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Severely impaired health-related quality of life in chronic hyperventilation patients: Exploratory data

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Summary
Patients with hyperventilation syndrome (HVS) report severe symptom-related suffering and often complain from insufficient medical attention. However, quality of life data in this context are scarce. We aimed at assessing the health-related quality of life (HRQoL) of HVS patients. Twenty-one HVS patients with extensive cardiorespiratory workup including cardiopulmonary exercise testing (CPET) filled in the generic SF-36 questionnaire and the results were compared to French normal values. Correlations between SF36 dimensions and clinical and functional data were established. All SF-36 scores were markedly decreased in HVS patients compared to healthy subjects: Physical Functioning: 44 ± 24, Social Functioning: 57 ± 27, Role Physical: 21 ± 32, Role Emotional: 48 ± 42, Mental Health: 51 ± 27, Vitality: 34 ± 20, Body Pain: 41 ± 21, General Health: 42 ± 21. These figures were all significantly lower in the HVS patients respective to the normal reference population. They were also lower than corresponding values published in patients with asthma or chronic obstructive pulmonary disease (COPD). "Vitality" and "Physical Functioning" scores were correlated with Nijmegen score ($r = -0.594$, $p = 0.047$) and peak respiratory frequency during CPET ($r = -0.644$, $p = 0.019$). The SF-36 Social Functioning score was correlated

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with the ventilatory threshold ($r = 0.629$, $p = 0.034$), peak $V'E/V'CO_2$ (ventilation/CO_2 production) ($r = 0.650$, $p = 0.016$) and peak $PaCO_2$ ($r = -0.664$, $p = 0.027$).

In conclusion, this study shows that HRQoL can be severely impaired in patients with HVS, which is one more reason to take this condition seriously.

Background

The term "hyperventilation syndrome" (HVS) designates a condition comprising a variety of somatic and psychological symptoms associated with physiologically inappropriate alveolar hyperventilation [1,2] that may be chronic or triggered by mental stress or exercise. The symptoms (primarily dyspnea, but also chest pain, anxiety or even panic attacks [3] and many other manifestations) are episodic in nature. No clear pathophysiological mechanism has been identified. HVS is difficult to diagnose because of the labile nature of the symptoms, the absence of any readily identifiable somatic abnormality, and the absence of a gold standard diagnostic method. HVS may be isolated, in the presence of normal cardiorespiratory function ("idiopathic HVS"), but can also occur in patients with other respiratory diseases (for example, asthma), which further complicates the diagnostic. In these settings, the diagnosis of HVS can be considered when the documented abnormalities are insufficient to explain the symptoms or blood gas abnormalities. Several diagnostic tools have been proposed, including the Nijmegen questionnaire [4], reproduction of symptoms during voluntary hyperventilation challenge [5—8], measurement of gas exchanges during exercise [9] or during a shift from the sitting to the standing position [10]. However, none of these diagnostic tools are completely satisfactory. Of note, arterial hypocapnia at rest is a useful clue to HVS, but is probably the hallmark of more chronic and/or more severe forms of the condition.

For the above reasons (diversity and lability of symptoms, their intricate association with anxiety, lack of clear pathophysiology, diagnostic difficulties), HVS tends to be poorly perceived and often neglected by both general practitioners and specialists. However, clinical experience suggests that HVS patients may suffer severely from their condition. Exercise intolerance [11] and an exaggerated feeling of the unpleasantness of dyspnea for a given level of perceptual intensity are probably important causes of this suffering [12]. HVS patients report that the limited attention paid by doctors to their condition also contributes to their distress. The impact of HVS on health-related quality of life (HRQoL) has however not been extensively described. We hypothesized that HVS would have a major negative impact on HRQoL, and tested this hypothesis by applying the French version of the generic SF-36 questionnaire [13] in a population of patients diagnosed with HVS.

Methods

Setting

The study was conducted in a tertiary referral dyspnea clinic run by the 86-bed respiratory medicine unit of a teaching hospital. All patients referred to this clinic are systematically assessed by pulmonary function tests (PFTs), room air arterial blood gases and Doppler echocardiography when not already available in their charts. Cardiopulmonary exercise testing (CPET) is also performed for the purposes of differential diagnosis and to evaluate the disproportionateness of dyspnea in cases of HVS associated with respiratory abnormalities. When HVS is suspected on the basis of these examinations, the Nijmegen questionnaire (16 items related to common complaints due to chronic hyperventilation) is also applied and a hyperventilation provocation test (HVPT) is performed (see below, Methods). The French Sadoul dyspnea scale [14] and the Baseline Dyspnea Index [15] are systematically measured. The present study was approved by the French learned society institutional review board ("*Société de Pneumologie de Langue Française*" reference number CEPRO2012-009) and patients gave their consent to anonymous use of their data for research purposes.

Inclusion criteria

Patients were included in the study when they met the following criteria:

- at least two compatible clinical symptoms among dyspnea, chest tightness, chest pain, palpitations, blurred vision, dizzy spells, bloated feelings in stomach, tingling fingers, stiff fingers or arms, feeling of tightness around the mouth, cold hands or feet, feeling tense or feelings of anxiety;
- resting hypocapnia with $PaCO_2$ <38 mmHg with a normal alveolar-arterial gradient for oxygen ($PA\text{-}aO_2$);
- absence of significant obstructive or restrictive ventilatory defects on PFTs;
- absence of pulmonary artery hypertension on Doppler echocardiography;
- absence of exercise-induced increase of $PA\text{-}aO_2$.
- at least two criteria among: Nijmegen score ≥ 23 [4]; reproduction of at least 2 usual symptoms during HVPT and delayed return of the end-tidal partial pressure of carbon dioxide in the expired gas ($PETCO_2$) to baseline during HVPT (see below).

Pulmonary function testing

Spirometry, plethysmography and single-breath lung diffusing capacity for carbon monoxide (D_LCO) were performed in all patients (Jaeger Masterscreens Body®) according to the joint guidelines of the American Thoracic Society and of the European Respiratory Society [16—18].