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SHORT REPORT

Treatment of ventilatory failure in the Prader-Willi syndrome

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Treatment of ventilatory failure in the Prader-Willi Syndrome. I.E. Smith, M.A. King, P.W.L. Siklos, J.M. Shneerson. ©ERS Journals Ltd 1998.

ABSTRACT: Hypercapnic respiratory failure is a common cause of death in the Prader-Willi syndrome. Its relationship to sleep-disordered breathing has not been established and there are no reports of its successful treatment.

We have retrospectively reviewed the records of four patients with the syndrome, who developed ventilatory failure. Daytime arterial blood gas tensions and overnight oximetry traces before and during treatment were compared.

Each patient had severe sleep-disordered breathing in association with daytime ventilatory failure. The median overnight mean arterial oxygen saturation (S_{a,O_2}) was 82% and the median minimum was only 41.5%. Initial treatment was with nasal intermittent positive pressure ventilation, and in each case the daytime arterial blood gas tensions were normalized. The patients were maintained on nasal continuous positive airway pressure at night after discharge. Compliance has been good, and at last follow-up (after a median of 4.8 yrs) the daytime arterial gas tensions remained normal, while the median overnight mean arterial oxygen saturation was 95.5% and the median minimum was 84.5%.

This study of patients with the Prader-Willi syndrome shows that daytime ventilatory failure is associated with sleep-disordered breathing. It can be reversed with nocturnal noninvasive ventilation and maintenance treatment with continuous positive airway pressure is well tolerated, with no deterioration in respiratory parameters.

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The Prader-Willi syndrome (PWS) is the most common congenital disorder leading to obesity. It presents in infancy with hypotonia and a failure to feed, and in later childhood may be diagnosed from the combination of mental retardation, hyperphagia, hypogonadism and characteristic dysmorphic features [1]. Hypersomnolence is a common but unexplained feature [2]. Ventilatory failure with cor pulmonale has been reported to be a common cause of death [3], but there are no published data on the successful treatment of ventilatory failure in adult patients. In this paper, we describe our experience of treating adults with the PWS using noninvasive ventilatory assistance.

Patients and methods

Between September 1988 and May 1996, seven adult patients with PWS were referred to the Respiratory Support and Sleep Centre (Papworth Hospital, Cambridge, UK) for assessment of snoring and daytime sleepiness. Four of these patients (three males and one female) have had an episode of ventilatory failure (arterial carbon dioxide tension (P_{a,CO_2}) >6.5 kPa, while self-ventilating awake breathing air) and have been treated with nasal intermittent positive pressure ventilation (NIPPV).

The records of the four patients were reviewed retrospectively and the results of investigations prior to the initiation of NIPPV extracted. Only those investigations which were felt to be essential to the management of the patients were performed. These included the haemoglobin concentration, electrocardiogram, plain chest radiograph, arterial blood gas tensions with the patient at rest breathing air, and the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) measured using a dry spirometer (Vitalograph, Maids Morton, Bucks, UK). The arterial oxygen saturation (S_{a,O_2}) was recorded continuously overnight using a Biox 3700 pulse oximeter (Ohmeda, Hatfield, Herts, UK) and saved as a hard copy using a chart recorder. These paper tracings were reviewed; the overnight minimum S_{a,O_2} level was measured and the overnight mean S_{a,O_2} and desaturation index (defined as the number of dips in S_{a,O_2} Š4%·h^{-1}) calculated.

All of the patients have been admitted periodically for reassessment. Results from the most recent admission, which for the surviving patients took place between December 1996 and March 1997, are also presented. Data are presented as median and range in parenthesis.

Results

All four patients were snorers and had excessive and increasing daytime somnolence. Parents and carers described long daytime naps and episodes where the patients had fallen asleep in inappropriate circumstances, such as in the

Table 1. – Characteristics of the patients studied and arterial blood gas tensions before and after nasal intermittent positive pressure ventilation (NIPPV)

		Pre-NIPPV				Post-NIPPV	
Pt No.	Sex	Age yrs	BMI kg·m^{-2}	P_{a,O_2} kPa	P_{a,CO_2} kPa	P_{a,O_2} kPa	P_{a,CO_2} kPa
1	M	43	28.6	4.8	8.4	11.7	6.4
2	M	32	63.6	8.5	8.4	9.4	5.5
3	F	38	65.3	5.2	9.8	8.3	6
4	M	30	51.9	7.2	7.6	9.3	6.3

Pt: patient; M: male; F: female; BMI: body mass index; P_{a,O_2}: arterial oxygen tension; P_{a,CO_2}: arterial carbon dioxide tension.

middle of meals and conversations. The median age of the patients at the initiation of NIPPV was 35 (30–43) yrs. Three had a body mass index (BMI) of >50 kg·m^{-2} (normal upper limit 30 kg·m^{-2}) (table 1). None of the patients consumed >10 units of alcohol·week^{-1} and none were taking sedative medication.

