Paraplegia (1995) 33, 94–97

Antidiuretic hormone levels and polyuria in spinal cord injury. A preliminary report

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Chronic cervical spinal cord injury is characterized by defects in sodium and water homeostasis and defects of adaptive hormonal responses. The plasma osmolality is maintained in a relatively narrow range, the lower limit of which is determined by osmotic threshold for vasopressin release and the upper limit by the thirst threshold. Antidiuretic hormone as an important mediator of fluid and electrolyte balance was well investigated in able bodied children comparing children with normal voiding pattern and children with enuresis. The normal subjects were found to have higher plasma ADH at night, not detected in the group with enuresis. The findings were similar in elderly patients with increased diuresis at night, suggesting an important role of ADH in nocturnal decrease of urine output. Investigators studied the effect of rapid tilt on plasma ADH in tetraplegic compared with normal subjects, but there are no data available in the literature regarding ADH and its effects on water and electrolyte balance in healthy tetraplegic subjects with a normal lifestyle. We decided to undertake a pilot study to attempt to establish baseline ADH levels in this subject group, to better understand and manage tetraplegic patients with water and electrolyte dysregulation. Our preliminary data suggest that these individuals lack the normal diurnal variation of ADH, a phenomenon similar to that demonstrated in enuretic children and elderly, and furthermore appear to have generally depressed ADH levels.

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

Introduction

Nocturnal polyuria is a common problem in individuals who have had a spinal cord injury, particularly in those with tetraplegia. It can cause significant inconvenience for patients and/or their caregivers. It may trigger dysreflexic crises from urinary bladder overdistention at night, and has been associated with low morning blood pressure and postural hypotension.[1,2]

Although the phenomenon of nocturnal polyuria has long been recognized, its cause remains unclear. It has been attributed, at least in part, to chronic autonomic failure with resultant loss of vascular tone in the lower extremities, pooling of body fluid in the legs and decreased intravascular volume in the daytime, followed by intravascular flooding and diuresis upon recumbence at night.[1,3,4] While these orthostatic factors play a role, other regulating mechanisms, including hormonal effects, may also be involved.

Water balance is, to a large extent, maintaining plasma osmolality within a narrow range. This constancy is achieved through osmoregulation of the antidiuretic hormone (ADH) release and thirst activation. When the plasma ADH level increases, it causes an increase in the permeability of the renal collecting ducts, resulting in renal water conservation and a decrease in urine output. Conversely, when the ADH level falls, urine output increases and diuresis occurs. The secretion of ADH by the neurohypophysis is controlled by at least two mechanisms: (1) changes in the plasma osmolality and (2) changes in the blood pressure and blood volume.

It is found that the secretion of ADH shows diurnal variation.[5,6] Sleeping increases ADH secretion in most normal healthy individuals. This increased nocturnal ADH secretion is believed to cause a smaller volume of concentrated urine at night. It has also been shown that children with enuresis and elderly men with nocturnal polyuria lack this normal nocturnal rise in ADH levels.[7–9] So, a lack of nocturnal increase in ADH levels may be involved in nocturnal polyuria in tetraplegic individuals.

However, to our knowledge, so far there is no data available in the literature studying the relationship of ADH to nocturnal polyuria in healthy tetraplegic subjects. We therefore undertook the present study to delineate the role of ADH in relation to nocturnal polyuria in this group of individuals.

Patients and methods

Ten subjects with spinal cord injury were studied. All were male, aged from 23 to 70 (mean 44 years). Nine were tetraplegic with levels of injury between C4 and C7, all of them with complete injury Frankel's class A, and one with L1 injury was also included in the study. The duration of injury ranged from 1 month to 48 years

(mean 10.9 years). They all used wheelchairs for mobility. All subjects claimed to have high nocturnal urine outputs. They all had normal renal function as shown by 24 h urinary creatinine clearance, serum blood urea nitrogen (BUN), creatinine and renal scan. No patients in the study had diabetes mellitus or any acute or chronic illness. None was taking any medications known to affect the ADH release or urine output.

Each subject was admitted to the hospital for the study. They were investigated for a 24 h period, beginning and ending at 0800. The subjects were instructed to follow their routine activities as closely as possible. Their water intake the day before and during the day of study was restricted to 3000 cc per day. They were instructed to have most of their fluid intake in the daytime before 1700.

