ORIGINAL ARTICLE

A retrospective review of the ambulatory blood pressure patterns and diurnal urine production in subgroups of spinal cord injured patients

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Study design: Retrospective study.

Objectives: To quantify diurnal blood pressure (BP) patterns and nocturnal hypertension and to measure diurnal urine production in spinal cord injury (SCI) patients with clinically significant disorders of BP control.

Setting: A specialist state-based spinal cord service in Victoria, Australia.

Methods: Medical records of patients with traumatic SCI who were referred to a specialist service for management of a BP disorder were examined. Ambulatory BP and nocturnal urine production were compared between groups of patients classified according to level, completeness and chronicity of SCI. Patients with night:day systolic BP <90% were classified as dippers, 90–100% as non-dippers and >100% as reversed dippers.

Results: Patients (44 tetraplegic, 10 paraplegic) were predominantly males (92.6%) aged 41 ± 2.5 years (mean $\pm$ s.e.m.). Referral was for orthostatic intolerance ($n=37$), autonomic dysreflexia ($n=6$), nocturnal polyuria ($n=4$), elevated BP ($n=1$) and peripheral oedema ($n=1$). The average BP was $111.1 \pm 1.4/65.0 \pm 1.2$ mm Hg. In 56% of patients ($n=30$), BP at night was higher than during the day and another 37% ($n=20$) were non-dippers. Nocturnal hypertension was present in 31% ($n=17$) of the patients. In the tetraplegic patients, urine flow rate was greater during the night than day (121 ± 9.5 ml h⁻¹ vs 89 ± 8.2 ml h⁻¹, $P=0.025$).

Conclusion: Ambulatory BP monitoring in patients with SCI and clinically significant BP disorders detected a high incidence of reversed dipping and nocturnal hypertension. We postulate elevated nocturnal BP may contribute to nocturnal diuresis that might cause relative volume depletion and thereby contribute to daytime orthostatic hypotension.

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INTRODUCTION

Abnormal blood pressure control resulting in orthostatic intolerance is a common and distressing disorder for both able-bodied and spinal cord injury (SCI) patients. At least for able-bodied patients with orthostatic hypotension, guidelines recommend measuring blood pressure over 24 h using an ambulatory device.^{1,2} Monitoring of ambulatory blood pressure in autonomic neuropathy detects episodes of otherwise undetectable hypotension and it can also determine whether night pressures are elevated, which is particularly important when contemplating drug treatments that may further increase already elevated nocturnal pressures. Also, it has been postulated that elevated nocturnal pressures in autonomic neuropathy may contribute to nocturnal diuresis and natriuresis, which in turn is proposed to cause volume depletion which may exacerbate postural hypotension.^{3–5} Thus, in addition to assisting in management of blood pressure disorders, measurement of ambulatory blood pressure may provide insight into the mechanisms contributing to orthostatic hypotension.

Although abnormalities in diurnal blood pressure have been found in patients with SCI, and clinical use of ambulatory blood pressure monitoring has been advocated,⁶ the clinical application of ambulatory blood pressure monitoring in SCI has been incompletely studied. This

is partly because previous studies have specifically excluded patients with 'orthostatic dysregulation' or 'cardiovascular disease'.^{7–9} Whether patients with symptomatic blood pressure disorders have abnormal diurnal variation or nocturnal diuresis, which could potentially contribute to orthostatic hypotension, has not been determined.

In this study, we examined the 24-h ambulatory blood pressure patterns in patients with SCI who had clinically significant problems with blood pressure control. We also measured the nocturnal urine production in a subset of those patients—17 tetraplegics—most of whom had long-term catheters (2 had condom drainage and 1 male did not use voiding aids). Patients included in this study had tetraplegic or paraplegic SCI, complete and incomplete SCI and acute and chronic SCI.

MATERIALS AND METHODS

The protocol for this study was approved by the Human Research Ethics Committee of Austin Health.

