Sleep, 4(2):139–146

Changes in Systemic Arterial Pressure During Sleep in Shy-Drager Syndrome

Paolo Martinelli, Giorgio Coccagna, Nicola Rizzuto, and Elio Lugaresi

Institute of Neurology, University of Bologna; and Institute of Neurology, University of Verona, Italy

Summary: Polygraphic findings during spontaneous nocturnal sleep of 2 patients suffering from Shy-Drager syndrome are reported. In both patients, total sleep time was reduced—sleep latency and awakening periods during the night being increased. Considerable reductions of rapid eye movement (REM) stage and, in 1 patient, also of deep non-REM (NREM; stages 3–4) were found. No apneas were recorded. In normal subjects, systemic systolic and diastolic pressure decreases during all the sleep stages; in our patients, arterial pressure values rose progressively during NREM sleep stages and showed a further increase in REM sleep. In all the sleep stages, sudden phasic swings of systemic arterial pressure were observed. **Key Words:** Shy-Drager syndrome—Sleep—Arterial pressure.

Orthostatic hypotension, urinary and rectal incontinence, and anhydrosis are the most important autonomic dysfunctions in Shy-Drager syndrome (SDS) (Shy and Drager, 1960). Alterations have also been observed in the circulation and respiration of SDS patients: Bannister et al. (1967) noticed an impaired reflex vasoconstriction in both resistance and capacity vessels in upper and lower limbs; Chokroverty et al. (1978) described periodic respiration in 4 patients; and considerable variations of supine blood pressure during wakefulness were observed in the cases reported by Mahoudeau et al. (1972) and by Chokroverty et al. (1969).

The behavior of arterial pressure during sleep has been studied in a few cases (Guilleminault et al., 1977; Briskin et al., 1978; Lehrman et al., 1978) in which SDS coexisted with a sleep apnea syndrome. These authors noticed that systemic arterial pressure increases were severely blunted during apneas.

We report here the results of nocturnal polygraphic studies of 2 patients with SDS, with particular emphasis on their arterial pressure behavior.

Accepted for publication February 1981.

Address correspondence and reprint requests to Dr. Martinelli at Institute of Neurology, Via Ugo Foscolo 7, Bologna, Italy.

MATERIALS AND METHODS

Case Reports

Patient I

A 68-year-old woman had a 2 year progressive history of ataxia and weakness of the lower limbs, urinary incontinence, dizziness when standing up or walking, and recent orthostatic syncopes.

Neurological examination revealed facial immobility and bradikinesis, as well as diffuse, symmetrical rigidity with irregular tremor in the arms and wasting of the leg muscles. The plantar reflex was elicited on the left side; tendon jerks were brisk and were more pronounced in the left lower limb than the right.

Laboratory data. The following laboratory examinations were found to be within normal limits: red cell and leucocyte counts, hematocrit, sedimentation rate, fasting blood sugar and oral glucose tolerance test, serum sodium, serum potassium, blood urea nitrogen, chest and skull radiographs, and a standard electroencephalogram (EEG) made in the recumbent position.

Clinical evolution. Treatment with L-DOPA (750 mg/day), plus a decarboxylase inhibitor, improved the extrapyramidal symptoms; the administration of 30 mg/day of cyproheptadine hydrochloride reduced the orthostatic hypotension and allowed the patient to walk.

Six months later, because of a femoral fracture, the patient was forced to remain in bed; she developed a bronchopneumonia and died. No neuropathological findings were available.

Patient II

The second patient was a 52-year-old man who presented with a 1 year history of urinary and rectal incontinence, an increasing difficulty in walking, dizziness, and recent orthostatic syncope with a fixed-pulse rate.

Laboratory data. The following tests all gave normal results: red cell and leucocyte counts, fasting blood sugar and oral glucose tolerance test, hematocrit, sedimentation rate, and radiographs of the cranium and chest in the recumbent position.

A pneumoencephalographic examination revealed a moderate atrophy of the cerebellum and of both cerebral hemispheres.

Clinical evolution. The patient's orthostatic hypotension became so severe that sitting up was enough to provoke syncope. The administration of cyproheptadine hydrochloride did not produce any improvement.

The patient died 10 months later of bronchopneumonia. His brain was made available for neuropathological examination.

Neuropathological findings. A gross examination of the brain showed severe cerebellar atrophy. The substantia nigra was less pigmented than normal, and the central part of pons was shrunken.

