Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension improves sleep-disordered breathing

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Rationale

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by chronic obstruction of the pulmonary arteries with organized clot[1]. Comorbid sleep-disordered breathing (SDB) could further aggravate pulmonary hypertension and adversely affect outcome. Limited data are available on the prevalence of SDB in CTEPH[2-4], and so far, the effect of balloon pulmonary angioplasty (BPA) on SDB has not been evaluated. We hypothesized that subjects with CTEPH have a high prevalence of SDB, both obstructive and central sleep apnea (CSA) with associated hypoxemia, which could improve with BPA.

Methods

50 consecutive patients with treatment-naïve CTEPH at Vienna General Hospital underwent pre- and post-BPA polygraphy (nasal pressure sensor, thermistor, sensors for thoracoabdominal excursions, pulse oximeter; Alice PDx, Philipps®) and hemodynamic and echocardiographic assessments. BPA consisted of 4 to 11 interventions per patient (median time of treatment: 12 months).

Results

Before BPA, prevalence of SDB (defined as an apnea-hypopnea index (AHI) >5 per hour) was 76%: 12 patients (24%) without SDB, 28 (56%) with predominantly obstructive sleep apnea (OSA; AHI= 24), and 10 (20%) with predominantly central sleep apnea (CSA; AHI= 32; see table 1). OSA was associated with male gender, and overnight fluid-shifts, whereas CSA was associated with increased right ventricular end-diastolic diameter. Patients with SDB had significantly higher oxygen-desaturation index (ODI), and tendency for worse nocturnal desaturation than those without SDB (Table 1).

After BPA, overall mean AHI and ODI decreased by 33% (p=0.006) and 26% (p=0.004), respectively (Table 2). In OSA patients, AHI decreased from 24 to 18 (p= 0.009) and in CSA patients AHI decreased from 32 to 18 (p= 0.018; Figure 1). Along with improvement in SDB, nocturnal desaturation decreased in both, CSA (T90% = time-below-90% SpO2 of time-in-bed) from 62% to 51%, p=0.009) and OSA (T90 from 46% to 39%, p=0.02, Figure 3). Oxygen desaturation index decreased by 23% in OSA (p= 0.003), and 38% in CSA (p=0.013; Figure 2). Mean nocturnal saturation increased by 1.9% in CSA (p= 0.020), and 0.7% in OSA (p= 0.045; Table 3+4).

Table 1. Baseline results (before BPA)

	No SDB (n=12)	OSA (n= 28)	CSA (n= 10)	p-value
Age (yrs.) (mean ± SD)	54.3 ± 16.1[c]	67.9 ± 12.1[a,c]	49.4 ± 18.8[a]	0.001
BMI (kg/m²) (mean ± SD)	31.26 ± 15.3	28.2 ± 6.6	27.5 ± 6.7	n.s
Male (n, %)	1 (8.3)[c]	15 (53.6)[c]	6 (60)	0.015
NYHA class III-IV (n, %)	7 (58.3)	12 (42.9)	6 (60.0)	n.s.
Mean PAP (mmHg) (mean ± SD)	51.7 ± 17.2	44.0 ± 11.5	48.1 ± 9.0	n.s
PVR (dyn·s·cm⁻⁵) (mean ± SD)	836.1 ± 473.1	606.2 ± 326.7	640.0 ± 170.5	n.s
PVR (Wood Units) (mean ± SD)	10.5 ± 5.9	7.1 ± 4.1	7.8 ± 2.1	n.s
Cardiac index (l/min/m²) (mean ± SD)	2.50 ± 0.46	2.47 ± 0.53	2.84 ± 0.73	n.s
Cardiac output (l/min) (mean ± SD)	4.51 ± 0.90	4.77 ± 1.21	5.60 ± 1.47	n.s
Stroke volume (ml) (mean ± SD)	59.4 ± 18.8	69.0 ± 18.0	71.6 ± 20.3	n.s
PAWP (mmHg) (mean ± SD)	10.6 ± 3.6	10.3 ± 4.1	10.8 ± 2.6	n.s
Diastolic gradient (mean ± SD)	20.1 ± 11.4	14.9 ± 9.8	17.4 ± 8.3	n.s
RVEDD >40 mm (n, %)	6 (50.0)[b]	6 (21.4)[a]	9 (90.0)[a,b]	<0.001
Epworth sleepiness scale (mean ± SD)	4.3 ± 3.0	7.0 ± 5.9	6.0 3.4	n.s
Fatigue severity index (mean ± SD)	3.2 ± 1.6	4.1 ± 1.8	5.0 ± 1.6	0.058
Neck circumference (cm) (mean ± SD)	37.5 ± 3.4	40.0 ± 3.4	39.1 ± 4.0	n.s
Calf diff. overnight (cm) (mean ± SD)	-0.13 ± 0.83	-0.80 ± 1.1	-0.55 ± 0.53	0.068
AHI (n/h) (mean ± SD)	3.6 ± 2.2[b,c]	23.9 ± 18.7[c]	31.7 ± 33.7[b]	<0.001
HI (n/h) (mean ± SD)	2.8 ± 1.9[b,c]	17.2 ± 15.5[c]	18.1 ± 14.7[b]	<0.001
ODI (n/h) (mean ± SD)	6.4 ± 3.4[b,c]	26.8 ± 20.0[c]	40.1 ± 34.9[b]	<0.001
T90 (% of sleep) (mean ± SD)	53.0 ± 34.6	50.5 ± 35.7	56.6 ± 37.0	n.s
Mean SpO2 (%) (mean ± SD)	91.3 ± 3.4	88.6 ± 3.4	88.5 ± 5.6	n.s
Lowest SpO2 (%) (mean ± SD)	85.0 ± 5.7[b,c]	78.9 ± 6.5[c]	76.5 ± 7.9[b]	0.010
Snoring (n, %)	3 (25.0)[c]	23 (82.1)[a,c]	4 (40.0)[a]	<0.001

