

## LETTER

## Effect of acute hypoxia on QTc interval in respiratory patients undergoing fitness to fly tests

## INTRODUCTION

Current UK guidelines recommend administration of in-flight supplemental oxygen to patients with chronic respiratory disease who have sea level arterial oxygen saturations <92% or partial pressure of oxygen (PaO<sub>2</sub>) <6.6 kPa (50 mm Hg) during a hypoxic challenge fitness to fly test.<sup>1</sup> Hypoxia has been shown to prolong cardiac repolarisation, assessed by the QT interval corrected for heart rate (QT<sub>c</sub>), and this may underlie the occurrence of potentially life-threatening cardiac arrhythmias<sup>2-4</sup>; however, few data exist about the cardiac response to hypoxia in patients with respiratory disease.

To establish whether hypoxia prolongs the QT<sub>c</sub>, potentially increasing the risk of significant arrhythmias in patients with respiratory disease, we analysed data from respiratory patients referred to our lung function department for fitness to fly testing.

## METHODS

Between 1 April 2008 and 27 February 2009, 101 patients (median age 57 years, range 20–87 years, 57.4% female) underwent hypoxic challenge (breathing 15% oxygen from a Douglas bag). Pulse oximetry was recorded continuously and an ECG recorded at baseline and after 15 min hypoxic exposure. In 65 patients (64.4%), capillary blood gases were analysed at the same time points. Further details are available online.

## RESULTS

Disease aetiology was interstitial lung disease (39.6%), chronic obstructive pulmonary disease (COPD) (11.9%), bronchiectasis (11.9%), sarcoidosis (7.9%), cystic fibrosis (6.9%), systemic sclerosis (5.9%), asthma (5.0%), extrinsic allergic alveolitis (3.0%) and other chronic lung conditions (7.9%). Fifteen subjects (14.9%) had known cardiac disease.

Following hypoxic exposure, mean±SEM arterialised capillary PO<sub>2</sub> decreased from 10.56±0.14 kPa to 6.82±0.09 kPa (p<0.001) and mean arterial oxygen saturation (SaO<sub>2</sub>) from 95.8±0.15% to 87.2±0.45% (p<0.001). Arterial carbon dioxide partial pressure, bicarbonate and transcutaneous carbon dioxide partial pressure also decreased (p<0.05, table 1).

Twenty patients (19.8%) became symptomatic during the test (combinations of dyspnoea, palpitations, nausea and dizziness). Eighty patients (79.2%) met the BTS criteria for use of supplemental oxygen in-flight.

Hypoxic challenge resulted in a significant increase in heart rate (from 83.2±1.48 bpm

**Table 1** Blood gas and ECG parameters at baseline and while breathing the 15% hypoxic mixture

Parameter	Mean	N	SD	SE mean	95% CI lower	95% CI upper	Significance
H <sup>+</sup> (0.21%)	36.58 nmol/l	65	2.35	0.29			
H <sup>+</sup> (0.15%)	36.06 nmol/l	65	2.41	0.30			
ΔH <sup>+</sup> (21–15%)	0.52 nmol/l	65	2.60	0.32	-0.1282	1.1590	0.12
Paco <sub>2</sub> (0.21%)	5.11 kPa	65	0.45	0.06			
Paco <sub>2</sub> (0.15%)	4.87 kPa	65	0.47	0.06			
ΔPaco <sub>2</sub> (21–15%)	0.25 kPa	65	0.40	0.05	0.14904	0.34942	<0.001
Pao <sub>2</sub> (0.21%)	10.56 kPa	65	1.17	0.14			
Pao <sub>2</sub> (0.15%)	6.82 kPa	65	0.77	0.09			
ΔPao <sub>2</sub> (21–15%)	3.75 kPa	65	1.06	0.13	3.48188	4.00920	<0.001
HCO <sub>3</sub> <sup>-</sup> (0.21%)	25.62 mmol/l	65	4.88	0.61			
HCO <sub>3</sub> <sup>-</sup> (0.15%)	24.46 mmol/l	65	2.33	0.29			
ΔHCO <sub>3</sub> <sup>-</sup> (21–15%)	1.16 mmol/l	65	4.15	0.51	0.1310	2.1860	0.03
BE (0.21%)	1.09 mmol	65	2.04	0.25			
BE (0.15%)	0.74 mmol	65	2.18	0.27			
ΔBE (21–15%)	0.35 mmol	65	1.7378	0.22	-0.0814	0.7798	0.11
Sao <sub>2</sub> (0.21%)	95.82%	65	1.19	0.15			
Sao <sub>2</sub> (0.15%)	87.15%	65	3.61	0.45			
ΔSao <sub>2</sub> (21–15%)	8.67%	65	3.38	0.42	7.8326	9.5090	<0.001
Ptcco <sub>2</sub> (0.21%)	5.12 kPa	39	0.69	0.11			
Ptcco <sub>2</sub> (0.15%)	4.84 kPa	39	0.74	0.12			
ΔPtcco <sub>2</sub> (21–15%)	0.28 kPa	39	0.28	0.05	0.1874	0.3715	<0.001
HR (21%)	83.22 bpm	101	14.97			1.49	
HR (15%)	86.89 bpm	101	15.09			1.50	
ΔHR (21–15%)	3.67 bpm	101	0.58	-4.809	-2.537	0.57	<0.001
PR (21%)	161.23 ms	96	16.09			1.64	
PR (15%)	158.01 ms	96	20.31			2.07	
ΔPR (21–15%)	3.22 ms	96	12.63	0.660	5.778	1.29	0.01
QRSD (21%)	91.93 ms	101	15.97			1.59	
QRSD (15%)	90.27 ms	101	15.92			1.58	
ΔQRSD (21–15%)	1.66 ms	101	9.13	-0.138	3.465	0.91	0.07
QT (21%)	357.75 ms	101	40.97			4.08	
QT (15%)	348.83 ms	101	35.03			3.49	
ΔQT (21–15%)	8.92 ms	101	24.05	4.173	13.669	2.39	<0.001
QTc (21%)	415.16 ms	101	25.86			2.57	
QTc (15%)	416.95 ms	101	24.02			2.39	
ΔQTc (21–15%)	1.79 ms	101	26.70	-7.062	3.478	2.66	0.50