Bladder management—seven patients were on a clean intermittent catheterization program, three patients had indwelling Foley catheters (C R Bard Inc, Covington, Georgia, USA). We divided the 24 h period into two sections: a 'day' (0800–2000) and a 'night' (2000–0800), to simulate normal daily routine. Urine samples were collected separately into two different containers during the two periods of time. At the end of the 12 h period of time, patients underwent clean catch catheterization and the obtained urine was the last volume to go into the previous collection, so that all the patients started the new 12 h period of time with an empty bladder. The total urine output was recorded and a sample sent for measurement of urine osmolality.

Blood samples for determination of ADH and plasma osmolality were obtained between 1400 and 1500 for the day and between 0200 and 0300 for the night. Radioimmunoassays for ADH were performed by the Smith-Kline Beecham Clinical Radioimmunoassays according to the methods described by Skowsky *et al*.[10] The sensitivity of the ADH assay was 0.9 pg ml^{-1}. Reference values were 2.00–12.00 pg ml^{-1}. Plasma osmolality was measured by the freezing point depression method.

Results

The mean total day urine output from 0800 to 2000 was 1525 cc and the mean total night urine output from 2000 to 0800 was 1100 cc. Therefore, as shown in Figure 1, the mean (±SE) rate of urine output in the day was 109 ± 18 cc h^{-1} and the night was 111 ± 9 cc h^{-1}. The difference was not statistically significant.

The mean (±SE) daytime plasma osmolality was 282 ± 3 mOsm kg^{-1} and the nocturnal plasma osmolality was 286 ± 1 mOsm kg^{-1} (P = NS, Figure 2), The mean (±SE) daytime urine osmolality was 404 ± 59 mOsm kg^{-1} and the nocturnal urine osmolality was 308 ± 46 mOsm kg^{-1} (P = NS, Figure 2).

There were no statistically significant differences between the day and the night ADH release in our quadriplegic subjects as shown in Figure 3. The mean daytime ADH level was 2.37 ± 0.73 pg ml^{-1} and the nocturnal ADH level was 1.97 ± 0.76 pg ml^{-1}.

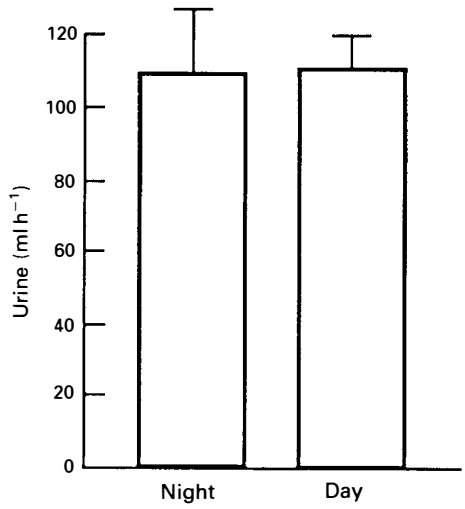

Figure 1 The mean (± SE) rate of urine output during the day and night

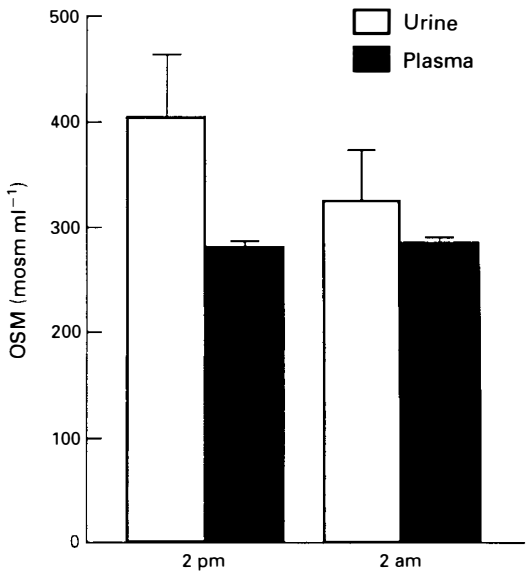

Figure 2 The mean (± SE) plasma and urine osmolality during the day and night

Discussion

In this study, we found no significant difference between day and night urinary output and urine osmolality in tetraplegic individuals. The day and night plasma ADH levels were also not significantly different. Compared to the diurnal rhythm of urine output, concentration and ADH secretion in normal healthy individuals,[5,6] our finding that tetraplegic individuals did not show such a diurnal rhythm may partly explain their relative nocturnal polyuria.

