Diurnal blood pressure variation in quadriplegic chronic spinal cord injury patients

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(Received 18 December 1989/15 October 1990; accepted 19 October 1990)

SUMMARY

1. Measurement of blood pressure and heart rate over a 24 h period was performed in 10 quadriplegic spinal cord injury patients and 10 immobilized, neurologically intact orthopaedic subjects by using the Spacelabs 90207 automated ambulatory monitoring system.

2. Systolic and diastolic blood pressure fell significantly at night in orthopaedic subjects but not in quadriplegic patients, and night-time blood pressures were similar in both groups.

3. Cumulative summation of differences from a reference value (cusum analysis) confirmed a markedly diminished diurnal blood pressure variation in the quadriplegic patients.

4. These findings could not be accounted for on the basis of blood pressure variations during chronic postural change.

5. Heart rate fell significantly at night in both groups.

6. The findings suggest that the increase in blood pressure during waking hours in neurologically intact subjects is a consequence of a diurnal variation in sympathetic activity (absent in quadriplegic patients with sympathetic decentralization) which is independent of changes in physical activity.

Key words: ambulatory monitoring, blood pressure, catecholamines, circadian variation.

INTRODUCTION

Diurnal variation of blood pressure is well described in normal subjects, with substantial falls in blood pressure occurring at night during sleep [1]. The mechanism for this diurnal variation is uncertain and controversy exists regarding the relative contribution of alterations in physical activity [2] as opposed to cyclical alterations in the activity of the sympathetic nervous system [3], the renin–angiotensin–aldosterone system [3–5], cortisol secretion [4–6] and atrial natriuretic peptide secretion [7], which are independent of physical activity.

In order to further investigate the role of the central and peripheral nervous system in the maintenance of diurnal blood pressure variation, we monitored blood pressure for 24 h to study day–night blood pressure differences in quadriplegic patients with neurologically complete lesions above the first thoracic spinal cord segment. These patients have decentralized spinal cord sympathetic outflow which is associated with markedly reduced plasma noradrenaline levels due to a decreased spillover rate of noradrenaline into the circulation from sympathetic nerve terminals [8].

As quadriplegic patients have reduced mobility and relatively low levels of physical activity, fully immobilized but neurologically intact orthopaedic patients were used as control subjects.

METHODS

Subjects

Ten chronic quadriplegic patients and ten age- and sex-matched orthopaedic control subjects underwent intermittent automated blood pressure monitoring over a 24 h period by an ambulatory blood pressure recorder. Fully informed consent was obtained from all subjects and the study protocol was approved by the Ethical Review Committee of Austin Hospital. Demographic data for all subjects are summarized in Table 1. None of the orthopaedic subjects had suffered from cardiovascular disease nor were they taking medication which may have affected blood pressure. All of the orthopaedic subjects had been immobilized for at least 5 days. The quadriplegic patients were not receiving medication known to affect the cardio-
Table 1. Demographic data of quadriplegic spinal cord injury patients and orthopaedic control subjects used for study of diurnal blood pressure variations

There were no statistically significant differences in ages between the two groups studied (Student's unpaired t-test). Age values are means ± SEM.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Smoking status</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of males</td>
<td>No. of females</td>
</tr>
<tr>
<td>Quadriplegic spinal cord injury patients (n = 10)</td>
<td>44.0 ± 6.64</td>
<td>8</td>
</tr>
<tr>
<td>Orthopaedic control subjects (n = 10)</td>
<td>41.7 ± 6.29</td>
<td>8</td>
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</table>

vascular system except for anticholinergic type medication in two patients (amitriptyline), which was not altered during the study period. Quadriplegic patients were also receiving bowel aperients, urinary antiseptics and muscle relaxants, which would not be expected to affect the cardiovascular system. Intake of alcohol and caffeine was prohibited from midnight before the day of ambulatory monitoring and for the duration of the monitoring period. All subjects were on a standard hospital diet and were taking free fluids. Cigarette smoking was permitted during the study period. There were three smokers in the orthopaedic group and four in the quadriplegic group. There were no restrictions on physical activity in the quadriplegic group, who were mostly independently mobile in wheelchairs. Orthopaedic subjects remained in bed throughout the study period and generally had a lower level of physical activity than the quadriplegic patients.

Blood pressure monitoring

Twenty-four hour blood pressure monitoring was performed by using the Spacelabs 90207 ambulatory blood pressure system (Spacelabs Inc., Redmond, WA, U.S.A). Systolic blood pressure, diastolic blood pressure and heart rate were recorded automatically half-hourly from 06.00 hours to 24.00 hours, then hourly overnight. The device was calibrated against a mercury sphygmomanometer before the commencement of recording in each patient. Recordings considered to be artefacts (pulse pressure less than 10 mmHg, heart rate less than 30 beats/min or greater than 100 beats/min) were excluded. At least 25 valid blood pressure and heart rate recordings were required within the 24 h period to be included in the study.

