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Awakening Blood Pressure Rise in a Patient with Spinal Cord Injury

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 66
Final Diagnosis: Awakening blood pressure rise
Symptoms: Syncope
Medication: —
Clinical Procedure: Ambulatory blood pressure monitoring
Specialty: Cardiology

Objective: Challenging differential diagnosis

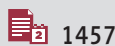
Background: The pathophysiological mechanism causing awakening blood pressure (BP) rise is not clear.

Case Report: We report the case of a 66-year-old man with a history of spinal cord injury, and who had remarkable awakening BP rise in ambulatory BP monitoring. The patient also had orthostatic hypotension and post-prandial hypotension associated with an increased insulin level. This case suggests that awakening BP rise can occur without increased physical activity or positional changes, in those with autonomic nerve dysreflexia associated with a spinal cord injury. The reduction of elevated awakening BP level can be affected by eating breakfast in association with an increased insulin level. However, in ambulatory BP monitoring, the awakening BP rise was reproducible, but this patient also exhibited evening BP rise in home BP monitoring when he took a nap.

Conclusions: Exaggerated awakening BP rise can occur in patients with spinal cord injury without positional change, and the recovery of BP may be modified by post-prandial and orthostatic BP drop.

MeSH Keywords: Baroreflex • Blood Pressure Monitoring, Ambulatory • Hypotension, Orthostatic • Spinal Cord Injuries

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/895825>



Background

BP tends to be higher upon awakening in the morning than at other times during ambulatory BP monitoring, and it has been reported that the elevated BP is associated with elevated incidence of cardiovascular events early in the morning [1,2]. However, the cause of BP elevation in the morning remains unclear. The possible mechanisms causing BP elevation in the morning are: (1) postural change (orthostatic hypertension) [3,4], (2) sympathetic nerve activation [5], (3) activation of the renin-aldosterone system, and (4) activation of the cortisol system. Kario et al. [4] hypothesized that subjects with awakening BP rise were associated with orthostatic BP rise after standing up. Stergiou et al. [6] also reported that BP rise after awakening can occur even after taking a nap. These reports suggest that the BP rise in the morning hours is a phenomenon that occurs after awakening (but it is not a chronological phenomenon).

Patients with spinal cord injury often have autonomic nerve dysfunction, which causes increased blood pressure variability; however, there is no previous report showing that awakening blood pressure rise could be observed in patients with spinal cord injury.

Case Report

Patient's history

A 66-year-old man was admitted to the hospital because of repeated syncope due to postprandial hypotension. The patient had sustained a spinal cord injury at the level between the 4th and 5th thoracic vertebra when he was 24 years old. After the injury, he had paraplegia and lies on the bed throughout the day, except when in a wheel chair in a passive sitting position. He had strong constipation and was obliged to use glycerin sp. for defecation on a regular basis.

Several months before the admission, the patient became unconscious just after eating and after sitting repeatedly, and he was therefore admitted to the hospital. On physical examination, he was alert when he was lying down on the bed. Blood pressures (BP) measured at the left upper arm in a supine position were 154/81 mmHg before breakfast, 69/43 mmHg after breakfast, 116/71 mmHg before dinner, and 84/54 mmHg after dinner. BP also dropped from 128/90 mmHg (pulse rate 62 beats per min) in a supine position to 89/61 mmHg (pulse rate 56 beats per min) after sitting-up for 30 min. His height was 150 cm, body weight was 50 kg, and body mass index was 22.2 kg/m². There were no bruits on the neck or abdomen. Heart and respiratory sounds were normal. The abdomen was not distended. There was no edema in his feet. The

patient was alert and had normal higher cerebral function, but he was paraplegic and had sensory disturbance at the level of the 4th thoracic vertebra. The chest x-ray and electrocardiogram were normal. There was no episode of arrhythmia suggesting Adam-Stokes attack in the continuous electrocardiogram monitor. In the laboratory examination (Table 1) there were no significant findings suggestive of anemia, diabetes, or secondary hypertension. Brain CT was normal. In the echocardiogram, the wall motion of the left ventricle was normal.

The results of BP during a 75-g glucose tolerance test are shown in Figure 1. The fasting glucose level was 102 mg/dl and increased to 171 mg/dl at 60 min after 75-g glucose ingestion. The level of serum insulin had a parallel change to serum glucose level. The BP had the opposite change to serum insulin level (i.e., it dropped until 60 min after 75-g glucose ingestion, and then recovered). Additionally, even when glucose was administered to the patient intravenously, there was a drop in BP at the time when the insulin level was elevated (Figure 2).

