CASE REPORT

Use of a new generation of adaptive servo ventilation for sleep-disordered breathing in patients with multiple system atrophy

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SUMMARY

A 70-year-old man (case 1) and a 64-year-old woman (case 2) with multiple system atrophy (MSA) and snoring were admitted for polysomnography. Their awake PaCO₂ indicated normocapnia. Apnoea–hypopnoea index (AHI), max transcutaneous carbon dioxide partial pressure (PtcCO₂) and ΔPtcCO₂ (max PtcCO₂ (during sleep)—baseline PtcCO₂ (while awake)) were 11.4/h, 63 mm Hg and 18 mm Hg, respectively, in case 1 and 53.1/h, 59 mm Hg and 13 mm Hg, respectively, in case 2. Their sleep-disordered breathing (SDB) was diagnosed as obstructive sleep apnoea with hypoventilation. We thought that variable expiratory positive airway pressure and pressure support ventilation (advanced-adaptive servo ventilation (ASV)) might be favourable for their SDB. Polysomnography after introducing advanced-ASV revealed that AHI, max PtcCO₂ and ΔPtcCO₂ were 0.2/h, 53 mm Hg and 5 mm Hg, respectively, in case 1 and 1.5/h, 56 mm Hg and 9 mm Hg, respectively, in case 2. Advanced-ASV for treating Cheyne-Stokes breathing may be helpful in SDB in patients with MSA.

CASE PRESENTATION

A 70-year-old man (case 1) had developed a gait disturbance at the age of 67 years. Thereafter, he developed gait and limb ataxia (cerebellar syndrome), orthostatic hypotension (autonomic failure) and bradykinesia and rigidity in the left elbow and wrist joints (parkinsonism). His predominant symptom was cerebellar ataxia. Brain MRI disclosed pontine atrophy and the ‘hot cross bun’ sign in the pons (additional feature). The latest criteria for the diagnosis of MSA established three levels of certainty: definite MSA for patients with autopsy confirmation, probable MSA for patients with autonomic failure plus poorly levodopa-responsive parkinsonism or cerebellar ataxia and possible MSA for patients with suggestions of autonomic failure in addition to parkinsonism or cerebellar ataxia and at least one additional feature, including findings according to history, clinical examination and neuroimaging.^{7 8} Therefore, he was diagnosed as having probable MSA with predominant cerebellar ataxia (MSA-C). At age 70 years, he was admitted to our department for the evaluation of habitual snoring. He had a medical history of diabetes mellitus and hypertension. He took taltirelin, metformin, glibenclamide, nifedipine, valsartan, doxazosin and trichlormethiazide. His body mass index (BMI) was 21.5 kg/m². The findings of a chest X-ray were normal. Pulmonary function testing showed a vital capacity (VC) of 3.31 L (100.9% predicted) and forced expiratory volume in 1 s (FEV₁) of 2.46 L (90.9% predicted). Results of analysis of arterial blood gas (ABG) in room air were PaO₂ of 85.5 mm Hg and PaCO₂ of 37.2 mm Hg. A polysomnography (PSG) study (Somnostar, SensorMedics) with audiovisual recording and transcutaneous monitoring (TOSCA, Linde Medical) revealed that the apnoea–hypopnoea index (AHI), max transcutaneous carbon dioxide partial pressure (PtcCO₂) and ΔPtcCO₂ (max PtcCO₂ (during sleep)—baseline PtcCO₂ (while awake)) were 11.4/h, 63 mm Hg and 18 mm Hg, respectively (table 1 and figure 1A). Data on PtcCO₂ could not be accepted from 2:00 because blood flow at the ear probe was greatly restricted because of the patient’s right side lateral position. Apnoea was defined as the cessation of airflow ≥10 s and hypopnoea was defined as a >30% decrease in a valid measurement of airflow or more lasting for at least 10 s, accompanied by oxygen desaturation of >4%. His SDB was diagnosed as OSA with hypoventilation.