Cumulative summation of differences from a reference value [cusum analysis] [9] was performed on mean hourly recordings for each patient to examine differences in blood pressure trends over the 24 h.

To ascertain whether blood pressure levels were altered by postural change (e.g. from bed to wheelchair) in quadriplegic patients, we compared the mean of three measurements of diastolic blood pressure and systolic blood pressure during awake bed rest and after 1 h of sitting in a wheelchair.

Statistical analysis

Differences in blood pressure levels during awake bed rest and 1 h of wheelchair sitting were compared by using Student's paired t-test.

The mean and SEM for systolic blood pressure, diastolic blood pressure and heart rate were obtained for day-time readings (06.00–24.00 hours) and night-time readings (24.00–06.00 hours) for each of the two groups.

Blood pressure and heart rate differences between the two groups and between day-time and night-time were analysed by two-way analysis of variance with pairwise comparisons by analysis of simple effects (using the CLR-ANOVA program). Linear regression of cusum slopes before (16.00–22.00 hours) and during (24.00–06.00 hours) sleep were determined in each patient. Two-way analysis of variance was performed to look for significant differences in these cusum slopes in both study groups.

RESULTS

The paired data for blood pressure levels during awake bed rest and 1 h of wheelchair sitting are presented in Fig. 1. There were no significant differences in blood pressure level between these two positions.

The mean and SEM of day-time and night-time readings for the 24 h blood pressure monitoring are summarized in Table 2. Mean day–night blood pressure and heart rate differences are presented in Fig. 2. Orthopaedic subjects had higher day-time systolic and diastolic blood pressures than quadriplegic patients, but this difference did not reach statistical significance. Systolic and diastolic blood pressures fell significantly at night in orthopaedic patients, but not in quadriplegic patients. Heart rate fell significantly at night in both groups, but there was a much larger fall in the orthopaedic group.

Pooled mean hourly recordings for systolic blood pressure and diastolic blood pressure in both the quadriplegic group and orthopaedic group are presented in Fig. 3.

These data demonstrate the maintenance of a diurnal variation in both systolic blood pressure and diastolic blood pressure in the orthopaedic subjects despite their physical immobility. No obvious diurnal variation is discernible in the quadriplegic group.
Diurnal blood pressure variation in quadriplegic patients

Pooled cusum analyses of mean hourly readings in each patient (reference value = 24 h mean of hourly recordings) are presented in Fig. 4 and individual cusum slopes derived from linear regression are presented in Table 3. There were significant differences in cusum slope around the time of sleep for both systolic and diastolic blood pressure in both groups; however, the 24.00–06.00 hours cusum slopes were significantly attenuated in the quadriplegic patients, suggesting a markedly attenuated nocturnal blood pressure fall in this group.

DISCUSSION

The marked diminution of diurnal variation of blood pressure in quadriplegic patients with sympathetic de-

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**Table 2. Average day-time and night-time blood pressures and heart rates in quadriplegic spinal cord injury patients and orthopaedic control subjects**

Although day-time systolic and diastolic blood pressures were lower in the quadriplegic group, this difference did not reach statistical significance. Day-time heart rate was significantly higher in the orthopaedic group than the quadriplegic group (*P*< 0.005). Systolic and diastolic blood pressures fell significantly at night in the orthopaedic group (††*P* < 0.005) but not in the quadriplegic group. Heart rate fell significantly at night in both orthopaedic subjects (‡*P*< 0.005) and quadriplegic patients (‡‡*P*< 0.005). Statistical analysis was performed by two-way analysis of variance with pairwise comparison of significant values by analysis of simple effects. Values are means ± SEM.

<table>
<thead>
<tr>
<th></th>
<th>Systolic blood pressure (mmHg)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>Heart rate (beats/min)</th>
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<tbody>
<tr>
<td></td>
<td>Day-time</td>
<td>Night-time</td>
<td>Day-time</td>
</tr>
<tr>
<td>Quadriplegic spinal cord injury patients (n = 10)</td>
<td>117.86 ± 7.23</td>
<td>116.26 ± 5.71</td>
<td>68.51 ± 3.21</td>
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<tr>
<td>Orthopaedic control subjects (n = 10)</td>
<td>126.13 ± 2.98</td>
<td>113.65 ± 3.13‡</td>
<td>73.40 ± 1.65</td>
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</table>
centralization demonstrates not only the importance of intact pathways between the central and peripheral nervous systems in the maintenance of blood pressure, but also of its diurnal rhythm in man. A number of studies have documented decreases in sympathetic activity at night in normal subjects, reflected by lower levels of urinary and plasma catecholamines [3–5]. In addition, circadian variation of urinary noradrenaline and adrenaline is maintained (but diminished) during 24 h bed rest in neurologically intact subjects [3]. Quadriplegic patients have very low levels of day-time sympathetic activity, resulting in low plasma noradrenaline levels and low systemic blood pressure levels. These patients are also unable to increase sympathetic nervous system activity in response to physiological stimuli such as the assumption of an upright posture from recumbency [10]. In addition, loss of a diurnal variation of sympathetic activity (measured by urinary catecholamine secretion) has been demonstrated [11]. Nocturnal plasma noradrenaline levels in normal subjects have been shown to decrease to levels similar to the low day-time levels observed in quadriplegic patients [4, 8, 10].

