Sleep-Disordered Breathing in 2 Pediatric Patients on Peritoneal Dialysis

Sleep-disordered breathing (SDB) is prevalent in children with chronic kidney disease (CKD), and has the potential to worsen vascular and neuro-cognitive health and quality of life. We present 2 children with CKD who experience central sleep apnea and nocturnal hypoventilation and discuss the possible underlying mechanisms in relation to CKD and dialysis.

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Sleep-disordered breathing (SDB) is prevalent in adult and pediatric patients with chronic kidney disease (CKD) (1,2) and in dialysis patients (3). Pediatric studies are based on questionnaire data only. To date, there are no published polysomnography (PSG) data in this population.

Sleep apnea (SA) has adverse effects on behavior (4), neuro-cognitive function (5), and school performance (6) in children. It is associated with vascular disease through altered

lipid homeostasis (7) and endothelial dysfunction (8). In CKD, SA potentially increases the pre-existing risk of morbidity and mortality from cardiovascular disease and reduces quality of life independently of CKD (3). Therefore, identification and treatment of SDB in CKD patients is especially important.

We review 2 pediatric patients with CKD and SDB in conjunction with their PSG results, and discuss the possible contributing factors.

PATIENT 1

Patient 1 is a 5-year-old male with steroid-resistant nephrotic syndrome secondary to focal segmental glomerulosclerosis due to a podicin mutation. After bilateral nephrectomies, continuous cycling peritoneal dialysis (CCPD) with Physioneal (bicarbonate 25 mmol/L + lactate 15 mmol/L; Baxter Healthcare Corporation, Deerfield, IL, USA) was started. Due to nocturnal oxygen desaturation while on CCPD, he underwent overnight oximetry. It showed multiple desaturations, with a minimum oxygen saturation of 80%. History was negative for nocturnal or daytime symptoms of SA. Lateral neck radiograph did not demonstrate adenotonsillar hypertrophy.

Polysomnography while on CCPD (Figure 1) demonstrated severe central sleep apnea (CSA) and nocturnal hypoventilation

Figure 1 — Polysomnography demonstrating severe central apnea in patient 1: the absence of air flow at the nose/mouth (arrow 1) and absence of chest (arrow 2) and abdominal wall (arrow 3) movement with associated oxygen desaturations. REM = rapid eye movement.

(Table 1). Computed tomography (CT) head was normal. As bi-level positive pressure ventilation was declined by the family, nocturnal supplementary oxygen was started. Overnight oximetry demonstrated improvement in oxygen saturation with no associated hypercapnia, and normalized after renal transplant.

PATIENT 2

Patient 2 is a 5-year-old female with membranoproliferative glomerulonephritis, who underwent bilateral nephrectomies for severe hypertension. Nocturnal intermittent PD (NIPD) using Physioneal was commenced. Within 3 months, she developed a metabolic alkalosis with hypercapnia.

History was positive for snoring, apneas, sleep talking, nocturnal awakenings, and daytime headaches. Lateral neck radiograph showed no adenotonsillar hypertrophy and she had no history of recurrent otitis media or tonsillitis.

Polysomnography demonstrated nocturnal hypoventilation and mild obstructive sleep apnea (OSA) and CSA (Table 1).

We hypothesized that the metabolic alkalosis developed secondary to bicarbonate absorption from the Physioneal.

Subsequent nocturnal hypoventilation increased her carbon dioxide (CO_2), thereby lowering her pH. A lactate-based PD solution, Dianeal (lactate 40 mmol/L; Baxter Healthcare Corporation, Deerfield, IL, USA) was initiated to test this hypothesis. Repeat PSG after 3 weeks demonstrated resolution of the nocturnal hypoventilation, and moderate OSA and CSA.

At the time of the second sleep study, history was positive for allergic rhinitis and nasal congestion, potentially explaining the increase in the obstructive events. The increase in central apnea may be explained by the development of an increased apnea threshold, secondary to chronic elevation in CO_2 (i.e. a higher level of CO_2 was required to stimulate breathing). Therefore normalizing the CO_2 may have subsequently predisposed her to unstable breathing patterns and apnea.

Her urea and creatinine levels were slightly higher at the time of the second PSG, which may have exacerbated sleep apnea through the effect of increased uremic toxins. The elevation in urea and creatinine may reflect altered clearance while on Dianeal possibly related to an impact on peritoneal transport; however, we do not have peritoneal equilibration testing to support this.

TABLE 1
Summary of PSG Findings

Sleep parameter	Patient 1	Patient 2 (PSG 1)	Patient 2 (PSG 2)	Patient 2 (PSG 3)
Type of dialysis	CCPD (Physioneal)	NIPD (Physioneal)	CCPD (Dianeal)	None (Post renal transplant)
Total sleep time (min)	454.0	339.0	410.5	448.8
Sleep efficiency (%)	98.5	85.6	89.3	89.8
% REM sleep	23.6	14.5	13.8	23.2
Arousal index (events per hour sleep)	4.5	8.8	12.3	8.2
Obstructive apnea hypopnea index (events per hour sleep)	4.0	1.6	6.8	0.1
Central apnea index (events per hour sleep)	15.0	2.1	5	0.9
Baseline mean SpO_2 (%)	94–95	98.3	97.6	99.5
SpO_2 nadir (%)	79	85.6	73.2	92
Time Pco_2 (transcutaneous) > 50 mmHg (% of night)	100	98	0	0
Capillary blood gas results & renal function	On Physioneal	On Physioneal	On Dianeal	Post renal transplant
pH	7.46	7.44	7.45	7.39
p CO_2 (mmHg)	50	57	46	38
p O_2 (mmHg)	95	86	68	77
Bicarbonate (mm/L)	35	38	31	22
Base excess	+10	+13	+7	-2
Urea (mmol/L)	10–20	20–25	25–30	5.9
Creatinine (umol/L)	800–850	600–700	700–800	34
PD prescription				
Nocturnal cycles and duration	6 cycles/12 hours	8 cycles/10 hours	8 cycles/10 hours	
Nocturnal fill volume (mL/m^2)	1,095	929	1,027	
Day dwell (mL/m^2)	890 (Icodextrin)		822 (Icodextrin)	

PSG = polysomnography; CCPD = continuous cycling peritoneal dialysis; NIPD = nocturnal intermittent peritoneal dialysis; REM = rapid eye movement; SpO_2 = oxygen saturation; p CO_2 = partial pressure of CO_2 ; CO_2 = carbon dioxide; PD = peritoneal dialysis.