The histopathological examination of the cerebral cortex revealed a loss of neurons, especially in the depths of the sulci; no senile plaques or neurofibrillary degenerations were found. The ganglia did not show any significant changes. In

the substantia nigra and locus coeruleus a severe loss of neurons was associated with gliosis and melanin-containing macrophages.

No Lewy bodies were visible. Demyelination and fibrillary gliosis were found in the transverse fibers of the pons as well as in the middle cerebellar peduncles. In the medulla, the inferior olive showed a decrease of nerve cells.

A severe loss of Purkinje and granule cells as well as pallor of the white matter of the hemispheres were found in the cerebellum; the dentate nucleus showed a mild loss of neurons.

Experimental Procedures

The 2 patients underwent a nocturnal polygraphic recording that included the simultaneous recording of the horizontal EEG, electro-oculogram (EOG), and electromyogram (EMG) of the mylohyoid muscle with surface electrodes. The sleep stages were classified according to the criteria suggested by Rechtschaffen and Kales (1968).

A subsequent polygraphic recording was performed on both patients, which included simultaneous recording of systemic arterial pressure, electrocardiogram (lead II), and nasal and thoracic respiration. The systemic arterial pressure was recorded continuously by means of a Teflon needle introduced percutaneously into the radial artery. The needle was connected to a Statham P23 dB transducer, which in turn was connected to a manometric preamplifier. The values of systolic and diastolic arterial pressure were taken every 30 sec during both wakefulness and sleep.

The findings obtained in the patients were compared with data from normal subjects previously studied in our laboratory (Coccagna and Lugaresi, 1978).

TABLE 1. *Sleep parameters and behavior of systemic arterial pressure (mm Hg) during sleep in the 2 patients studied and in the control group*

Sleep parameter	Patient 1	Patient 2	Control group
Recording time (hr)	9.0	8.12	8.5
Sleep time (hr)	4.65	6.28	7.5
Sleep (% of recording time)	51.6	77.3	84
Sleep latency (min)	127	50	20
First REM latency (min)	466	260	84
Awakening after sleep onset (*n*)	10	4	2.3
Sleep stages (%)			
1	44.1	21.2	11
2	28.0	22.3	37
3–4	12.2	52.5	29
REM	15.7	4.0	23
Systemic arterial pressure (systolic/diastolic)			
Wakefulness	145/72	146/72	129/60
Stage 1	145/71	153/78	125/57
Stage 2	147/74	155/77	118/54
Stage 3–4	153/75	150/75	112/52
REM	171/90	169/89	120/58

Table 1 reports the mean of all the values for these 2 patients and the control group.

RESULTS

Sleep Data

The sleep data are reported in Table 1. The 2 patients showed a reduction in total sleep time due to increased sleep latency and to several prolonged awakenings during the night. The sleep percentages were found to be modified in both patients, mainly because of a considerable reduction of the rapid eye movement (REM) stage and, in one case, of NREM stages 3–4 (see Table 1). Their sleep showed no morphologic alterations, and no apneas appeared during sleep.

Cardiac and Hemodynamic Findings

On assuming the orthostatic position during waking hours, both patients showed a rapid decrease in arterial pressure. Their heart rate, however, after an initial slight decrease, remained constant. When their arterial pressure dropped to under 40 mm Hg, slow waves appeared in the EEG. One patient experienced syncope (Fig. 1). In both patients, the Valsalva maneuver did not produce the normal hypertensive rebound or variations in heart rate.

In both patients, the systolic and the diastolic arterial pressures showed a substantial increase during NREM stages 3–4, and a further increase during REM sleep, as compared with waking state values (Fig. 2, Table 1).