A retrospective review of the records in the Blood Pressure Clinic database identified patients with a history of traumatic SCI who were referred to our Blood Pressure Service for blood pressure management between June 2008 and May 2011.

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Demographic details of SCI (date, mechanism of injury, level and completeness of injury), ambulatory blood pressure monitoring results and diurnal urine production were obtained from medical records. The level and completeness of injury were evaluated according to the international standards for neurological classification by the American Spinal Injury Association (ASIA) on admission to the hospital with SCI and on discharge from rehabilitation. The most recent level and ASIA impairment scale (AIS) noted in the medical history were recorded for the purposes of this study.

Ambulatory blood pressure monitoring

Ambulatory blood pressure monitor results were analysed according to mean 24-h, day (0700–2300) and night (2300–0700) values for systolic blood pressure, diastolic blood pressure and pulse rate, obtained from half-hourly measurements during the day and hourly measurements overnight during 24 h of monitoring.

The nocturnal dip was the ratio of night to day systolic blood pressure, expressed as a percentage. Patients with a nocturnal dip of <90% (the normal pattern) were classified as 'dippers', 90–100% as 'non-dippers' and >100% as 'reversed dippers'.¹⁰ Hypertension was defined as a 24-h blood pressure greater than 130/80 mm Hg, daytime hypertension as a daytime blood pressure above 135/85 mm Hg and nocturnal hypertension as a night blood pressure above 120/70 mm Hg.¹¹

Nocturnal urine production

Urine volumes were recorded over three consecutive days, generally within a week of blood pressure monitoring. Measurements reported were average values for the 3 days. Nocturnal urine production was the volume of urine produced overnight, including urine passed on first waking for the day, expressed as a percentage of the entire day's urine output. Nocturnal polyuria was defined as a nocturnal urine volume being >33% of the total daily volume.¹¹

Study groups

Patients were divided firstly according to level of injury, where tetraplegia was defined as a level of injury above T1 and paraplegia, T1 and below. These were then subdivided into patients with complete (AIS A) and incomplete (all others) injury. Next, they were grouped according to whether the SCI was acute (occurring within the past 1 year) or chronic (occurring more than 1 year before the blood pressure monitoring).

Statistical analysis

Analysis was performed using Microsoft Excel. The Student's *t*-test was used to compare continuous variables between study groups (such as blood pressure and nocturnal urine production). The chi-square test was used for categorical variables (such as gender and dipping status). Significance was set at $P < 0.05$. Range intervals represent standard error of the mean (s.e.m.).

RESULTS

Study group characteristics

The patients ($n = 54$) were predominantly male (92.6%), aged 41 ± 2.5 years (mean $\pm$ s.e.m.) and mainly tetraplegic (Table 1). Of the 10 patients with paraplegia, 7 had SCI between T3 and T5, most were complete and all had acute injuries; therefore, paraplegics were only considered as a single group, with insufficient numbers for subgroup

Table 1 Characteristics of study group

	Tetraplegia ($n = 44$)	Paraplegia ($n = 10$)
Level of SCI	C1–C7	T3–12
Complete/incomplete	22/18	9/1
Acute/chronic	29/15	10/0

Abbreviation: SCI, spinal cord injury.

analysis. Records of nocturnal urine production were available for 17 patients with tetraplegia.

Referral to the Blood Pressure Service was for clinically significant blood pressure management issues with referring clinicians specifically requesting assistance with orthostatic intolerance ($n = 37$), autonomic dysreflexia ($n = 6$), nocturnal polyuria ($n = 4$), elevated blood pressure ($n = 1$) and peripheral oedema ($n = 1$). Co-morbidities include sleep apnoea ($n = 6$), hypertension ($n = 3$), diabetes mellitus ($n = 3$), atrial fibrillation ($n = 2$) and congestive cardiac failure ($n = 1$). Medications taken by patients during ambulatory blood pressure monitoring included anti-hypertensives ($n = 4$), pseudoephedrine 30–60 mg daily ($n = 4$) and sodium chloride and/or fludrocortisone 0.1–0.2 mg daily ($n = 3$).