Each of the patients had a restrictive deficit on spirometry, the median FEV1 and FVC were 1.54 L (0.9–1.8) and 1.92 L (1.16–2.22), respectively. None of the patients were polycythaemic and only one had evidence of right ventricular hypertrophy on the electrocardiogram. Arterial blood gas tensions prior to the initiation of NIPPV are recorded in table 1. The median overnight mean S_{a,O_2} for the four patients was 82% (66–86), and the median overnight minimum S_{a,O_2} was only 41.5% (15–55). The median desaturation index was 35 (11–65) episodes·h^{-1}.

The patients were treated with NIPPV, using either the PB2800 (Nelcor Puritan Bennett, Bistor, Oxon, UK) or the BiPAP ST (Respironics, Bognor Regis, W. Sussex, UK) with standard nasal masks (Respironics). No supplementary oxygen or respiratory stimulants were used. At the time of discharge from hospital, NIPPV was used at night only and the daytime arterial blood gas tensions were normal.

All patients were converted to nasal continuous positive airway pressure (CPAP) during review admissions. The median duration of follow-up from the initiation of NIPPV was 4.8 yrs. At their most recent admission, each patient was using the CPAP for Š6 h·night^{-1} (recorded using a concealed clock on the CPAP unit). The parents or carers of the patients reported a sustained improvement in daytime somnolence. One patient (no. 1) died, 1.04 yrs after referral, from an acute gastric haemorrhage. The other patients remain well. The most recent results for arterial blood gas tensions are presented in table 1. The median overnight mean S_{a,O_2} from the most recent follow-up was 95.5% (93–97) and the median minimum S_{a,O_2} was 84.5% (84–85). The median desaturation index was 5 (1–7) episodes·h^{-1}.

Discussion

PWS is an uncommon condition in which the life expectancy is unknown. There are few published reports of patients >30 yrs of age. Ventilatory failure appears to be a frequent cause of death but this has hardly been investigated. In one series of 33 patients, nine died and in each case cardiorespiratory failure was given as the cause of death, although no details of the clinical features or treatment were available [3].

Whilst there are several isolated case reports of sleep-disordered breathing (SDB) in patients with PWS [4–7], these have suggested that it is mild, its prevalence is low and its association with daytime ventilatory failure is unproven [6]. However, most of the patients studied previously have been younger than those in the present series, and in some cases overnight oximetry was not performed [7]. Each of the patients with ventilatory failure had severe SDB and all four have maintained normal daytime arterial blood gas tensions while using mechanical ventilatory support at night only. These results suggest that SDB precedes daytime ventilatory failure in PWS.

The successful reversal of respiratory failure using weight loss and progesterone as a respiratory stimulant has been described in children with PWS [8]. However, weight loss is much harder to achieve in adult patients [4], and one of the patients studied was not obese. The treatment of obstructive sleep apnoea in the absence of ventilatory failure using CPAP has been reported in a series of seven patients with the PWS [9], although it was concluded that compliance was sometimes poor due to behavioural and learning difficulties. There have been two case reports of the attempted treatment of ventilatory failure with mechanical ventilatory support in patients with the PWS, but both were unsuccessful [10, 11].

In contrast to these earlier reports, we have successfully treated four adult PWS patients with ventilatory failure using NIPPV until the daytime arterial blood gas tensions were normal and then using nocturnal CPAP in the maintenance phase. In each case, after the patients had felt the benefit of the treatment there were no problems with compliance. We cannot tell whether these patients predominantly had obstructive or central sleep apnoeas or hypopnoeas before treatment, but all patients have subsequently been effectively managed with nocturnal CPAP. The successful treatment of central apnoeas with CPAP has been reported previously [12]. Polysomnography was not attempted, since our priority was the initiation of treatment. Patients with PWS are liable to behavioural problems and we felt that only investigations essential to clinical management should be performed in an attempt to maximize the co-operation of the patient.

It has been our experience that by using structured follow-up, which allows the benefits of treatment to be reinforced, long-term compliance has been very good and prolonged survival on treatment has been demonstrated. We would recommend that any adult patient with Prader-Willi syndrome who complains of excessive sleepiness and snoring should be investigated with measurement of daytime arterial blood gas tensions and overnight oximetry, as a treatable cause of morbidity may be revealed.

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