[a]p< 0.05 CSA vs OSA. [b]p< 0.05 CSA vs No SDB. [c]p< 0.05 OSA vs No SDB.

Table 2. Hemodynamic changes after BPA

	Pre-BPA	Post-BPA	p-value
Mean PAP (mmHg) (mean ± SD)	46.7 ± 12.7	33.8 ± 12.0	<0.001
Sys. PAP (mmHg) (mean ± SD)	80.2 ± 24.7	58.8 ± 21.7	<0.001
Diast. PAP (mmHg) (mean ± SD)	27.1 ± 9.0	18.8 ± 9.1	<0.001
PVR (dyn·s·cm⁻⁵) (mean ± SD)	670.8 ± 332.0	401.9 ± 258.3	<0.001
PVR (Wood Units) (mean ± SD)	8.2 ± 4.2	4.9 ± 3.2	<0.001
Cardiac index (l/min/m²) (mean ± SD)	2.55 ± 0.57	2.72 ± 0.58	n.s.
Cardiac output (l/min) (mean ± SD)	4.88 ± 1.24	5.18 ± 1.33	n.s.
Stroke volume (ml) (mean ± SD)	67.24 ± 18.80	72.8 ± 16.7	0.045
PAWP (mmHg) (mean ± SD)	10.5 ± 3.7	10.6 ± 3.8	n.s.
Diastolic gradient (mean ± SD)	16.6 ± 9.9	8.2 ± 7.2	<0.001
NT-proBNP (ng/l) (mean ± SD)	1620.3 ± 2318.0	675.1 ± 1545.9	<0.001

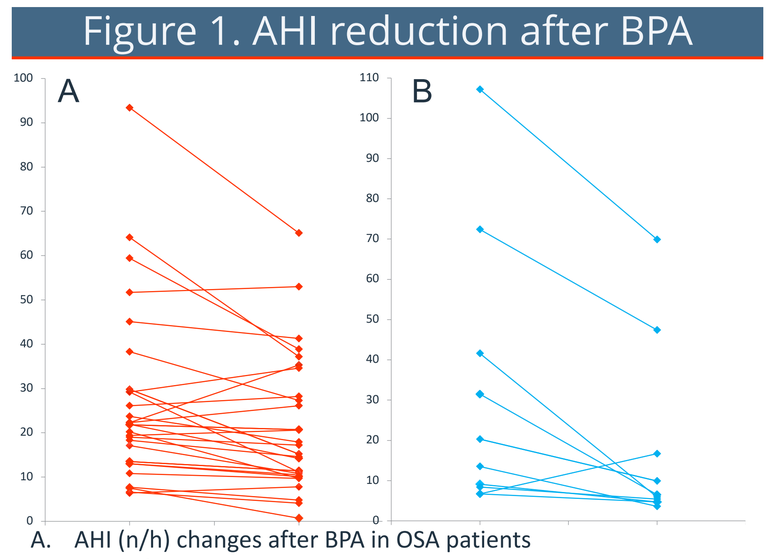
Table 3. OSA after BPA

OSA patients (n= 28)	Pre-BPA	Post-BPA	p-value
AHI (n/h) (mean ± SD)	23.9 ± 18.7	17.7 ± 12.1	0.009
ODI (n/h) (mean ± SD)	26.8 ± 20.0	21.3 ± 15.5	0.003
T90 (% of sleep) (mean ± SD)	50.5 ± 37.5	42.9 ± 34.4	0.046
Mean SpO2 (%) (mean ± SD)	88.6 ± 3.4	89.3 ± 3.5	0.045
Lowest SpO2 (%) (mean ± SD)	78.9 ± 6.5	78.4 ± 6.8	n.s.
Snoring (n, %)	23 (82.1)	18 (64.3)	n.s
Mean heart rate (bpm) (mean ± SD)	65.9 ± 8.0	65.8 ± 8.0	n.s.
Max. heart rate (bpm) (mean ± SD)	92.8 ± 10.2	101.5 ± 23.2	n.s.
Epworth sleepiness scale (mean ± SD)	7.0 ± 5.9	5.6 ± 5.0	0.009
Fatigue severity index (mean ± SD)	4.1 ± 1.8	3.2 ± 1.7	<0.001
Calf diff. overnight (cm) (mean ± SD)	-0.80 ± 1.1	-0.66 ± 1.0	0.023