All patients

Of the 54 patients studied, only 4 (7%) had the normal dipping pattern of blood pressure. Thirty (56%) patients had higher pressures at night than during the day (Table 2). Reversed dipping patterns tended to be more common amongst the tetraplegics than paraplegics. Nocturnal hypertension was present in 17 (31%) patients (2 of whom were paraplegic), whereas daytime hypertension and elevated 24-h blood pressure were only present in 2 and 3 tetraplegic patients, respectively. The pulse rate was lower in the tetraplegic compared with the paraplegic patients and both groups had a nocturnal fall in pulse rate.

Mean total daily urine volume in the 17 tetraplegics was 2570 ± 164 ml. An average of $50 \pm 3.3\%$ volume of urine was passed overnight. Urine flow rate was higher during the night than day (121 ± 9.5 ml h⁻¹ vs 89 ± 8.2 ml h⁻¹, $P = 0.025$). The proportion of

Table 2 Blood pressure and pulse rate for all patients, tetraplegics and paraplegics

	All patients ($n = 54$)	Tetraplegics ($n = 44$)	Paraplegics ($n = 10$)	P-value
Age (years)	40.8 ± 2.5	42.8 ± 2.9	32.4 ± 4.2	0.113
Systolic BP (mm Hg)				
24 h	111.1 ± 1.4	110.5 ± 1.6	113.5 ± 2.1	0.392
Day	110.5 ± 1.5	109.5 ± 1.7	114.9 ± 2.1	0.162
Night	112.0 ± 1.6	112.2 ± 1.8	110.7 ± 2.8	0.717
Night:day (%)	101.7 ± 1.3	102.9 ± 1.5	96.5 ± 2.2	0.055
Reversed dippers	30 (56%)	27 (61%)	3 (30%)	0.072
Diastolic BP (mm Hg)				
24 h	65.0 ± 1.2	65.1 ± 1.3	64.4 ± 2.6	0.826
Day	65.9 ± 1.3	65.7 ± 1.4	66.8 ± 2.6	0.736
Night	63.3 ± 1.2	64.0 ± 1.4	59.8 ± 2.9	0.188
Hypertension				
24 h	3 (5.6%)	3 (7%)	0	0.396
Day	2 (3.7%)	2 (5%)	0	0.492
Night	17 (31.5%)	15 (34%)	2 (20%)	0.387
Pulse rate (bpm)				
24 h	72.3 ± 1.9	70.1 ± 1.9	82.1 ± 4.4	0.011
Day	74.4 ± 1.9	71.8 ± 1.9	86.0 ± 4.3	0.002
Night	68.5 ± 2.2	67.0 ± 2.3	74.4 ± 6.2	0.205
Day-Night	5.9 ± 1.4	4.6 ± 1.3	11.6 ± 4.9	0.053

Abbreviation: BP, blood pressure. *P*-values are for comparison between tetraplegics and paraplegics. *P*-values <0.05 are indicated in bold.

urine produced at night was inversely correlated with the 24 h systolic pressure ($r^2=0.25$, $P=0.043$) and day systolic pressure ($r^2=0.30$, $P=0.022$) and there was a trend to a direct correlation with the night: day systolic pressures ($r^2=0.19$, $P=0.078$).

Complete vs incomplete tetraplegia

Compared with those with incomplete injuries, tetraplegic patients with complete injuries were younger, had lower day blood pressures and a greater incidence of reversed dipping (Table 3). In incomplete injuries, pressures at night were lower than day values for both diastolic ($P<0.001$) and systolic pressure ($P=0.166$), whereas night systolic pressures were higher than the day measurement for complete injuries ($P=0.003$). Compared with day values, the pulse rate fell in both groups at night ($P<0.05$).