The result of 24-h ambulatory BP monitoring (taken at 15-min intervals) is shown in Figure 3. The mean 24-h ambulatory BP was 122/74 mmHg (pulse rate 62 beats/min). The blood pressure decreased remarkably after eating in a supine position. Moreover, awakening systolic BP was increased by 78 mmHg (from the night-time lowest systolic BP 89 mmHg to morning systolic BP 167 mmHg), according to the definition in a previous report [2]. Percutaneous oxygen saturation during sleeping hours was normal, and the patient was unlikely to have had sleep-disordered breathing. The result of heart rate variability showed that there were no findings suggestive of sympathetic nerve activation, as measured as low-frequency (LF)/high-frequency (HF) component, in the morning hours, although parasympathetic nerve activations, measured as HF component, were observed after breakfast. The patient was evaluated for serum catecholamine, renin activity, aldosterone, and cortisol levels just before sleeping and after awakening (in the same supine position). On another day of 24-h BP monitoring, the serum adrenaline and cortisol levels in the morning hours were slightly higher than those in the evening (adrenaline, 9.0 to 13.0 pg/ml; cortisol, 5.3 to 9.5 µg/dl), but the levels of dopamine, noradrenaline, and aldosterone, as well as plasma renin activity, in the morning hours were slightly lower than those in the evening (dopamine 24.0 to <5.0 pg/ml, noradrenaline, 297.0 to 251.0 pg/ml; renin activity, 0.3 to 0.2 ng/ml/hr; aldosterone, 65.4 to 42.3 pg/ml).

The awakening BP rise was reproducible in a repeated ambulatory BP monitoring; however, this patient demonstrated BP rise not only in the morning, but also in the evening when he took a nap during home BP monitoring. The patient was prescribed Droxidopa 200 mg p.o. at 30 min before eating, and was discharged from the hospital without unconscious events after eating.

Table 1. Laboratory data.

	Value	Normal range	Unit
White blood cell	5300	3900~9800	/ μ l
Red blood cell	364	427~570	$\times 10^6$ / μ l
Hemoglobin	11.2	13.5~17.6	g/dl
Hematocrit	34.2	39.8~51.8	%
Platelet	19.9	13.1~36.2	$\times 10^9$ / μ l
Total protein	6.2	6.5~8.2	g/dl
Aspartate amino transferase (AST)	19	9~30	IU/l
Alanine aminotransferase (ALT)	19	4~35	IU/l
Lactate dehydrogenase (LDH)	116	80~260	IU/l
Creatine phosphokinase (CPK)	226	14~170	IU/l
Fasting glucose	91	70~110	mg/dl
Fasting insulin	5.50	0~17	μ U/ml
Hemoglobin A1c	4.9		%
Uric acid	3.5	4~7	mg/dl
Blood Urea Nitrogen (BUN)	10.2	8~20	mg/dl
Creatinine	0.41	0.6~1.06	mg/dl
Sodium	127	132~148	mEq/l
Potassium	4.2	3.6~5.0	mEq/l
Chloride	95	96~110	mEq/l
Low-density lipoprotein (LDL) cholesterol	81	70~139	mg/dl
High-density lipoprotein (HDL) cholesterol	43	40~86	mg/dl
Triglyceride	50	40~130	mg/dl
Urine			
Protein	(-)		
Glucose	(-)		
Occult blood	(-)		
Ketone	(-)		

Discussion

The patient in this case report was unable to sit down by himself and remained lying down during the ambulatory BP monitoring. The remarkable awakening BP rise in the patient occurred without postural change or increased physical activity. The awakening BP rise in ambulatory BP monitoring was reproducible, but the patient also exhibited evening BP rise in home BP monitoring when he took a nap.

Sympathetic nerve activity, measured as the LF/HF component of heart rate variability, was not elevated in the morning hours during the 24-h BP monitoring. The patient had slightly higher adrenaline and cortisol levels in the morning hours than in

the evening, but the changes were clinically subtle. It has been reported that blood vessels in the upper portion of the body receive sympathetic nerve innervations from the Th1 to Th5 spinal sympathetic neurons, while the major vasculature beds in the splanchnic region and lower extremities are under the control of the more caudal Th6 to L2 sympathetic preganglionic neurons. Therefore, pronounced cardiovascular dysfunction occurred by the spinal cord injury above Th6 [7] and the level of spinal cord injury in our patient was Th4.

After awakening in the morning, BP level decreased after eating breakfast, with increased parasympathetic activity measured as HF component. It was reported that parasympathetic nerve activity can be preserved in patients with spinal cord

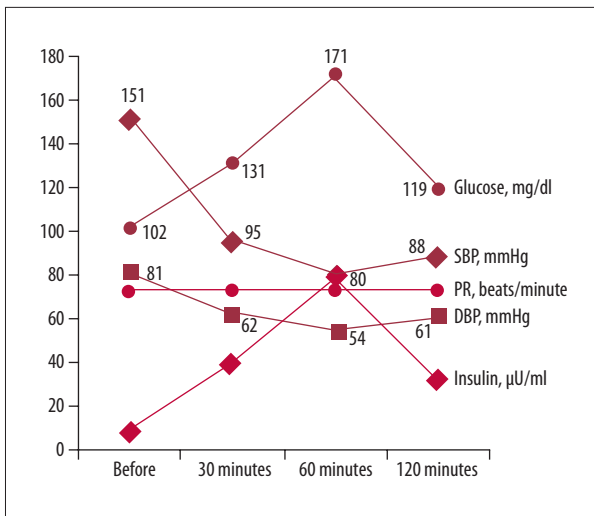


Figure 1. Change in blood pressure and pulse rate during a 75-g glucose tolerance test.

