Diurnal variation of antidiuretic hormone and urinary output in spinal cord injury

S Kiliç^{*1}, MN Akman¹, F Levendoğlu¹ and R Özker¹

¹Baskent University School of Medicine, Department of Physical Medicine and Rehabilitation, Ankara, Turkey

Introduction: Healthy individuals have a nocturnal decrease in urine output due to increased plasma antidiuretic hormone levels at night. This does not occur in spinal cord injury and most patients experience nocturnal polyuria, which triggers dysreflexic crises secondary to urinary bladder overdistension, and interferes with patients' sleep due to the need for extra catheterization.

Objective: To evaluate the diurnal variation in ADH level, urinary output, and plasma and urine osmolality in SCI patients with regard to their level of injury and in comparison with age- and sex-matched healthy individuals.

Materials and methods: Sixteen ASIA-A spinal cord-injured patients, eight with paraplegia, eight with tetraplegia, and eight healthy individuals, were evaluated for urinary output, urine and serum osmolality, and antidiuretic hormone levels during day and night hours.

Results: Absence of diurnal variation in urinary output and antidiuretic hormone secretion was detected in both paraplegic and tetraplegic patients, while antidiuretic hormone levels rose significantly at night in the control group.

Conclusion: Antidiuretic hormone levels should be monitored both day and night in spinal cord injury patients with severe nocturnal polyuria. Treatment with desaminocystein-D-arginine vasopressin can be attempted when conservative measures fail to control nocturnal polyuria, especially in patients who are on an intermittent catheterization program.

Keywords: antidiuretic hormone; nocturnal polyuria; urine and serum osmolality; spinal cord injury

Introduction

It is commonly observed that spinal cord-injured (SCI) patients, particularly those with cervical injuries, have a significantly higher urinary output at night than in daytime. Patients on an intermittent catheterization program (ICP) and who freely void upon reflex bladder contraction are thus at greatest risk for excessive bladder distension at night and need to be catheterized/void more frequently. This interferes with the patients' and/or caregivers' sleep and quality of life. Psychological problems may appear upon bed wetting, and patients may lose their self-confidence as they need to use diapers or a condom at night. Nocturnal polyuria in patients with chronic autonomic failure is associated with low morning blood pressure, which aggravates the symptoms of orthostatic hypotension.

Nocturnal polyuria in SCI patients has been widely attributed to defective autonomic regulatory mechanisms causing loss of vascular tone and pooling of body fluid in the lower extremities during the day, followed by intravascular flooding and diuresis at night.^{1–4} It

has been suggested that lack of normal diurnal variation of antidiuretic hormone (ADH) may play a role in the nocturnal polyuria of tetraplegic patients, a phenomenon similar to that documented in enuretic children and the elderly.^{5,6} The purpose of this study was to evaluate the diurnal variation in ADH level, urinary output, and plasma and urine osmolality in SCI patients with regard to their level of injury and in comparison with age- and sex-matched healthy individuals.

Methods

Sixteen complete SCI patients (five females, 11 males) with ASIA score A and duration of injury of at least 3 months, and eight healthy controls (two females, six males) were studied. The SCI patients were assigned to groups I and II according to their neurological level of injury. Group I: eight patients (three female, five male) with lesions at T-6 and above, and Group II: eight patients (two female, six male) with lesions below T-6. Patients with any known illness and those who were on medication which might have affected ADH levels, serum osmolality, or electrolytes were excluded. All

*Correspondence: S Kiliç, Baskent University School of Medicine, Department of Physical Medicine and Rehabilitation 16 Sokak No11, 06490 Bahçelievler, Ankara, Turkey

were participants in the active inpatient rehabilitation program, which included standing with the aid of an assistive device and using wheelchairs. All patients had been on ICP for at least 3 weeks and all but one had slight to moderate spasticity, Ashworth grade 1–2, at the lower extremities. The one exception, with flask paralysis, had a lesion at L-1. All the patients and control subjects gave written informed consent for blood sampling and urine collection. Twenty-four-hour creatinine clearance, blood urea nitrogen, serum creatinine, and electrolyte levels were within normal limits in all patients and controls. Each individual was allowed a maximum daily liquid intake of 2000 ml including fluid content of the food and was instructed to stop drinking liquids or eating juicy food after 2000 h.

Urine samples of all subjects were collected separately in two containers during the day (between 0800–2200 h) and at night (between 2200–0800 h). After the totals of day and night urine output were recorded, samples were sent for measurement of urine osmolality. Blood samples for the measurement of serum osmolality, ADH, and

total protein levels were drawn at 1500 h for day and 0300 h for night. Serum ADH levels were determined with the double-antibody radioimmunoassay method, using an ethanol extraction. Serum osmolality was measured by the freezing point depression method.⁷ Statistical analysis was performed with the computer software program SPSS for Windows, utilizing the Wilcoxon matched-pairs signed-ranks test for paired samples, and the one-way ANOVA test.