There was a higher total daily urine volume in patients with a complete injury, and their urine flow rate at night was significantly higher than in the day ($P=0.035$).

Table 3 BP and urine measurements for complete and incomplete tetraplegics

	Complete (n = 22)	Incomplete (n = 18)	P-value
Age (years)	37 ± 3.4	51 ± 4.3	0.011
Systolic BP (mm Hg)			
24 h	109.0 ± 2.3	113.0 ± 2.5	0.255
Day	106.5 ± 2.3	114.3 ± 2.9	0.037
Night	113.4 ± 2.9	110.7 ± 2.6	0.449
Night:Day (%)	106.7 ± 1.9	97.2 ± 1.9	0.002
Reversed dippers	16 (73%)	7 (39%)	0.031
Diastolic BP (mm Hg)			
24 h	63.7 ± 1.7	68.3 ± 2.1	0.101
Day	63.1 ± 1.6	70.5 ± 2.3	0.011
Night	64.9 ± 2.1	64.1 ± 2.0	0.805
Hypertension			
24 h	1 (5%)	2 (11%)	0.433
Day	0	2 (11%)	0.109
Night	10 (45%)	4 (22%)	0.125
Pulse rate			
24 h	70.9 ± 2.7	69.7 ± 2.9	0.759
Day	72.7 ± 2.6	71.1 ± 3.0	0.688
Night	67.6 ± 3.3	66.9 ± 3.1	0.880
Urine Measures	Complete (n = 10)	Incomplete (n = 7)	P-value
Volumes (ml)			
Total	2867 ± 193	2140 ± 206	0.023
Day	1439 ± 198	1123 ± 160	0.265
Night	1428 ± 105	1017 ± 197	0.065
Nocturnal (%)	52.0 ± 4.0	46.1 ± 5.7	0.399
Flow rates (ml h ⁻¹)			
Day	95 ± 12	80 ± 11	0.378
Night	132 ± 7.0	105 ± 20	0.172
Night:Day	1.6 ± 0.2	1.5 ± 0.4	0.789

Abbreviation: BP, blood pressure. P-values <0.05 are indicated in bold.

Acute vs chronic tetraplegics

Patients with acute injuries were younger than those with chronic injuries (Table 4). The average time between monitoring and SCI was 3.1 months (1.1–6.0 months) in the acute group. Patients in the chronic group had had SCI for an average of 32.5 years (4–48 years).

Compared with patients with chronic injuries, patients with acute injury had lower blood pressure, particularly the diastolic pressure, higher night:day systolic pressure and a greater proportion of reversed dippers. Pulse rates for both groups were similar, including the presence of nocturnal fall.

Compared with the chronic tetraplegics, acute tetraplegics had lower day urine production and passed a greater proportion of their urine at night, and had a significantly higher night urine flow rate than that in the day ($P=0.002$).

Table 5 summarises the nocturnal blood pressure dipping ratios and nocturnal urine volumes for subgroups of tetraplegics.