It is possible that, by measuring ADH levels of each subject only once during day and night periods, we have missed the peaks and troughs of each individual's ADH pattern. However, this sampling strategy was meant only to detect differences in ADH secretion

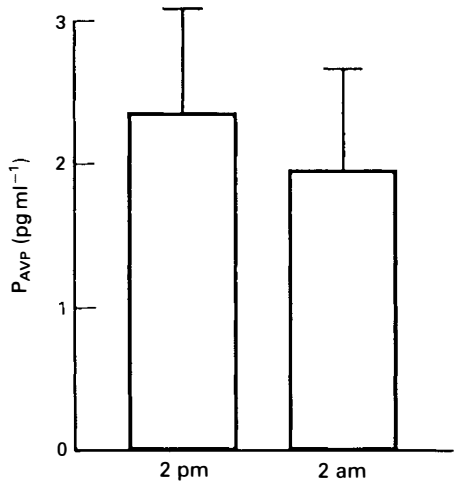

Figure 3 The mean (± SE) antidiuretic hormone secretion during the day and night

from day to night, and for that we believe it to be adequate. George *at al*[5] and Rittig *at al*[7] demonstrated that in normal young males and in normal children, respectively, the nocturnal rise in ADH appears to be sustained over the nocturnal hours, peaking between 2400 and 0400 h. Thus, even if we detected a difference in ADH secretion we would very likely have detected a difference in ADH secretion from day to night. It is unlikely that we would have missed large ADH changes from day to night from mere sampling error. Thus, we believe our study demonstrated attenuation of normal diurnal ADH patterns in tetraplegic subjects.

Our other finding is the low normal levels of ADH (along with low urine osmolality) in the presence of low normal serum osmolality. Low ADH levles have been noted in tetraplegic subjects,[4,11] but only in conjunction with low serum osmolality and hyponatremia, attributed to chronically high fluid intake and possibly resetting of the osmostat, which does not appear to apply to our subjects. Several studies have demonstrated exaggerated ADH response to osmotic and non-osmotic (ie orthostatic) stimuli in tetraplegic individuals relative to able bodied subjects.[2,4,11–13] Our subjects do not seem to follow this pattern, having relatively normal ADH levels for their respective serum osmolality.

In tetraplegic subjects, the efferent pathways from the central nervous system that are normally involved in maintaining cardiovascular homeostasis in postural changes are defective.[14] They are unable to increase the sympathetic activity in the erect posture,[15] causing a fall in the blood pressure and an increased release of ADH.[13,16] This increased postural release of ADH may be an important cause of relative low urine output often seen in tetraplegic individuals during long periods of sitting in the daytime.[17]

Conversely, when tetraplegic individuals lie down at night, the blood pressure increases relative to the sitting position. The blood volume also increases from decreased urine output in daytime and from redistribution of extravascular fluid into intravascular space. The increase in blood pressure and blood volume causes a reduction in the ADH secretion, independent of plasma osmolality, increasing the urine output. In addition, the increase in blood pressure itself can also cause increased urine output due to pressure diuresis.[18]

Therefore, at night, recumbency is associated with a higher urine output in tetraplegic individuals relative to able bodied subjects, a result of multiple factors. These include increased renal perfusion from a rise in blood pressure and redistribution of extravascular fluid into intravascular space. We have demonstrated that the attenuation of the diurnal rhythm of ADH secretion also plays a role.

In conclusion, we have shown that healthy tetraplegic individuals lack the normal nocturnal rise in ADH, a phenomenon similar to that demonstrated in enuretic children[7,8] and in enuretic elderly male patients.[9] This finding provides at least a partial explanation of the relative nocturnal polyuria seen in this group of individuals. Since this study was performed as a preliminary investigation to determine the relationship between ADH and nocturnal polyuria in healthy tetraplegic individuals, further investigations are needed to establish a better understanding of the various factors involved.

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