Resumption of Physioneal resulted in a recurrence of metabolic alkalosis with compensatory hypercapnia. Four months after renal transplantation, PSG demonstrated complete resolution of SDB.

SLEEP-DISORDERED BREATHING IN CHRONIC KIDNEY DISEASE

Our patients were both on PD with bicarbonate/lactate-containing solutions (total buffer 40 mmol/L), which may be one explanation for the metabolic alkalosis and subsequent nocturnal hypoventilation. In addition, patient 1 typically absorbed 200 mL of his 650-mL Icodextrin day dwell, contributing to fluid overload at the onset of sleep. Both patients had CSA, and patient 2 also had OSA, illustrating that other types of SDB also occur in CKD patients, with multiple contributing factors.

CENTRAL SLEEP APNEA

Central sleep apnea describes the cessation of respiratory effort and air flow for at least 20 seconds, or less if associated with a desaturation, arousal, or awakening (9). The pathophysiology of CSA is related to ventilatory instability. In non-REM (rapid eye movement) sleep, ventilatory control is determined by the ventilatory recruitment threshold (level of CO_2 required to trigger ventilation) (10). Chronic kidney disease patients frequently have metabolic disturbances, usually metabolic acidosis and uremia (11). These can alter chemoreceptor sensitivity (over-sensitivity to CO_2) (12) and increase ventilatory drive and ventilatory over-shoot, driving CO_2 below the apnea threshold and resulting in apnea (13). This is supported by case reports demonstrating resolution of CSA after renal transplantation (14).

HYPOVENTILATION

Metabolic alkalosis-related complications include hypokalemia and arrhythmia. Compensatory nocturnal hypoventilation (defined by a CO_2 measurement of more than 50 mmHg for more than 25% of total sleep time [9]) and retention of CO_2 to normalize pH is unexpected because the resultant hypoxemia is not physiologic (15). However, human studies demonstrated a reduction in minute volume in response to induced metabolic alkalosis (16). Furthermore, blunting of the chemoreceptor stimulus in the face of metabolic alkalosis results in dependence on hypoxic drive for ventilation (17). We identified one other pediatric case report describing a patient on PD (Physi-oneal) with nocturnal hypoventilation as a consequence of bicarbonate-based dialysis fluid (18).

HYPERCAPNIA

Our patients pose a clinical dilemma regarding the consequences of chronic hypercapnia. Sleep-disordered breathing is associated with impaired verbal memory (19) in adults and behavioral problems (4) in children, but the underlying mechanisms are unclear. One theory suggests induction of

endothelial nitric oxide synthase alters cerebral perfusion (20). Cerebral hypercapnia may adversely affect neuropeptides and neurotransmission (21). Hypoxia leads to pulmonary vascular remodeling and pulmonary hypertension (22). Hypercapnia may worsen this process by inhibiting angiogenesis stimulated by hypoxia (22). In chronic obstructive pulmonary disease patients, hypercapnia is associated with increased morbidity and mortality (22), suggesting that hypercapnia may be detrimental with or without hypoxia.

OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea is defined as the cessation of airflow in the presence of respiratory effort for at least 2 breaths (9). Pediatric OSA is frequently related to adenoidal/tonsillar hypertrophy (23). In the context of CKD, rostral fluid shifts and uremia play a significant role. Obstructive sleep apnea is more common in patients with peripheral edema (24), suggesting fluid shift in the recumbent position leads to swelling of the peripharyngeal tissues and venous distention, predisposing to OSA. Studies in adult heart failure patients show a correlation between overnight fluid displacement from the legs and neck and more severe OSA (25,26). A study of adult CKD patients demonstrated a similar correlation (27).

Uremia contributes by reducing airway muscle tone during sleep (20), likely related to neuronal depressive effects of uremic toxins causing a reduction in airway muscle tone (20). This is further supported by studies demonstrating improvement of SA with improved dialytic clearance of fluid and uremic waste (11,28).

CONCLUSION

Sleep-disordered breathing is common in children with CKD, based on questionnaire data, but PSG data are lacking in this group. In patients using PD with bicarbonate-containing solutions, consideration of SDB is important as subsequent metabolic alkalosis can potentially lead to hypoventilation and hypercapnia. Other metabolic disturbances frequently seen in CKD such as metabolic acidosis may predispose to CSA. Obstructive sleep apnea, while most commonly due to adenoidal/tonsillar enlargement, may be related to rostral fluid shifts and upper airway muscle weakness secondary to uremia. It is imperative for clinicians to be aware that patients with CKD and PD patients using bicarbonate-containing solutions may be especially predisposed to SDB. Treatment of SDB improves quality of life, and may reduce additional morbidity and mortality.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

Neha Sharma¹
Elizabeth Harvey²
Reshma Amin^{1*}

Division of Respiratory Medicine¹
Hospital for Sick Children
Division of Nephrology²
Hospital for Sick Children
University of Toronto, Toronto, Canada

*Email: reshma.amin@sickkids.ca

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