

## Clinical Report

# Desmopressin use prior to renal transplant biopsy—does it fit?

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### Abstract

Desmopressin acetate (DDAVP), a selective agonist of type 2 vasopressin receptors, is sometimes used prior to percutaneous renal biopsy to reduce the risk of bleeding complications. DDAVP increases free water reabsorption in renal collecting ducts, potentially leading to water intoxication or dilutional hyponatraemia. We present two cases, where DDAVP was used prior to percutaneous renal transplant biopsy and was associated with severe hyponatraemia and neurological sequelae. With DDAVP being advocated in many centres prior to percutaneous renal biopsy, these cases highlight the need for increased awareness regarding side effects. In this report, we provide suggestions on strategies to minimize hyponatraemia in this context.

**Keywords:** biopsy; drug toxicity; electrolyte management; kidney (allograft) function/dysfunction; kidney transplant/nephrology; patient safety

## Background

Desmopressin acetate, also known as DDAVP (1-deamino-8-D-arginine vasopressin), a selective agonist of type 2 vasopressin receptors, is sometimes used prior to percutaneous renal biopsy to reduce the risk of bleeding complications [1–4]. DDAVP was first used in the 1970s in patients with haemophilia A and von Willebrand disease prior to surgical interventions to minimize the need for blood products. Studies have demonstrated that infusion of DDAVP elicits a rapid, transient increase in the levels of von Willebrand factor (vWF) and plasma factor VIII (FVIII), reaching a maximum between 90 min and 2 h post-administration [3, 5]. DDAVP has been shown to enhance platelet adhesion to vessel walls and transiently releases tissue plasminogen activator into plasma [6].

Uraemia has been associated with a prolonged bleeding time, and the use of intravenous DDAVP has been shown to normalize bleeding time for up to 8 h despite these patients having normal factor VIII and vWF [4]. A recent randomized controlled trial suggested that DDAVP administration decreases the risk of bleeding and haematoma size in patients undergoing percutaneous kidney biopsy [7]. Potential side effects of DDAVP include headache, facial flushing, hypotension and tachycardia [5]. As a synthetic antidiuretic hormone, DDAVP increases free water reabsorption in renal collecting ducts and this may lead to water intoxication or dilutional hyponatraemia [5, 8]. Therefore, the use of DDAVP for anti-haemophilic purposes always requires a tight control of fluid balance.

We present two cases of DDAVP use prior to percutaneous renal transplant biopsy, which were associated with severe hyponatraemia and neurological sequelae.

## Case 1

A 67-year-old female, with end-stage renal failure secondary to IgA nephropathy, who was 30 months out from receiving a deceased-donor renal transplant, was scheduled to have a transplant biopsy due to deteriorating graft function. Her creatinine had risen to 142  $\mu\text{mol/L}$  from a baseline creatinine of 87  $\mu\text{mol/L}$  over 3 months, with a corresponding reduction in estimated glomerular filtration rate (eGFR) from 60 to 34  $\text{mL/min/1.73 m}^2$  according to the Modification of Diet in Renal Disease (MDRD), and this was associated with proteinuria (330 mg in 24 h) although no donor-specific antibody was detected. She had been compliant with her immunosuppression regimen of azathioprine 25 mg once daily and ciclosporin 75 mg twice daily. She had recently been commenced on nortriptyline 10 mg once daily for persistent headaches but was not taking diuretic therapy. Other medications included 1- $\alpha$ -calcitriol 0.25  $\mu\text{g}$  once daily, aspirin 75 mg once daily, doxazosin 8 mg twice daily, epoetin alfa 2000iu twice weekly, ferrous sulphate 200 mg three times a day, irbesartan 150 mg once daily, simvastatin 20 mg once daily, beclomethasone inhaler two puffs twice daily and salbutamol inhaler as required. Of note, she had been drinking 4–5 L of fluid per day in an attempt to improve her graft function and her initial sodium concentration was 127  $\text{mmol/L}$  (normal range, 135–145  $\text{mmol/L}$ ).

She was given an infusion of 12  $\mu\text{g}$  of intravenous DDAVP over 20 min in preparation for biopsy and she was observed for 6 h post-biopsy, remaining haemodynamically stable with no macroscopic haematuria. During her journey home, she developed headache, nausea and muscle cramps. The following day, she had a self-terminating tonic-clonic

seizure at home and was admitted to the intensive therapy unit (ITU) of her local hospital, with a Glasgow Coma Scale (GCS) of 7/15 and a sodium concentration of 107 mmol/L on admission. After eliminating other possible causes of hyponatraemia with biochemical testing, CT and MRI scans of the brain and investigation for potential para-neoplastic syndromes, the hyponatraemia was presumed to be related to a combination of excess fluid intake and administration of DDAVP. Fortunately, the patient recovered following a short ITU stay with fluid restriction leading to a gradual correction of hyponatraemia, without any permanent neurological sequelae.