Results

The mean ages ($\pm$ s.d.) for groups I and II and the controls were 32.1 ± 5.7 years, 31.2 ± 9.4 years and 30.4 ± 9.8 years, respectively, with no significant differences between the groups identified. The data regarding serum ADH levels and urinary output rates for study and control groups are shown in Table 1. There was no significant difference between day and night urine output rate in Groups I and II. However, the night-time urine output of the control subjects was significantly decreased compared to day time

Table 1 Serum ADH levels and urinary output rates for study and control groups

	ADH level (pg/dl) at 03:30	ADH level (pg/dl) at 15:00	Urine out put (ml/h) night time	Urine output (ml/h) day time
<i>Group I</i>				
1	4.5	1.3	56.26	62.50
2	2.7	2.5	50.00	62.50
3	9.5	10.0	50.00	40.50
4	3.6	7.0	106.25	53.12
5	1.4	2.7	93.70	50.00
6	2.5	2.0	100.00	62.5
7	1.4	5.8	93.00	53.13
8	1.7	1.6	31.25	118.75
mean $\pm$ s.d.	3.41 ± 2.89	4.11 ± 3.14	72.56 ± 28.64	62.87 ± 23.84
<i>Group II</i>				
1	2.4	1.3	74.20	50.00
2	3.6	3.0	93.20	67.00
3	3.2	3.1	112.50	62.00
4	2.8	4.0	72.30	60.45
5	4.0	5.2	50.00	50.00
6	2.9	3.0	45.60	67.40
7	1.7	7.3	50.00	49.70
8	2.5	2.5	42.50	70.70
mean $\pm$ s.d.	2.89 ± 0.72	3.68 ± 1.85	67.54 ± 25.27	59.66 ± 8.68
<i>Control</i>				
1	1.2	1.0	54.00	62.50
2	12.0	3.0	17.00	37.00
3	6.0	3.0	20.00	39.70
4	3.3	1.7	28.50	84.00
5	1.1	1.0	69.50	87.50
6	5.5	2.5	37.75	110.00
7	4.9	1.3	26.00	95.50
8	3.6	3.0	25.00	56.00
mean $\pm$ s.d.	4.7 ± 3.46	2.06 ± 0.91	34.72 ± 18.25	71.53 ± 26.71

($P < 0.05$), as shown in Figure 1. Night-time urine osmolality was significantly higher than the day-time figure in control subjects (day = 385.88 ± 146.68 mOsm/kg, night = 517.75 ± 150.45 mOsm/kg), but this was not the case for the SCI subjects (Group I: day = 400 ± 194.85 mOsm/kg, night = 336.142 ± 59.03 mOsm/kg; Group II: day = 344.5 ± 90.28 mOsm/kg, night = 387.71 ± 171.96 mOsm/kg) (Figure 2). There were no statistically significant differences between the night and day ADH levels in the two SCI groups. However, there was a significant increase in ADH level for control subjects at night ($P < 0.05$) (Figure 3).

Serum osmolality and total protein levels for day and night in study and control groups are shown in Table 2. Differences between the subject groups' day and night levels were not statistically significant. Total protein levels measured during the day and at night for Group I, Group II and controls were also similar.

Figure 1 The mean rate of urine output (ml/h)

Figure 2 The mean urine osmolality (mOsm/kg)

Discussion

Studies of cervical SCI patients have clearly shown that urine production is decreased in the sitting as compared to the lying position.^{2,3} Due to the interruption of the descending sympathetic pathways and abolished orthostatic reflexes in tetraplegic patients, upright posture causes pooling of blood in the legs which leads to a decrease in circulating blood volume.^{8,9} During recumbency, the redistribution of extracellular fluid and expansion of blood volume in circulation leads to an increase in blood pressure and a drop in ADH secretion, resulting in nocturnal polyuria.² Recently, Szollar *et al* noted that tetraplegic patients lack the normal nocturnal rise in ADH secretion, a phenomenon similar to that seen in enuretic children and elderly males.^{5,6} Unfortunately, their study included neither paraplegic patients nor age-matched control groups.