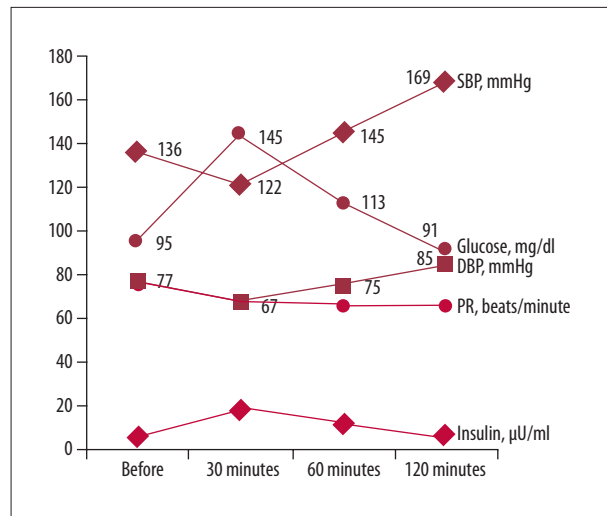


Figure 2. Change in blood pressure and pulse rate during intravenous administration of glucose (25 g).

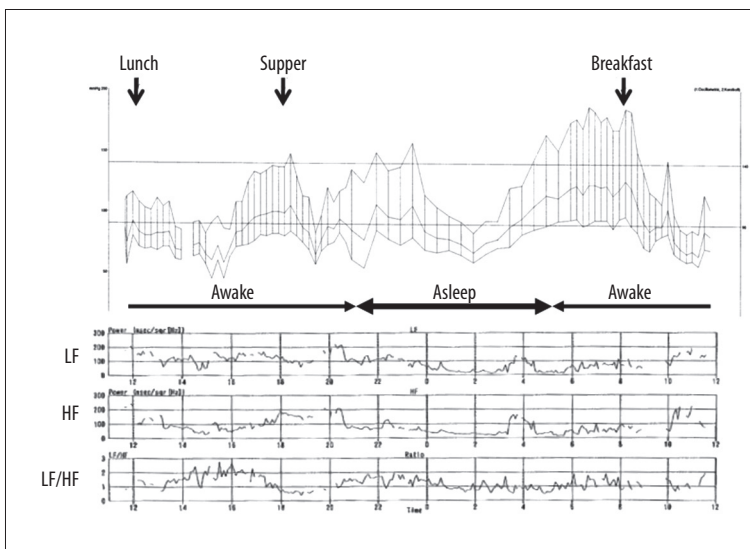


Figure 3. Ambulatory blood pressure monitoring. Awakening blood pressure (BP) was 123/75 mmHg (pulse rate 63 beats/min), asleep BP was 119/71 mmHg (pulse rate 57 beats/min) (nocturnal BP fall 3%), 24-h average BP was 122/74 mmHg (pulse rate 62 beats/min), night-time BP (the lowest) was 89/63 mmHg (pulse rate 55 beats/min), morning BP was 167/93 mmHg (pulse rate 70 beats/min), and morning BP surge was 78 mmHg.

injury of Th4 [7]. The “lowest” BP in the sleeping hours was associated with the parasympathetic nerve activity without eating. The parasympathetic nerve activation during the sleeping hours might help cause extreme-dipping status.

Awakening BP rise is a normal physiological response in general, but exaggerated BP rise could be pathogenetic. The exaggerated awakening BP rise could be caused by autonomic dysreflexia [7] and impaired baroreflex response [8,9] associated with spinal cord injury. Impaired baroreflex response causes hypertensive crisis, volatile hypertension, orthostatic tachycardia, and malignant vagotonia [10]. As seen in the results of the home BP monitoring, an exaggerated BP rise can occur even in the evening when taking a nap. Therefore, the term “morning BP rise” is inappropriate and we should use “awakening BP rise”.

The cardiovascular risk associated with awakening BP rise is still controversial. In retrospective analysis of prospective cohorts in Japan, exaggerated awakening BP rise was reported to be associated with stroke events in elderly hypertensive patients [2] and with cerebral hemorrhage in a general population [11], but there is no prospective study that confirms the results by predefined hypothesis. Moreover, many cohorts in Europe demonstrated that a greater awakening BP rise was associated with a lower risk of cardiovascular events. Therefore, we focused on the background causing exaggerated awakening BP rise. Patients with spinal cord injury were reported to have an increased risk of cardiovascular mortality [12].

Postprandial hypotension in the present case was managed successfully with droxidopa taken before eating, but the effect of droxidopa for neurogenic orthostatic hypotension is

controversial [13]. We did not prescribe antihypertensive medication to manage the awakening BP rise, because the exaggerated awakening blood pressure rise was reduced after eating or sitting-up. Moreover, there are no data showing that a reduced awakening BP rise is associated with reduced hypertensive organ damage.

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Conclusions

We treated a patient with spinal cord injury and autonomic nerve dysreflexia, who exhibited exaggerated awakening BP rise in ambulatory BP monitoring, without changes in physical activity or position. Postprandial and orthostatic hypotension could be associated with exaggerated awakening BP rise.