Other studies have also documented loss of nocturnal blood pressure falls (or day-time rises) in subjects with autonomic dysfunction including the Shy–Drager syndrome [12] and cardiac transplantation (where cardiac sympathetic denervation occurs) [13].

It is possible that other vasoactive hormones play a role in diurnal variation of blood pressure. Unlike noradrenaline, however, plasma renin, aldosterone and arginine vasopressin demonstrate normal or exaggerated responses to physiological manoeuvres such as orthostasis in patients after spinal cord injury [10, 14, 15], and may mediate the recovery of cardiovascular homeostatic mechanisms in these subjects. Alterations in the secretion of these hormones would therefore appear unlikely to contribute to the loss of diurnal blood pressure variation in quadriplegic patients.

The present study also demonstrates that the lack of diurnal variation in quadriplegic patients cannot be
Diurnal blood pressure variation in quadriplegic patients

Table 3. Slope of cusum deviation from mean

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<thead>
<tr>
<th></th>
<th>Quadriplegic patients</th>
<th>Orthopaedic subjects</th>
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<tr>
<td></td>
<td>SBP 16.00-22.00 hours</td>
<td>DBP 16.00-22.00 hours</td>
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<tr>
<td>Slope</td>
<td></td>
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<tr>
<td></td>
<td>1.4</td>
<td>-10.2</td>
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<tr>
<td></td>
<td>1.8</td>
<td>-12.4</td>
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<td></td>
<td>4.5</td>
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<td>6.3</td>
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<tr>
<td></td>
<td>8.9</td>
<td>-10.4</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>-3.0</td>
</tr>
<tr>
<td></td>
<td>2.1</td>
<td>-16.1</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>-33.2</td>
</tr>
<tr>
<td></td>
<td>3.9</td>
<td>-17.0*</td>
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<tr>
<td>Mean</td>
<td>1.36</td>
<td>-3.30</td>
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<td></td>
<td>3.28</td>
<td>3.77</td>
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<td>3.05</td>
<td>4.58</td>
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Slope of cusum deviation from the mean derived from linear regression of cusum values before (16.00-22.00 hours) and during (24.00-06.00 hours) sleep. There were significant differences in cusum slope between the two time points in both quadriplegic patients (systolic blood pressure, $P=0.015$; diastolic blood pressure, $P=0.002$) and orthopaedic control subjects (systolic blood pressure, $P=0.000$; diastolic blood pressure, $P=0.000$). There were no significant differences in cusum slope at 16.00-22.00 hours between the two study groups for systolic blood pressure ($P=0.274$) and diastolic blood pressure ($P=0.981$). There were significant differences in cusum slope at 24.00-06.00 hours between the two study groups for systolic blood pressure ($*P=0.000$) and diastolic blood pressure ($**P=0.001$), suggesting a significant attenuation of diurnal blood pressure variation in the quadriplegic group. Statistical analysis was performed by two-way analysis of variance with pairwise comparisons by analysis of simple effects. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

ACKNOWLEDGMENTS

H.K. is a National Health and Medical Research Council of Australia Postgraduate Medical Research Scholar. This work was supported by the Austin Hospital Medical Research Foundation and a NH & MRC Program Grant.

REFERENCES


accounted for on the basis of postural change from night-time recumbency to day-time sitting (in a wheelchair). Postural hypotension is much less of a problem in the chronic compared with the acute spinal cord injury patient, and if it occurs is usually an acute short-term phenomenon. In the present study, the lack of an overall reduction in blood pressure on changing from awake bed rest to wheelchair sitting would appear to confirm this finding. In addition, there were no symptomatic complaints of postural hypotension during the period of monitoring.

Loss of diurnal blood pressure variation has also been demonstrated in acute post spinal injury patients during their immediate management in the emergency room [16]. However, the period of study involved continual management interventions by staff in an area of continuous lighting and noise. It is therefore difficult to separate these effects from the direct effect of the spinal cord injury itself.

The present study has also documented significant reductions in heart rate at night in both groups. Heart rate reductions in normal man are mediated by increased vagal tone to the heart as well as the withdrawal of sympathetic activity. As efferent vagus innervation is intact in quadriplegic patients, increased vagal tone appears likely to account for the small but significant fall in heart rate at night in these patients. It is possible that the smaller fall in heart rate at night in spinal cord injury patients was due in part to the anticholinergic drug therapy.

In summary, this study demonstrates that nocturnal falls in blood pressure are markedly diminished in quadriplegic patients but are maintained in neurologically intact orthopaedic subjects who were almost totally immobile. The findings suggest that the increase in blood pressure during waking hours compared with night-time is a consequence of a diurnal variation in sympathetic activity which is relatively independent of changes in physical activity.