Table 4 BP and urine measurements for acute and chronic tetraplegics

	Acute (n = 29)	Chronic (n = 15)	P-value
Age (years)	38 ± 3.8	52 ± 3.2	0.029
Systolic BP (mm Hg)			
24 h	109.4 ± 1.8	112.7 ± 3.2	0.326
Day	107.4 ± 1.6	113.7 ± 3.8	0.084
Night	113.1 ± 2.4	110.6 ± 2.9	0.526
Night:Day (%)	105.4 ± 1.6	98.1 ± 2.7	0.017
Reversed dippers	21 (72%)	6 (40%)	0.036
Diastolic BP (mm Hg)			
24 h	62.8 ± 1.3	69.6 ± 2.6	0.011
Day	63.0 ± 1.3	70.9 ± 3.1	0.008
Night	62.4 ± 1.6	67.1 ± 2.4	0.104
Hypertension			
24 h	1 (3%)	2 (13%)	0.218
Day	0	2 (13%)	0.044
Night	9 (31%)	6 (40%)	0.552
Pulse rate			
24 h	71.9 ± 2.2	66.6 ± 3.6	0.191
Day	73.7 ± 2.1	67.9 ± 3.6	0.141
Night	68.8 ± 2.9	63.9 ± 3.8	0.319
Urine Measures	Acute (n = 12)	Chronic (n = 5)	P-value
Volumes (ml)			
Total	2448 ± 172	2854 ± 374	0.272
Day	1133 ± 123	1731 ± 297	0.040
Night	1315 ± 126	1123 ± 235	0.447
Nocturnal (%)	54.1 ± 3.4	38.8 ± 5.6	0.029
Flow rates (ml h ⁻¹)			
Day	77 ± 6.6	117 ± 19	0.019
Night	127 ± 12	106 ± 16	0.319
Night:Day	1.8 ± 0.2	1.0 ± 0.2	0.051

Abbreviation: BP, blood pressure. P-values <0.05 are indicated in bold.

Table 5 Nocturnal dipping ratio and urine volumes for subgroups of tetraplegics

	Complete	Incomplete
<i>Night:Day SBP (%)</i>		
Acute	108.5 ± 1.8 (n = 16)	98.9 ± 2.5 (n = 9)
Chronic	102.1 ± 5.1 (n = 6)	95.5 ± 3.0 (n = 9)
<i>Nocturnal urine volume (%)</i>		
Acute	53.1 ± 4.3 (n = 8)	56.0 ± 6.0 (n = 4)
Chronic	47.5 ± 13.5 (n = 2)	33.0 ± 0.6 (n = 3)

Abbreviation: SBP, systolic blood pressure.

DISCUSSION

In our population of SCI patients who were referred for blood pressure management, ambulatory monitoring revealed a substantial prevalence of reversed dipping or nocturnal hypertension, despite a relatively low prevalence of 24-h or daytime hypertension, and these abnormalities tended to be more frequent amongst patients with acute, complete or tetraplegic injuries. In addition to the higher incidence of reversed dipping of blood pressure, we also found higher nocturnal urine production in patients with acute or complete SCI when compared with patients with chronic or incomplete injuries, respectively (Table 5).

The mechanisms explaining these findings are uncertain. One explanation for the reversed diurnal variation of blood pressure is that interruption of sympathetic nervous system tracts rendered our patients unable to maintain blood pressure when upright during the day. This is in keeping with the observation that patients with incomplete SCI, who presumably have more intact sympathetic nervous system tracts, tended to have a lower incidence of non-dipping. It is also consistent with the high incidence of non-dipping seen in autonomic neuropathy, which is another condition associated with impaired orthostatic blood pressure control.^{12,13} However, in both SCI and autonomic failure, not all patients have non-dipping, implying that factors other than damage to the autonomic nervous system cause changes in diurnal blood pressure profiles. For example, the lower incidence of abnormal blood pressure or urine production in our patients with chronic injury suggests that at a time that is more than 6 months after SCI, adaptive mechanisms unrelated to spinal cord function might develop to modulate blood pressure control.

Similarly, the mechanism explaining nocturnal polyuria is unclear. In general, the patient groups in our study that had a higher incidence of non-dipping also had a relatively higher rate of nocturnal urine flow, raising the possibility that the diuresis may have been directly related to renal perfusion pressures. However, at least in patients with autonomic failure, natriuresis can be independent of elevated nocturnal pressures.⁵

The importance of these findings relates to a potential role for nocturnal blood pressure elevation in orthostatic intolerance. It has been proposed that attenuating the excessive natriuresis of autonomic failure by selectively reducing nocturnal blood pressure may provide relief from orthostatic symptoms. In autonomic neuropathy, sleeping with a head up tilt was suggested to attenuate orthostatic hypotension by reducing renal perfusion pressure and thereby reducing diuresis.¹⁴ Similarly, short-acting nocturnal anti-hypertensive agents have reduced nocturnal blood pressure and nocturnal natriuresis in patients with primary autonomic failure.^{15–17} However, head up tilt is problematic in the SCI population, because their sleeping position is determined by other considerations, such as prevention of pressure

injury. Short-acting nocturnal anti-hypertensives are a potential pharmacological alternative to head up tilt, but their role in SCI has not been examined.

