Dynamic respiratory mechanics and exertional dyspnoea in pulmonary arterial hypertension

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ONLINE DATA SUPPLEMENT

METHODS

Patients and controls

We studied 25 consecutive clinically stable patients with idiopathic or heritable PAH [1], diagnosed according to the current evidence-based clinical practice guidelines [2, 3]. Patients were included in the study irrespective of the treatment received, if they had been clinically stable during the 3 preceding months, and if they were scheduled for CPET within the frame of their clinical follow-up at the reference center. Exclusion criteria were: *1*) past or current tobacco-smoking history; *2*) spirometric evidence of an obstructive ventilatory defect as defined by a reduced FEV_1/VC ratio below the 5^{th} percentile of the predicted value [4]; *3)* body mass index (BMI) >30 $kg.m^{-2}$; *4)* use of supplemental oxygen; *5)* PAH induced by drugs and toxins; *6)* PAH associated with other conditions, including connective tissue diseases, congenital heart diseases, portal hypertension, and HIV infection [1]; *7)* chronic thromboembolic pulmonary hypertension [1]; *8)* other respiratory, cardiac and other diseases that could contribute to dyspnoea or exercise limitation; or *9*) contraindications to clinical exercise testing [5].

Procedures

Pulmonary function tests were performed using automated equipment (Masterscreen MS Body and Diffusion, tyb B/IEC 601-1/IP20, Jaeger, Germany) according to recommended standards [6-8]. Measurements were expressed as percentages of predicted normal values [9]; predicted

inspiratory capacity (IC) was calculated as predicted total lung capacity (TLC) minus predicted functional residual capacity (FRC). Symptom-limited incremental CPETs were conducted on an electrically braked cycle ergometer (Ergoline 100P mitBD; Medisoft, Sorinnes, Belgium) with a cardiopulmonary exercise testing system (Ergocard model E, Medisoft, Sorinnes, Belgium). To ensure safety, oxygen saturation (SpO_2), heart rate (HR), cardiac rhythm and ST-segment changes, and blood pressure (indirect sphygmomanometry) were evaluated at rest and throughout exercise testing. Breath-by-breath cardiopulmonary and metabolic data were collected at baseline and throughout exercise while subjects breathed through a mouthpiece with nasal passages occluded by a nose-clip. Exercise variables were measured and averaged over the last 20 seconds of each minute and at peak exercise. Exercise variables were compared with the predicted normal values of Jones [10]. Maximum ventilatory capacity (MVC) was estimated as $35 \times FEV_1$[11]. Measurements of arterial partial pressure of CO_2 ($PaCO_2$, Torr) were obtained at rest and at peak exercise only in PAH patients. The physiological dead space-to-tidal volume ratio (V_D/V_T) and the gradient between arterial and end-tidal carbon dioxide partial pressure [$P(a\text{-}ET)CO_2$] were also calculated [12].

TABLES

Table 1. Specific pulmonary arterial hypertension (PAH) pharmacotherapy in patients who developed dynamic lung hyperinflation (PAH-H) during exercise and in those who did not (PAH-NH)

	PAH-H (n = 15)	PAH-NH (n = 10)
Oral anticoagulants	11	5
Diuretics	10	3
Digoxin	0	0
Calcium channel blockers	3	3
Prostanoids:		
Epoprostenol	6	1
Iloprost	0	0
Treprostinil (IV)	2	1
Beraprost	0	0
Endothelin receptor antagonists:		
Bosentan	10	6
Sitaxentan	0	0
Ambrisentan	0	0
Phosphodiesterase type-5 inhibitors:		
Sildenafil	9	6
Tadalafil	1	0

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