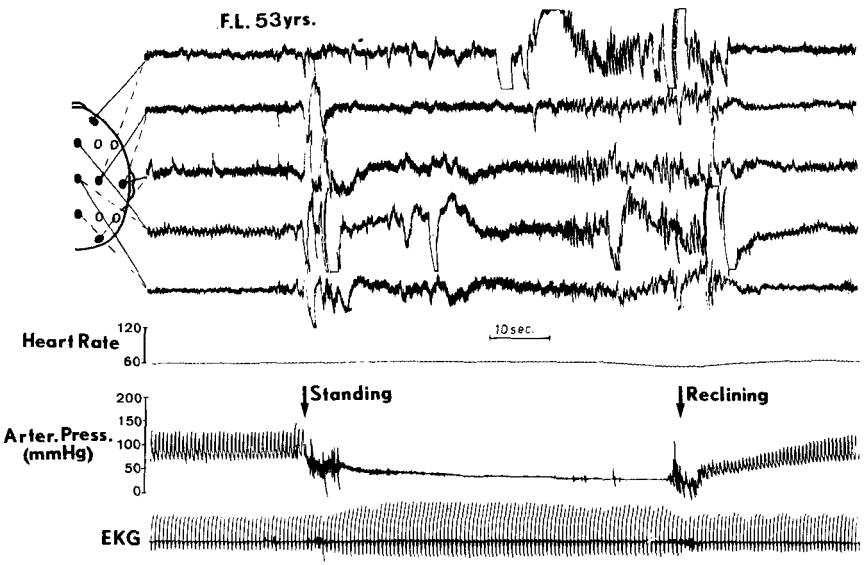

FIG. 1. Patient 2 showed a rapid drop in arterial pressure on moving from the recumbent to the standing position. After about 20 sec, slow hypoxic waves appeared in the EEG and syncope was observed clinically; heart rate did not change. When the patient lay down again, pressure values rapidly returned to previous levels.

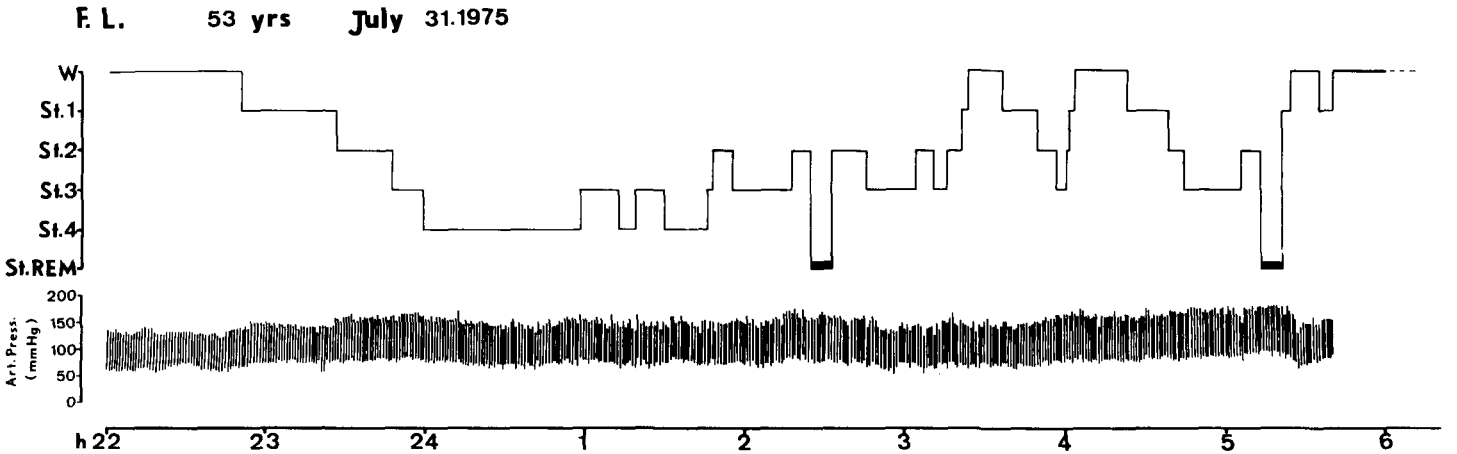

FIG. 2. Sleep histogram (**top**) and arterial pressure values (**bottom**) during sleep in patient 2. Note the considerable reduction of REM stage; a marked increase of REM latency and awakening periods was observed. Pressure values show an extremely irregular pattern, with no relation to sleep stages.

Sudden swings of arterial pressure, already present in the waking state, appeared in all stages, regardless of body movements; these sudden variations were not accompanied by changes in heart rate or respiration (Fig. 3).

DISCUSSION

Nocturnal sleep changes in SDS similar to those observed in our patients have been reported by several authors (Cotrufo and Bonavita 1976; Bergonzi et al., 1977; Castaigne et al., 1977; Guilleminault et al., 1977; Briskin et al., 1978; Lehrman et al., 1978). All these authors pointed out that the main impairment of nocturnal sleep consisted in the reduction of the duration of deep NREM (stage 3–4) and REM sleep.