Our results differ from previous studies that found a loss of diurnal variation in blood pressure only in patients with chronic and complete tetraplegics, but not in incomplete tetraplegics or complete paraplegics.^{7–9} To some extent, this difference may be explained by those studies excluding patients with conditions such as known cardiovascular disorders, autonomic dysreflexia and orthostatic dysregulation, thus potentially excluding a population of patients in whom disruption of blood pressure control may be greatest.

The other interesting aspect of our study is our measurement of the prevalence of nocturnal hypertension in patients with SCI, a parameter that has not previously been reported in similar studies. Reversed dipping and nocturnal hypertension may have implications for risk of cardiovascular disease, which may be elevated in patients with SCI.¹⁸ Studies in the general population have found that night blood pressure and reversed diurnal variation are important factors in predicting cardiovascular risk^{19–21} and it may be that the results of ambulatory monitoring can be used to detect patients who would benefit from treatments aimed at reducing cardiovascular risk.

In addition to orthostatic intolerance, autonomic dysreflexia is the other major blood pressure problem seen in SCI. It has been proposed that the loss of diurnal blood pressure variation may be a feature of tetraplegic patients with dysreflexia.²² However, autonomic dysreflexia was a relatively uncommon cause of referral in our study group (6 of 44 tetraplegic patients), yet almost all patients exhibited an abnormal diurnal blood pressure pattern. Further studies should be directed towards examining whether abnormalities of diurnal blood pressure variation are more common or contribute to autonomic dysreflexia in SCI.

Although our study was retrospective and limited to a relatively small number of patients, its strength was that it only included patients who had a clinical reason for measurement of ambulatory blood pressure. The high incidence of abnormalities in this group suggests that the role of measuring ambulatory monitoring should be further explored in these patients.

CONCLUSION

We conclude that ambulatory blood pressure monitoring is a useful diagnostic method for nocturnal hypertension and reversed dipping in patients with SCI who are referred for blood pressure management. The reversal of diurnal blood pressure variation, elevation of nocturnal blood pressure and increased night urinary flow rates support the nocturnal blood pressure as a potential therapeutic target.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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- 1 Head GA, McGrath BP, Mihailidou AS, Nelson MR, Schlaich MP, Stowasser M *et al*. Ambulatory blood pressure monitoring in Australia: 2011 consensus position statement. *J Hypertens* 2011; **30**: 253–266.
- 2 Ejaz AA, Kazory A, Heinig ME. 24-hour blood pressure monitoring in the evaluation of supine hypertension and orthostatic hypotension. *J Clin Hypertens (Greenwich)* 2007; **9**: 952–955.

