@saitama-med.ac.jp

Tsuneo Takenaka
Hiroshi Takane
Hirokazu Okada
Yoichi Ohno
Hiromichi Suzuki

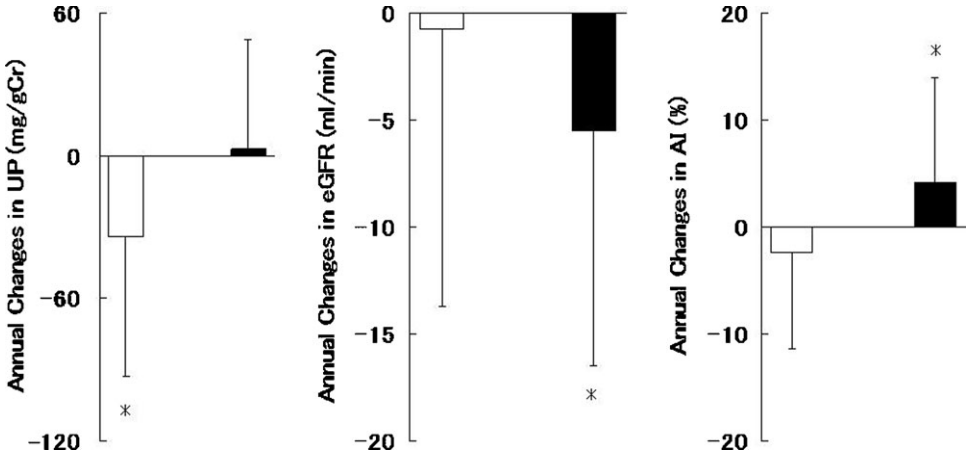

Fig. 1. Annual changes in urinary protein (UP, left panel), estimated glomerular filtration rate (eGFR, middle panel) and augmentation index (AI, right panel). *$P < 0.05$ from zero. Significant decreases in UP (116 ± 93 to 82 ± 67 mg/g creatinine, $n = 27$, $P < 0.005$) and eGFR (53 ± 53 to 47 ± 49 ml/min, $n = 26$, $P < 0.01$) were observed in the benidipine (open bar) and amlodipine groups (closed bar), respectively. AI (79 ± 14 to 84 ± 14, $n = 26$, $P < 0.05$) and serum creatinine (3.8 ± 3.5 to 4.1 ± 3.6 mg/dl, $n = 26$, $P < 0.01$) were considerably increased in the amlodipine group.

1. Takenaka T, Mimura T, Kanno Y *et al*. Qualification of arterial stiffness as a risk factor to the progression of chronic kidney diseases. *Am J Nephrol* 2005; 25: 417–424
2. Mimura T, Takenaka T, Kanno Y *et al*. Vascular compliance is secured under angiotensin inhibition in non-diabetic chronic kidney diseases. *J Hum Hypertens* 2008; 22: 38–47
3. Hayashi K, Wakino S, Homma K *et al*. Pathophysiological significance of T-type Ca^{2+} channels: role of T-type Ca^{2+} channels in renal microcirculation. *J Pharmacol Sci* 2005; 99: 221–227
4. Takenaka T, Suzuki H, Okada H *et al*. Transient receptor potential channels in rat renal microcirculation: actions of angiotensin II. *Kidney Int* 2002; 62: 558–565
5. Günther W, Lüchow A, Cluzeaud F *et al*. ClC-5, the chloride channel mutated in Dent's disease, colocalizes with the proton pump in endocytotically active kidney cells. *Proc Natl Acad Sci USA* 1998; 95: 8075–8080

doi: 10.1093/ndtplus/sfp014

Potentially serious medication errors with a new once-daily preparation of tacrolimus (Advagraf™)

Sir,

Tacrolimus is a widely used immunosuppressant drug in solid-organ transplantation. A new once-daily formulation (Advagraf™, Astellas, Tokyo) has been licensed in Europe in 2007 and shown to be safe and efficacious [1,2]. It is conceivable that the new formulation offers an advantage regarding compliance when compared to twice-daily Tacrolimus (Prograf™, Astellas) although this remains unproven.

A 31-year-old renal transplant recipient with stable transplant function [glomerular filtration rate (GFR) 27 ml/min] was maintained on Prograf™ 2.5 mg BD and prednisolone. While participating in a teaching event in November 2008, she produced a box of once-daily Tacrolimus (Advagraf™) and stated that she had taken this 'new' drug twice daily for 2 months. A mild rise in Tacrolimus blood levels was noted although her GFR had remained stable. We prescribed Prograf™ and investigated the incident. It transpired that she ordered repeat prescriptions through a web-based system (EMISaccess™, Egton Ltd, Leeds, UK). When updating her medication, the GP had erroneously chosen Advagraf™ M/R (modified release) from the two options for Tacrolimus that the software provided but maintained treatment twice daily. Advagraf™ had then been dispensed. However, the patient had not read the package insert and taken Advagraf™ twice daily, as suggested by her medication plan, thus maintaining her previous total Tacrolimus dose. In December 2008, we double-checked her medication again. It turned out that she now took Prograf 2 mg BD and Advagraf 0.5 mg BD. Again, we rectified the error while GFR and Tacrolimus levels remained stable.

We [3] and others [4] have previously voiced concern regarding two different formulations of Tacrolimus being available concurrently. This incident underpins our concern. No untoward consequences have occurred, chiefly because the patient took Advagraf™ twice daily. Had she taken the drug according to the package insert, and halved her daily Tacrolimus dose, she may have sustained rejection and graft loss. Conversely, if transplant patients erroneously take Advagraf™ twice daily, this may cause over-immunosuppression and infection with a potentially fatal outcome.

Various healthcare providers are involved in prescribing the immunosuppression in transplant recipients. All of them should be very aware of this potentially life-threatening issue. We appreciate that Astellas takes this matter very seriously and we understand that the company plans additional warning labels on the package. Prescribing software should feature similar warnings and should not allow treatment with Advagraf™ twice daily. Others, such as the health authorities in Wales, have decided against Advagraf™ to avoid errors and because they feel that the drug does not convey any particular advantage over Prograf™ [5]. We have alerted general practitioners and begun to scrutinize patients on Tacrolimus. We consider approaching all our transplant patients. Finally, we now provide an