Minute-Ventilation Variability During Cardiopulmonary Exercise Test Is Higher In Idiopathic Dyspnoea Subjects Compared To Subjects With Breathing Pattern Disorder.

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Research Article

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Abstract

Background: Patients with abnormal breathing responses often report presenting with debilitating symptoms that negatively impact both physical and mental quality of life.

Objective: To compare time-domain variability of ventilatory components of Idiopathic dyspnoea and Breathing Pattern Disorder during a progressive maximal exercise test, evaluating their relationship to other variables usually obtained during a cardiopulmonary exercise test.

Methods: Analysis of time-domain variability (RMSSD) of minute-ventilation (VE) during a maximal cardiopulmonary exercise test of 13 subjects with Idiopathic dyspnoea and 13 subjects with dysfunctional breathing pattern. Data was compared by a two-tailed Student T-test.

Results: Idiopathic dyspnoea subjects exhibited a greater Minute-Ventilation Variability (31.5 ± 6.2 Vs 25.4 l/min ± 8.0 , $p > 0.05$). Inspiratory tidal volume time ratio (VT_{in}/t_i) (1.96 ± 0.7 Vs 2.58 ± 0.6 , $p > 0.05$) and Breathing Frequency (35 ± 9.3 Vs 43 breath/min ± 8.2 $p > 0.05$) were also significantly lower in Idiopathic Dyspnoea compared to Breathing Pattern Disorder subjects.

Conclusions: Time-domain variability of minute ventilation during exercise is greater in Idiopathic Dyspnoea compared to the Breathing Pattern Disorder subject's possible highlighting a lower ventilatory threshold.

Introduction

Many patients with Idiopathic dyspnoea (ID) or Breathing Pattern Disorder (BDP) such as Postural Orthostatic Tachycardia Syndrome, Hyperventilation or Dysautonomia present with debilitating symptoms that negatively impact both physical and mental quality of life¹. Changes in normal breathing can result in symptoms of; dizziness, blood pressure fluctuations, paraesthesia and tachypnoea^{2,3}. Furthermore, abnormal breathing patterns are routinely seen in 20% of individuals with asthma⁴.

Therefore the quantitation of ventilatory variability may prove a significant prognostic indicator in this subject group.

Methods

Dyspnoea is defined as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity"^{5,6}. BPD was determined by either Physiotherapist assessment or by using The Brompton Breathing Pattern Assessment Tool (BPAT). A BPAT > 4 was seen as positive⁷.

26 subjects (13 ID, 13 BPD) underwent cardiopulmonary exercise test as part of routine clinical care. Table 1 shows the primary diagnoses for the ID cohort.

This study was approved by the Respiratory Medicine Research Committee at St Barts NHS Trust.

Table 1: Idiopathic dyspnoea primary diagnoses	
Primary Diagnosis	Number of Subjects
Asthma	1
Chronic Cough	1
Gastro-Oesophageal Reflux Disease	2
Obstructive Sleep Apnoea	1
Pulmonary Embolism	3
Shortness Of Breath On Exertion	2
Unexplained Breathlessness	3

Time-domain variability analysis of data was applied retrospectively. Root mean square successive difference (RMSSD) (Figure 1) is widely used in cardiology to quantify heart-rate variability and is appropriate for this subject group^{8,9,10}.

Study Protocol

This was a retrospective, single centre study, all subjects performed a maximal cardiopulmonary exercise test using an electrically-braked cycle ergometer (VIAsprint 150 cycle ergometer, Vyair Medical Products Ltd, Basingstoke, UK) following an individualised incremental ramp protocol up to exhaustion. All tests achieved at least two of the following criteria to be considered maximum: Post-exercise blood lactate levels ≥ 8 mmol·L⁻¹, VE_{peak} / MVV % ≥ 85 , or a respiratory exchange ratio ≥ 1.05 .⁶

Cardiopulmonary exercise tests were performed with gas exchange and ventilatory variables being analysed breath-by-breath using a calibrated computer-based exercise system (Vyntus CPX Metabolic Cart, Vyair Medical Products Ltd, Basingstoke, UK). The O₂ and CO₂ analysers were calibrated before each test using a reference gas (12% O₂; 5% CO₂; nitrogen balance). The pneumotachograph used was also calibrated, with an automatic differential flow profile.

During each cardiopulmonary exercise test, a 12-lead electrocardiogram was continuously recorded (Vyntus ECG 12-lead PC-ECG) and heart rate automatically derived. Heart Rate (HR), Breathing Frequency (BF), Minute Ventilation (VE) Oxygen Uptake (VO₂) and ventilatory parameters of Inspiratory Time/Total Inspiratory and Expiratory Time Ratio (ti/ttot), Inspiratory And Expiratory Time Ratio (ti/te), Inspiratory Tidal Volume Time Ratio (VT_{in}/ti) and Breathing Frequency Tidal Volume Ratio (BF/VT_{ex}) were measured by breath-by-breath.