## Case 2

A 69-year-old female with end-stage renal failure secondary to hypertension was scheduled for a renal transplant biopsy to investigate deteriorating graft function 13 months after receiving a deceased-donor renal transplant. Her creatinine rose to 205  $\mu\text{mol/L}$  from a baseline creatinine of 78  $\mu\text{mol/L}$  over 8 months (MDRD eGFR 67 mL/min/1.73 m<sup>2</sup> to 22 mL/min/1.73 m<sup>2</sup>) in the presence of a donor-specific antibody but no significant proteinuria. She had been compliant with her immunosuppression regimen of prednisolone 5 mg once daily and ciclosporin 35 mg twice daily. She was not receiving diuretic therapy and other medications included alfacalcidol 0.25  $\mu\text{g}$ , aspirin 75 mg, atorvastatin 20 mg, bisoprolol 1.25 mg, co-trimoxazole 480 mg and ranitidine 150 mg twice daily. Of note, she had been advised to increase her daily oral fluid intake in an attempt to improve graft function. Her sodium concentration prior to desmopressin use was 129 mmol/L.

She presented for a day-case renal transplant biopsy and was given an infusion of 12  $\mu\text{g}$  intravenous DDAVP over 20 min prior to the procedure. She was discharged following a 6-h observation period. After leaving the hospital, she developed symptoms of nausea, feeling generally weak and unwell. The following day, she was found collapsed at home and had a witnessed self-terminating generalized tonic-clonic seizure. She was found to have a sodium concentration of 124 mmol/L on admission to her local hospital (normal range, 135–145 mmol/L). She was treated with fluid restriction and despite initial correction of the hyponatraemia, 2 months later, her sodium concentration remains 132 mmol/L.

In both of these cases, patients had been encouraged to increase oral fluid intake in light of the declining graft function and in preparation for biopsy. Sodium levels were <130 mmol/L on pre-admission blood tests prior to DDAVP administration, although they had been previously within the normal range. They had not received clear enough instructions to alter their water intake following the use of DDAVP and both patients continued to consume their standard post-transplant fluid intake.

## Discussion

Although these cases are relatively uncommon in our experience of elective renal transplant biopsies, the severity of the clinical presentations render them clinically significant. Since DDAVP is being used in several renal centres in the UK prior to percutaneous renal biopsy, these cases highlight the need for increased awareness regarding

side effects, in particular hyponatraemia. It is common practice to encourage oral fluid intake in the presence of declining graft function and in preparation for biopsy.

As a synthetic antidiuretic hormone, DDAVP increases free-water reabsorption in renal collecting ducts and this may lead to dilutional hyponatraemia, if appropriate fluid restriction is not instigated. Certainly, there have been reports, predominantly in the paediatric literature, of hyponatraemia-related seizures following treatment with DDAVP [8]. DDAVP itself does not cause hyponatraemia, and it is only with subsequent excessive water intake that this complication can develop.

However, dilutional hyponatraemia is largely preventable with appropriate fluid intake restriction. According to the U.S. Food and Drug Administration Agency, the half-life of DDAVP in patients with severe renal impairment is 9 h. Therefore, it follows that patients should be advised to restrict fluid intake from 1 h before to 9 h after administration of DDAVP [5].

The use of DDAVP as a haemostatic agent to reduce bleeding time prior to percutaneous kidney biopsy continues to be a common practice with potential to decrease the risk of bleeding and haematoma size post-biopsy [1–3, 7].

Other potential causes of hyponatraemia, include

- (i) Psychogenic polydipsia
- (ii) Drugs—e.g. thiazide diuretics, selective serotonin reuptake inhibitors, tricyclic antidepressants, antipsychotics, non-steroidal anti-inflammatory, carbamazepine, sulphonylureas, dopamine agonists, opiates, oxytocin, theophylline, clofibrate, angiotensin-converting enzyme inhibitors, angiotensin-II receptor antagonists, melphalan, proton pump inhibitors and amiodarone
- (iii) Endocrine disorders—hypothyroidism, Addison's disease
- (iv) Syndrome of inappropriate antidiuretic hormone secretion
- (v) Heart failure
- (vi) Chronic liver disease

The use of DDAVP in these patients requires careful consideration of sodium concentrations and current fluid balance as well as the likely fluid intake over the next 24 h and, given the usual practice of liberal fluid intake in renal transplant recipients, DDAVP should be used with extreme caution and close monitoring in any such individual, particularly those with low or borderline-low serum sodium levels. In retrospect, the use of DDAVP in Case 1 who had a pre-biopsy serum sodium of 127 mmol/L should have been contraindicated.

All patients receiving DDAVP therapy should be observed for symptoms associated with hyponatraemia, such as headache, nausea/vomiting, restlessness, fatigue, lethargy, disorientation, depressed reflexes, loss of appetite, irritability, muscle weakness, muscle spasms or cramps and abnormal mental state such as agitation, hallucinations, decreased consciousness and confusion. Severe symptoms may include one or a combination of the following: seizure, coma and/or respiratory arrest [5]. Patients should be advised to contact a doctor immediately if they feel unwell or experience unusual symptoms.

In summary, these cases highlight the importance of appropriate fluid restriction and monitoring following administration of DDAVP prior to renal biopsy. To prevent recurrence of similar cases, we have altered our hospital policy to include the points listed below and have included

information on the side effects of DDAVP in our renal biopsy patient information leaflet.

### Learning points

- (i) Review sodium concentrations prior to administration of DDAVP and avoid DDAVP use if serum sodium is <130 mmol/L
- (ii) Caution in patients predisposed to polydipsia
- (iii) Fluid restrict patients 1 h prior to and 9 h after administration of DDAVP
- (iv) Advise patients to be vigilant of any non-specific symptoms in the first 24 h following DDAVP use, with advice to contact a doctor to have repeat serum sodium measurements.

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