In our study, SCI patients with intact sympathetic pathways (lesions below T-6) and those with defective sympathetic activity (lesions at T-6 or above) showed no diurnal variation in urine output or serum ADH level, while both parameters varied from day to night in age-matched controls. ADH secretion by the posterior pituitary gland is controlled not only by changes in blood volume but by changes in plasma osmolality.¹⁰ Iso-osmotic reduction in central blood volume induced by upright posture or hemorrhage of up to 10% of blood volume did not result in non-osmotic stimulation of ADH secretion in the absence of hypotension.^{11,12} However, relatively modest but

Figure 3 The mean ADH level (pg/ml)

Table 2 Serum osmolality and total protein levels for day and night time

	Serum osm* for day (mOsm/kg)	Serum osm* for night (mOsm/kg)	Total protein for day (mg/dl)	Total protein for night (mg/dl)
Group I	261.85 ± 31.24	274.57 ± 37.02	7.14 ± 0.4	7.0 ± 0.3
Group II	264.85 ± 24.45	251.85 ± 21.77	7.2 ± 33	7.0 ± 0.23
Control	255.13 ± 27.68	262.13 ± 29.26	7.2 ± 0.5	7.3 ± 0.4

*osm = osmolality

prolonged reduction in central venous pressure has been shown to enhance the ADH response to osmotic stimulation in normal individuals and sitting tetraplegic subjects.¹³ During the day, paraplegic patients with low-level cord lesions experience increased pooling of blood in their paralyzed lower extremities as well as prolonged reduction of central venous pressure, since they are sitting in a wheelchair or walking or standing at a parallel bar for a long period of time. Our data suggest that nocturnal polyuria occurs in both tetraplegic and paraplegic patients due to a lack of diurnal variation in ADH secretion, and pooling of blood in the lower extremities seems to be the primary cause of this condition. Theoretically, spasticity should play a preventive role for venous pooling of blood, but it is commonly observed that spasticity does not manifest in the sitting position unless elicited by cutaneous stimulus.

In conclusion, patients should be encouraged to use compressive stockings and an abdominal binder in order to prevent hypotension, peripheral pooling, edema, and reduction in urine output rate. If these precautions, in addition to liquid intake regulation, fail to control nocturnal polyuria and the condition is interfering with a patient's quality of life, ADH levels should be checked. Szollar *et al* suggest the use of desaminocysteine D-arginine vasopressin (DDAVP), a synthetic analog of ADH, at a dose of 20–40 micrograms given at bedtime.⁶ Although long-term follow-up of this medication is lacking for SCI patients, DDAVP therapy can be attempted in patients with severe nocturnal polyuria.

References

- 1 Leehey DJ, Picache AA, Robertson GL. Hyponatremia in quadriplegic patients. *Clin Sci* 1988; **75**: 441–444.
- 2 Kooner JS *et al*. Haemodynamic, hormonal and urinary responses to postural change in tetraplegic and paraplegic men. *Paraplegia* 1988; **26**: 233–237.
- 3 Williams HH *et al*. Non-osmotic stimuli alter osmoregulation in patients with spinal cord injury. *J Clin Endocrinol Metab* 1990; **71**: 1536–1543.
- 4 Krum H *et al*. Diurnal blood pressure variation in quadriplegic chronic spinal cord injury patients. *Clin Science* 1991; **80**: 271–276.
- 5 Szollar SM, North J, Chung J. Antidiuretic hormone levels in spinal cord injury. A preliminary report. *Paraplegia* 1995; **33**: 94–97.
- 6 Szollar SM, Dunn KL, Brandt S, Fincher J. Nocturnal polyuria and antidiuretic hormone levels in spinal cord injury. *Arch Phys Med Rehabil* 1997; **78**: 455–458.
- 7 George CPL *et al*. Diurnal variation of plasma vasopressin in man. *J Clin Endocrinol Metab* 1975; **41**: 332–338.
- 8 Soni BM, Vaidyanathan S, Watt JWH, Krishnan KR. A retrospective study of hyponatremia in tetraplegic/paraplegic patients with a review of the literature. *Paraplegia* 1994; **32**: 597–607.
- 9 Sved AF, McDowell FH, Blessing WW. Release of antidiuretic hormone in quadriplegic subjects in response to head-up tilt. *Neurology* 1985; **35**: 78–82.
- 10 Raff H. Glucocorticoid inhibition of neurohypophysial vasopressin secretion. *Am J Physiol* 1987; **252**: R635–R644.
- 11 Goetz KL, Bond GC, Smith W. Effect of moderate hemorrhage in humans on plasma ADH and renin. *Proc Soc Exp Biol Med* 1974; **145**: 277–280.
- 12 Davies R, Slater H, Forsling L, Payne N. The response of arginine vasopressin and plasma renin to postural change in normal man, with observations on syncope. *Clin Sci* 1976; **51**: 267–274.
- 13 Wall BM *et al*. Altered sensitivity of osmotically stimulated vasopressin release in quadriplegic subjects. *Am J Physiol* 1990; **258**: R827–R835.