It is well known that in normal subjects the systemic arterial pressure decreases progressively in the successive stages of sleep; during REM sleep, values are similar to those in stage 2 sleep (Coccagna et al., 1971). Sudden swings of the arterial pressure appear only in connection with body movements or during REM sleep.

The behavior of the systemic arterial pressure during sleep in SDS has previously been studied in only a few patients who, in addition to SDS, were all suffering from a sleep apnea syndrome.

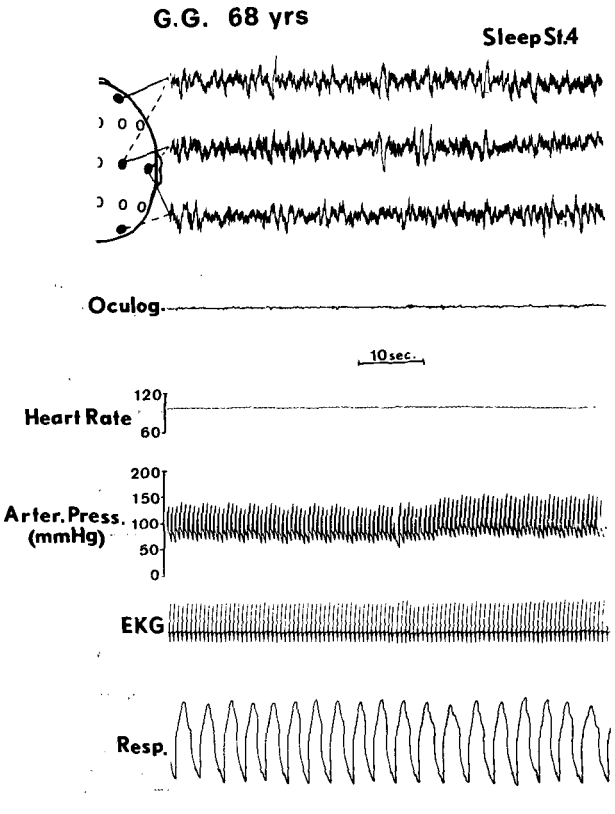

FIG. 3. Arterial pressure in patient 1 showed a sudden phasic swing during a slow wave sleep. No concomitant apneas, changes in heart rate, or body movements were observed.

Guilleminault et al. (1977) noted a moderate pulmonary hypertension in their patient, but no development of systemic hypertension during apneas was observed. In 2 similar cases studied by Briskin et al. (1978), the patients developed wide swings of pulmonary arterial pressure with obstruction; in contrast, systemic arterial pressure elevation was severely blunted. Lehrman et al. (1978), in another case of SDS plus sleep apnea syndrome, found periods of transient pulmonary hypertension but no changes in systemic arterial pressure. A complete autonomic denervation was hypothesized by these authors to explain the lack of arterial pressure elevations during apneas; the significant pulmonary arterial pressure increase could also be related to hypoxia or pulmonary vascular reflexes.

To our knowledge, there are no data in the literature about systemic arterial pressure variations during sleep in patients suffering from SDS only. In our 2 patients, who had no apneas during sleep, systemic arterial pressure increased during REM sleep, contrary to what is observed in normal subjects; furthermore, sudden swings of arterial pressure were present during every sleep stage, with no relation to body movements. In SDS, the autonomic system is greatly impaired; it seems unlikely that it causes both the sudden arterial pressure swings during wake time and sleep and the tonic arterial pressure increase during sleep.

Given the lack of nervous control in SDS, we advance the hypothesis that biochemical factors provoke variations in arterial pressure. Some findings suggest that the renin-angiotensin system could play a certain role: (1) angiotensin acts directly on the smooth arterial muscle and thus would not be affected by impairment of the autonomic system; (2) the hypertensive response to angiotensin, as well as to norepinephrine, infusion is exaggerated in SDS patients (Lehrman et al., 1978); and (3) in 1 of the 2 patients studied by Diamond et al. (1970), the hypotensive response to head-up tilt maneuvers was followed, on returning to the horizontal position, by a hypertensive period with a simultaneous increase of plasma renin activity levels.

It can be argued that in some patients the physiological hypotension during sleep is counterbalanced by an increased activity of the renin-angiotensin system.

Further studies of biochemical data coupled with arterial pressure variations during sleep are needed to evaluate this hypothesis.

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