- 3 Mathias CJ. Orthostatic hypotension and paroxysmal hypertension in humans with high spinal cord injury. *Prog Brain Res* 2006; **152**: 231–243.
- 4 Omboni S, Smit AA, van Lieshout JJ, Settels JJ, Langewouters GJ, Wieling W. Mechanisms underlying the impairment in orthostatic tolerance after nocturnal recumbency in patients with autonomic failure. *Clin Sci (Lond)* 2001; **101**: 609–618.
- 5 Okamoto LE, Gamboa A, Shibao C, Black BK, Diedrich A, Raj SR *et al*. Nocturnal blood pressure dipping in the hypertension of autonomic failure. *Hypertension* 2009; **53**: 363–369.
- 6 Hubli M, Krassioukov AV. Ambulatory blood pressure monitoring in spinal cord injury: clinical practicability. *J Neurotrauma* 2014; **31**: 789–797.
- 7 Munakata M, Kameyama J, Kanazawa M, Nunokawa T, Moriai N, Yoshinaga K. Circadian blood pressure rhythm in patients with higher and lower spinal cord injury: simultaneous evaluation of autonomic nervous activity and physical activity. *J Hypertens* 1997; **15**: 1745–1749.
- 8 Nitsche B, Perschak H, Curt A, Dietz V. Loss of circadian blood pressure variation in complete tetraplegia. *J Hum Hypertens* 1996; **10**: 311–317.
- 9 Krum H, Louis WJ, Brown DJ, Jackman GP, Howes LG. Diurnal blood pressure variation in quadriplegic chronic spinal cord injury patients. *Clin Sci* 1991; **80**: 271–276.
- 10 Ohkubo T, Imai Y, Tsuji I, Nagai K, Watanabe N, Minami N *et al*. Relation between nocturnal decline in blood pressure and mortality. The Ohasama Study. *Am J Hypertens* 1997; **10**: 1201–1207.
- 11 Cannon A, Carter P, McConnell A, Abrams P. Desmopressin in the treatment of nocturnal polyuria in the male. *BJU Int* 1999; **84**: 20–24.
- 12 Mann S, Altman D, Raftery E, Bannister R. Circadian variation of blood pressure in autonomic failure. *Circulation* 1983; **68**: 477–483.
- 13 Sommer S, Aral-Becher B, Jost W. Nondipping in Parkinson's disease. *Parkinsons Dis* 2011; **2011**: 897586.
- 14 Mathias CJ. Autonomic dysfunction and hypotension. In Willerson JT, Wellens HJ, Cohn JN, Holmes DR (eds). *Cardiovascular Medicine*, 3rd edn, Springer: London, UK, 2007, pp 1883–1910.
- 15 Jordan J, Shannon JR, Pohar B, Paranjape SY, Robertson D, Robertson RM *et al*. Contrasting effects of vasodilators on blood pressure and sodium balance in the hypertension of autonomic failure. *J Am Soc Nephrol* 1999; **10**: 35–42.
- 16 Shannon J, Jordan J, Costa F, Robertson RM, Biaggioni I. The hypertension of autonomic failure and its treatment. *Hypertension* 1997; **30**: 1062–1067.
- 17 Shibao C, Gamboa A, Abraham R, Raj SR, Diedrich A, Black B *et al*. Clonidine for the treatment of supine hypertension and pressure natriuresis in autonomic failure. *Hypertension* 2006; **47**: 522–526.
- 18 Lee C-S, Lu Y-H, Lee S-T, Lin C-C, Ding H-J. Evaluating the prevalence of silent coronary artery disease in asymptomatic patients with spinal cord injury. *Int Heart J* 2006; **47**: 325–330.
- 19 Hoshida S. Associations between nondipping of nocturnal blood pressure decrease and cardiovascular target organ damage in strictly selected community-dwelling normotensives. *Am J Hypertens* 2003; **16**: 434–438.
- 20 Boggia J, Li Y, Thijs L, Hansen TW, Kikuya M, Björklund-Bodegård K *et al*. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. *Lancet* 2007; **370**: 1219–1229.
- 21 Fagard RH, Thijs L, Staessen JA, Clement DL, De Buyzere ML, De Bacquer DA. Prognostic significance of ambulatory blood pressure in hypertensive patients with history of cardiovascular disease. *Blood Press Monit* 2008; **13**: 325–332.
- 22 Curt A, Nitsche B, Rodic B, Schurch B, Dietz V. Assessment of autonomic dysreflexia in patients with spinal cord injury. *J Neurol Neurosurg Psychiatry* 1997; **62**: 473–477.