BACKGROUND

Sleep-disordered breathing (SDB) such as obstructive and central apnoea and hypopnoea and stridor are common and associated with sudden death in patients with multiple system atrophy (MSA).^{1–3} There are several treatment options: continuous positive airway pressure (CPAP), non-invasive positive pressure ventilation (NPPV) and tracheostomy. When a patient with MSA has obstructive sleep apnoea (OSA) only, we use CPAP.⁴ When the patient has hypoventilation during sleep according to the progression of the disease, we begin to use NPPV.⁵ It is difficult for clinicians to know when to change therapeutic methods from CPAP to NPPV. Indeed, some patients have several types of SDB as in the cases reported here. Advanced-adaptive servo ventilation (ASV) is an NPPV instrument. This device can automatically adjust the expiratory positive airway pressure (EPAP) for correcting obstructive SDB events and pressure support (PS) to maintain the patient’s ventilation.⁶ We report that two patients with MSA diagnosed as having OSA with normocapnia while awake and hypoventilation during sleep were treated with advanced-ASV. We propose advanced-ASV as a new non-invasive treatment option for MSA with SDB.

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Table 1 Polysomnographic analysis of cases 1 and 2 before and after the introduction of ASV

Case	1		2	
Introduction of advanced-ASV	Before	After	Before	After
TST, min	283	356.5	186.5	393.5
Sleep efficacy (%)	57.1	82	36.2	84.8
Sleep stage (%)				
I	19.8	19.6	10.2	22.7
II	54.6	62.3	84.7	64.4
Slow wave sleep	45.5	3.1	5.1	0
REM	20.1	15.6	0	12.7
AHI (/h)	11.4	0.2	53.1	1.5
Obstructive apnoea (/h)	2.1	0	17.7	0
Hypopnoea (/h)	9.1	0.2	33.8	0.6
Central apnoea (/h)	0.2	0	1.6	0.9
Minimum SpO ₂ (%)	84	88	85	87
SpO ₂ <90% (min)	3.4	0	21.1	0.3
Arousal index (/h)	30.5	22.2	30.6	22.1
Transcutaneous monitoring				
Mean SpO ₂ (%)	98.4	99.19	96.38	97.55
Mean PtcCO ₂ (mm Hg)	61	46	52	51
ΔPtcCO ₂ * (mm Hg)	18	5	13	9
Max PtcCO ₂ (mm Hg)	63	53	59	56

*ΔPtcCO₂=max PtcCO₂ (during sleep)–baseline PtcCO₂ (while awake).

AHI, apnoea–hypopnoea index; ASV, adaptive servo ventilation; PtcCO₂, transcutaneous carbon dioxide partial pressure; REM, rapid eye movement; SpO₂, percutaneous oxygen saturation; TST, total sleep time.

Case 2 was of a 64-year-old woman. At age 62 years, she had experienced a gait disturbance and clumsiness in her left hand. Thereafter, she developed gait ataxia with cerebellar dysarthria (cerebellar syndrome), significant orthostatic blood pressure decline (suggesting autonomic dysfunction) and bradykinesia and rigidity in both elbows and wrist joints (parkinsonism). Her predominant symptom was cerebellar ataxia. Brain MRI findings disclosed cerebellar and pontine atrophy (additional feature). According to the above diagnostic criteria,^{7 8} she was diagnosed as having possible MSA-C. At age 64 years, she was admitted to our department for the evaluation of high-pitched snoring.

She had no other medical history. She took taltirelin and carbidopa/levodopa. Her BMI was 23.3 kg/m². The findings of a chest X-ray were normal. Pulmonary function testing showed a VC of 2.25 L (91.1% predicted) and FEV₁ of 1.88 L (99.5% predicted). Results of analysis of ABG in room air were PaO₂ of 73.8 mm Hg and PaCO₂ of 42.6 mm Hg. Although fiberoptic laryngoscopy did not reveal vocal cord abductor paralysis while awake, a PSG study identified the presence of nocturnal stridor. Her AHI, max PtcCO₂ and ΔPtcCO₂ were 53.1/h, 59 mm Hg and 13 mm Hg, respectively (table 1). Her SDB was diagnosed as OSA with hypoventilation as shown in case 1.

