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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 (Pa_{O_2}) <6.6 kPa (50 mm Hg) during a hypoxic challenge fitness to fly test.[1] Hypoxia has been shown to prolong cardiac repolarisation, assessed by the QT interval corrected for heart rate (QT_c), and this may underlie the occurrence of potentially life-threatening cardiac arrhythmias[2–4]; however, few data exist about the cardiac response to hypoxia in patients with respiratory disease.

To establish whether hypoxia prolongs the QT_c, 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 P_{O_2} decreased from 10.56±0.14 kPa to 6.82±0.09 kPa (p<0.001) and mean arterial oxygen saturation (Sa_{O_2}) 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 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_c 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_c and Pa_{O_2}/Sa_{O_2}. 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_c. ECG responses did not differ between those

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^+ (0.21%)	36.58 nmol/l	65	2.35	0.29			
H^+ (0.15%)	36.06 nmol/l	65	2.41	0.30			
ΔH^+ (21−15%)	0.52 nmol/l	65	2.60	0.32	−0.1282	1.1590	0.12
Pa_{CO_2} (0.21%)	5.11 kPa	65	0.45	0.06			
Pa_{CO_2} (0.15%)	4.87 kPa	65	0.47	0.06			
ΔPa_{CO_2} (21−15%)	0.25 kPa	65	0.40	0.05	0.14904	0.34942	**<0.001**
Pa_{O_2} (0.21%)	10.56 kPa	65	1.17	0.14			
Pa_{O_2} (0.15%)	6.82 kPa	65	0.77	0.09			
ΔPa_{O_2} (21−15%)	3.75 kPa	65	1.06	0.13	3.48188	4.00920	**<0.001**
HCO_3 (0.21%)	25.62 mmol/l	65	4.88	0.61			
HCO_3 (0.15%)	24.46 mmol/l	65	2.33	0.29			
ΔHCO_3 (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
Sa_{O_2} (0.21%)	95.82%	65	1.19	0.15			
Sa_{O_2} (0.15%)	87.15%	65	3.61	0.45			
ΔSa_{O_2} (21−15%)	8.67%	65	3.38	0.42	7.8326	9.5090	**<0.001**
$Ptcc_{O_2}$ (0.21%)	5.12 kPa	39	0.69	0.11			
$Ptcc_{O_2}$ (0.15%)	4.84 kPa	39	0.74	0.12			
$\Delta Ptcc_{O_2}$ (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_2 hypoxic mixture for 15 min; BE, base excess; ΔBE, change in base excess between 21% and 15% O_2; H^+, hydrogen ion concentration; ΔH^+, change in hydrogen ion concentration between 21% and 15% O_2; HCO_3, bicarbonate ion concentration; $\Delta HCO_3{}^+$, change in bicarbonate ion concentration between 21% and 15% O_2; HR, electrocardiographic heart rate; ΔHR, change in heart rate between 21% and 15% O_2; Pa_{CO_2}, partial pressure of CO_2; ΔPa_{CO_2}, change in partial pressure of CO_2 between 21% and 15% O_2; Pa_{O_2}, partial pressure of O_2; ΔPa_{O_2}, change in partial pressure of O_2 between 21% and 15% O_2; PR, electrocardiographic PR interval; ΔPR, change in PR interval between 21% and 15% O_2; $Ptcc_{O_2}$, transcutaneous CO_2; $\Delta Ptcc_{O_2}$, change in transcutaneous CO_2 between 21% and 15% O_2; QRSD, electrocardiographic QRSD interval; ΔQRSD, change in QRSD interval between 21% and 15% O_2; QT, electrocardiographic QT interval; ΔQT, change in QT interval between 21% and 15% O_2; QT_c, electrocardiographic QT_c interval; ΔQT_c, change in QT_c interval between 21% and 15% O_2; Sa_{O_2}, oxygen saturation; ΔSa_{O_2}, change in oxygen saturations between 21% and 15% O_2.

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_c in patients with chronic respiratory disease, in contrast to the QT_c prolongation seen in healthy subjects at altitude.[2 4 5] The absence of response might be due to hypoxic preconditioning[6 7] or drug effects upon autonomic efferent response (eg, salmeterol, ipratropium) or through other means (eg, renin-angiotensin system antagonists[8]). Given the association between prolonged QT_c and sudden death in COPD,[9] 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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