All breath-by-breath results were exported to an Excel spreadsheet (Microsoft Corporation, USA), where root mean square successive difference (RMSSD) of minute ventilation during exercise test was calculated for each subject. Data was normalised to reduce the risk of observation bias.

We hypothesised that time-domain ventilatory variability during exercise would be greater in Idiopathic Dyspnoea subjects than in Dysfunctional Breathing subjects due to a lower ventilatory threshold¹⁴. Therefore the present study was designed to compare time-domain minute-ventilation variability of these groups during a progressive maximal exercise test.

Statistical Analysis

Statistical analysis was performed using the software Graphpad 7.0 (Graphpad Software Inc, USA). Variables from the cardiopulmonary exercise tests showed normal distribution when analysed by the Shapiro Wilk’s test. Exercise variables in both groups were compared by paired two-tailed Student T test. Significance was set at $p < 0.05$. Results are presented as mean $\pm$ standard deviation. Based on similar studies a sample size of 26 individuals (13 in each group) would be needed to provide an $>80\%$ power with a 2-sided alpha of 0.05 ⁷.

Results

There were no differences in demographic and anthropometric characteristics of both groups (Table 2). Peak cardiopulmonary exercise data of both groups are shown in Table 3.

The ID group were significantly lower difference in *Breathing Frequency*, *Minute Ventilation* and *Inspiratory Tidal Volume Time Ratio* compared BPD group. Furthermore, ID subjects exhibited a significantly higher time-domain variability of minute-ventilation than BPD subjects during cardiopulmonary exercise test, as shown in Figure 1.

Table 2 – Demographic And Anthropometric Data (n = 26)

Idiopathic Dyspnoea				Breathing Pattern Disorder			
Variable							p-value
Age	51	$\pm$	17	51	$\pm$	21	0.94
Height (Cm)	168	$\pm$	10	166	$\pm$	9	0.56
Weight (Kg)	84	$\pm$	17	72	$\pm$	27	0.18
BMI	30	$\pm$	5	26	$\pm$	8	0.16

*Comparison between groups by student T test. BMI: body mass index.

Table 3 – Peak Exercise Data During Graded Maximal Cardiopulmonary Exercise Test

Idiopathic Dyspnoea

Breathing Pattern Disorder

							p-value
HR (beats/min)	139	±	26.8	152	±	25.6	0.23
BF (breaths/ min)	35	±	9.3	43	±	8.2	0.03*
VE (L)	50	±	19.2	67	±	14.5	0.02*
RMSSD VE (L)	31.5	±	6.2	25.4	±	8.0	0.03*
V'O ₂ /kg (mL/kg/min)	17	±	4.8	21	±	7.3	0.15
ti/ttot	55	±	9.9	56	±	8.0	0.75
ti/te	118	±	32.8	126	±	34.0	0.57
VTin/ti	1.96	±	0.7	2.58	±	0.6	0.02*
BF/VTex	51	±	15.2	52	±	16.3	0.82

Heart Rate (HR), Breathing Frequency (BF), Minute Ventilation (VE) Oxygen Uptake (VO₂), Inspiratory Time/Total Inspiratory and Expiratory Time ratio (ti/ttot), Inspiratory and expiratory time ratio (ti/te), Inspiratory tidal volume time ratio (VTin/ti) and Breathing Frequency tidal volume ratio (BF/VTex). *Comparison between groups by student T test

Discussion

The current study has shown that subjects with ID have greater minute ventilation variability during cardiopulmonary exercise than subjects with BPD. Interestingly however further analysis showed that ID subjects exhibit a reduction in Breathing Frequency and Inspiratory Tidal Volume Time Ratio during maximal graded exercise compared to BPD subjects.

From these findings have emerged two conflicting conclusions; (1) that a lower ventilatory threshold was seen in the Idiopathic Dyspnoea compared to the other group. It is known that in chronic populations such as Chronic Obstructive Pulmonary Disease a diminishing ventilatory threshold has if often the resultant of changes in pH and HCO₃ this may be cause of rapidly developing tachypnoea⁸.

(2) The conflicting conclusion, do subjects with BPD in fact exhibit and abnormal ventilatory response whereas ID subjects have better chemoreceptor control and therefore breathe in a deeper and more efficient manner?

Conclusions

The present study adds information regarding the quantification of exercise minute-ventilation variability however the exact triggers that influence ventilatory variability during exercise remain unclear.

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Declarations

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Figures

Figure 1

Minute-ventilation variability (RMSSD) of Idiopathic Dyspnoea subjects and Breathing Pattern Disorder subjects during a graded maximal exercise test. * $p < 0.05$