TREATMENT

Since hypoventilation was not evident while the two patients were awake, we first intended to treat them with CPAP. However, PtcCO₂ in cases 1 and 2 increased to 18 and 13 mm Hg from baseline and reached 63 and 59 mm Hg during the night, respectively. CPAP cannot provide ventilatory support (prevent hypoventilation) during sleep, and MSA is usually progressive so that hypoventilation becomes worse according to the progression of the disease.^{9 10} Next, we considered the use of NPPV. However, their awake PaCO₂ indicated normocapnia. If NPPV-derived ventilatory support would produce hypocapnia at the start stage of NPPV use, this hypocapnia would sometimes induce the serious side effect of upper airway obstruction (glottis closure).¹¹ We decided on using advanced-ASV which was made to treat Cheyne-Stokes breathing with OSA. Advanced-ASV provides breath by breath auto-PS with auto-CPAP.⁶ We thought that EPAP only increased without PS if CPAP was sufficient to treat this patient. EPAP and PS were set from 4 to 8 cm H₂O and from 0 and 8 cm H₂O, respectively. PSG on the second day of advanced-ASV revealed that AHI, max PtcCO₂ and ΔPtcCO₂ were 0.2/h, 53 mm Hg and 5 mm Hg, respectively, in case 1 (table 1 and figure 1B) and 1.5/h, 56 mm Hg and 9 mm Hg, respectively, in case 2 (table 1).

OUTCOME AND FOLLOW-UP

In addition to the PSG parameters such as AHI, minimum SpO₂, time of SpO₂<90% and arousal index and the mean PtcCO₂, ΔPtcCO₂ and maximum PtcCO₂ during sleep were much improved in cases 1 and 2 (table 1). These two patients

Figure 1 (A) Data obtained on case 1 by a diagnostic polysomnogram. Depicted derivations include (from top to bottom) percutaneous oxygen saturation (SpO₂); sleep stage; body position; transcutaneous carbon dioxide partial pressure (PtcCO₂). *Data on PtcCO₂ after 2:00 were deleted because blood flow at the ear probe was greatly restricted while the patient was in the right lateral position. (B) Data on case 1 from a therapeutic polysomnogram with advanced-adaptive servo ventilation. Depicted derivations include (from top to bottom) SpO₂; sleep stage; body position; PtcCO₂. *Data on PtcCO₂ after 2:00 were deleted from comparison of compare the data before treatment at the same intervals in order to compare the data before treatment at the same intervals

Figure 2 Data on case 1 (A) and case 2 (B) downloaded from the memory card showing expiratory and inspiratory positive airway pressure automatically titrating at home during the night. (A) Expiratory positive airway pressure (EPAP) and pressure support (PS: inspiratory positive airway pressure (IPAP)—EPAP) were set from 4 to 8 cm H₂O and from 0 and 8 cm H₂O, respectively. (B) EPAP and PS were set from 4 to 7 cm H₂O and from 0 and 9 cm H₂O, respectively.

used the advanced-ASV at home. Figure 2 showed that EPAP and inspiratory positive airway pressure were automatically titrated at home during sleep for more than 2 years in both cases.

DISCUSSION

We report that two patients with MSA with normocapnia who were diagnosed as having OSA with hypoventilation during sleep were treated with advanced-ASV in which EPAP and PS were varied according to the patients' types of SDB. To the best of our knowledge, this is the first report that an advanced-ASV was used to control hypoventilation during sleep with SDB and MSA.