21%, baseline measurement while breathing room air; 15%, test measurement after breathing 15% O<sub>2</sub> hypoxic mixture for 15 min; BE, base excess; ΔBE, change in base excess between 21% and 15% O<sub>2</sub>; H<sup>+</sup>, hydrogen ion concentration; ΔH<sup>+</sup>, change in hydrogen ion concentration between 21% and 15% O<sub>2</sub>; HCO<sub>3</sub><sup>-</sup>, bicarbonate ion concentration; ΔHCO<sub>3</sub><sup>-</sup>, change in bicarbonate ion concentration between 21% and 15% O<sub>2</sub>; HR, electrocardiographic heart rate; ΔHR, change in heart rate between 21% and 15% O<sub>2</sub>; Paco<sub>2</sub>, partial pressure of CO<sub>2</sub>; ΔPaco<sub>2</sub>, change in partial pressure of CO<sub>2</sub> between 21% and 15% O<sub>2</sub>; Pao<sub>2</sub>, partial pressure of O<sub>2</sub>; ΔPao<sub>2</sub>, change in partial pressure of O<sub>2</sub> between 21% and 15% O<sub>2</sub>; PR, electrocardiographic PR interval; ΔPR, change in PR interval between 21% and 15% O<sub>2</sub>; Ptcco<sub>2</sub>, transcutaneous CO<sub>2</sub>; ΔPtcco<sub>2</sub>, change in transcutaneous CO<sub>2</sub> between 21% and 15% O<sub>2</sub>; QRSD, electrocardiographic QRSD interval; ΔQRSD, change in QRSD interval between 21% and 15% O<sub>2</sub>; QT, electrocardiographic QT interval; ΔQT, change in QT interval between 21% and 15% O<sub>2</sub>; QT<sub>c</sub>, electrocardiographic QT<sub>c</sub> interval; ΔQT<sub>c</sub>, change in QT<sub>c</sub> interval between 21% and 15% O<sub>2</sub>; Sao<sub>2</sub>, oxygen saturation; ΔSao<sub>2</sub>, change in oxygen saturations between 21% and 15% O<sub>2</sub>.

to 86.9±1.50 bpm; p<0.001) and decrease in PR interval (161.2±1.64 ms to 158.0±2.07 ms; p=0.02). In keeping, the QT interval decreased (357.8±4.08 ms to 348.8±3.49 ms; p<0.001). However, ECG frontal axis and QT<sub>c</sub> did not change (415.2±2.57 ms to 417.0±2.39 ms; p=0.50).

There was no correlation between changes in QT<sub>c</sub> and PaO<sub>2</sub>/SaO<sub>2</sub>. No patient suffered arrhythmias or ischaemic ECG changes. The presence of cardiac disease was not associated with differences in baseline measures or hypoxia response, including variation in QT<sub>c</sub>. ECG responses did not differ between those

who had capillary blood gases performed (n=65) and those who did not (n=36; p>0.5 in all cases)

## DISCUSSION

Exposure to acute hypoxia (15% fractional inspired oxygen) is not associated with significant changes in cardiac QT<sub>c</sub> in patients with chronic respiratory disease, in contrast to the QT<sub>c</sub> prolongation seen in healthy subjects at altitude.<sup>2 4 5</sup> The absence of response might be due to hypoxic preconditioning<sup>6 7</sup> or drug effects upon autonomic efferent response (eg, salmeterol, ipratropium) or through other means (eg, renin-angiotensin system antagonists<sup>8</sup>). Given the association between prolonged QT<sub>c</sub> and sudden death in COPD,<sup>9</sup> these data are reassuring to patients with chronic lung disease who wish to fly. However, further studies are needed to confirm these findings, as well as the effects of prolonged hypoxia and exercise.

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