Table 4. CSA after BPA

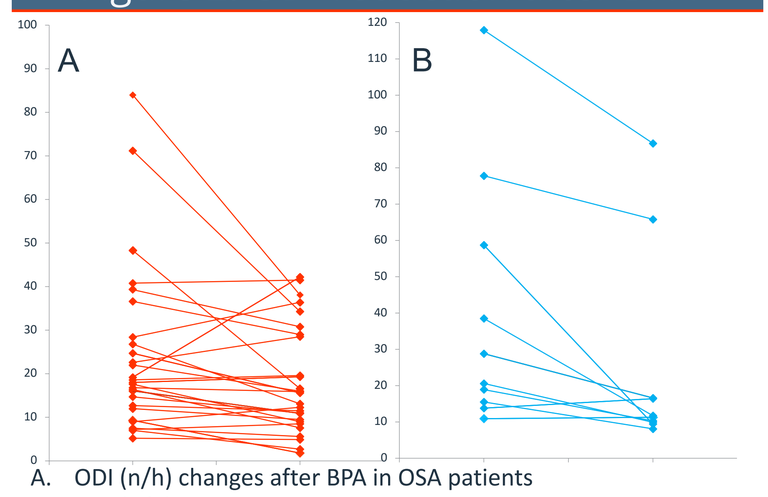
CSA patients (n= 10)	Pre-BPA	Post-BPA	p-value
AHI (n/h) (mean ± SD)	31.7 ± 33.7	17.5 ± 22.7	0.018
ODI (n/h) (mean ± SD)	40.1 ± 34.9	24.6 ± 27.8	0.013
T90 (% of sleep) (mean ± SD)	56.6 ± 37.0	36.5 ± 38.5	0.004
Mean SpO2 (%) (mean ± SD)	88.5 ± 5.6	90.4 ± 3.0	0.020
Lowest SpO2 (%) (mean ± SD)	76.5 ± 7.9	82.1 ± 4.6	0.008
Snoring (n, %)	4 (40.0)	2 (20.0)	n.s.
Mean heart rate (bpm) (mean ± SD)	65.1 ± 13.1	65.1 ± 13.1	n.s.
Max. heart rate (bpm) (mean ± SD)	102.7 ± 35.7	112.7 ± 51.2	n.s.
Epworth sleepiness scale score (mean ± SD)	6.0 ± 3.4	5.4 ± 2.9	n.s.
Fatigue severity index (mean ± SD)	5.0 ± 1.6	3.5 ± 1.2	0.011
Calf diff. overnight (cm) (mean ± SD)	-0.55 ± 0.53	-0.10 ± 0-50	0.039

Figure 1. AHI reduction after BPA



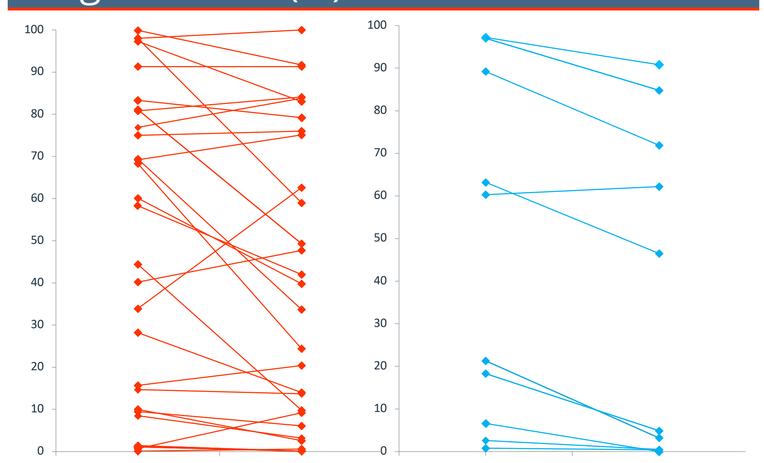
A. AHI (n/h) changes after BPA in OSA patients
B. AHI (n/h) changes after BPA in CSA patient

Figure 2. ODI reduction after BPA



A. ODI (n/h) changes after BPA in OSA patients
B. ODI (n/h) changes after BPA in CSA patient

Figure 3. T90(%) reduction after BPA



A. T90 (%) changes after BPA in OSA patients
B. T90 (%) changes after BPA in CSA patient

Conclusion

In CTEPH, there is a high prevalence of OSA and CSA. OSA was associated with nocturnal rostral fluid shifts and CSA was associated with right ventricular dilatation.

We found that BPA significantly improved SDB breathing and associated nocturnal desaturations. Future studies will show if effective treatment of SDB will enhance improvement of hemodynamics, morbidity and mortality in CTEPH, in addition to mechanical treatments.

Contact

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