SDB such as obstructive and central apnoea and hypopnoea is common in patients with MSA.¹ In the course of MSA, hypoventilation progresses.^{9–10} It is difficult for clinicians to properly use CPAP or NPPV for patients with MSA who usually have several progressive types of SDB and hypoventilation during sleep. In the cases described here, diagnostic PSG showed significant hypoventilation ($\Delta\text{PtcCO}_2 \geq 10$ mm Hg) with mainly obstructive SDB (table 1), while the awake PaCO_2 showed normocapnia. If we had not measured the PtcCO_2 , we would have used CPAP in these patients because they did not have hypercapnia while awake.⁴ Usually, we consider starting NPPV therapy for patients with MSA with SDB whose PaCO_2 becomes hypercapnic while awake.⁵ Since hypoventilation during sleep induces hypercapnia while awake,¹² it is desirable to use support ventilation during sleep. However, it is known that upper airway obstruction, namely glottis closure, can be caused by hypocapnia induced by NPPV.¹¹ In patients with MSA, it is said that vocal cord abduction paralysis by denervation of the vocal cord abductors and abnormal overactivation of the vocal cord adductors can occur and induce nocturnal or diurnal stridor, which is considered to be related to sudden death during sleep and short survival.^{2–3} Therefore, in patients with MSA, hypocapnia induced by the start of NPPV can worsen glottis closure and cause or worsen stridor. Therefore, it may be reasonable for patients with MSA with SDB to be treated with CPAP while normocapnic and with NPPV during hypoventilation.

The first-generation ASV was made for the treatment of Cheyne-Stokes breathing, and is also used to treat a complex sleep apnoea syndrome (central sleep apnoea following CPAP treatment). Indeed, Suzuki *et al*¹³ reported that a patient with MSA without hypoventilation but with complex sleep apnoea following CPAP was treated by this conventional ASV. In

advanced-ASV, EPAP is adjusted automatically by algorithms aimed at correcting obstructive-disordered breathing.⁶ PS is determined to target peak flow from the data from the previous 4 min of breathing (peak flow), and adjusted automatically.⁶ The algorithms are aimed at correcting hypoventilation or hyperventilation breath by breath.⁶ Therefore, advanced-ASV works as an auto-CPAP machine while the patient is awake or when the ventilation is sufficient. In addition, we supposed that advanced-ASV works as a PS machine when the ventilation of patients is decreased. Indeed, in this report, the machine worked well while changing EPAP and PS automatically (figure 2). However, in the future, we should again carefully investigate the future disease profiles of the patients reported here because the usefulness of advanced-ASV for patients with MSA is not yet convincing. In addition, CPAP was reported to exacerbate SDB in patients with MSA with a floppy epiglottis,¹⁴ which resulted in the short-term CPAP treatment.¹⁵

We report that two patients with normocapnic probable or possible MSA-C diagnosed as having OSA with hypoventilation during sleep were treated with advanced-ASV. We concluded that new-ASV, which was made for the treatment of Cheyne-Stokes breathing, would be also useful for SDB such as snoring (stridor), apnoea and hypoventilation in patients with MSA, because it is difficult for clinicians to use proper CPAP or NPPV treatment for patients with MSA who usually have several progressive or combined SDB conditions.

Learning points

- ▶ Patients with multiple system atrophy can have OSA with moderate hypoventilation during sleep without hypercapnia while awake.
- ▶ Breath by breath auto-pressure support with an auto-continuous positive airway pressure machine (advanced- adaptive servo ventilation) can work as a therapy for sleep-disordered breathing (obstructive sleep apnoea with hypoventilation) in patients with MSA who have moderate hypoventilation during sleep while their awake PaCO_2 is normocapnic.
- ▶ Advanced-ASV may be used for patients with Cheyne-Stokes breathing or complex sleep apnoea, as well as patients with simultaneous OSA with mild to moderate hypoventilation, if the monitoring can ascertain the effects of the treatment.

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