individual behaviours of sleepy drivers. Our data, albeit from a limited number of patients with OSAS, support the reliability of a driving simulator approach for the identification of patients with OSAS at risk: poor performers have high risk if they keep on driving when sleepy. Accordingly, poorer simulated driving performance was associated with crash history only in our subjects with ‘risky’ behaviour. Nevertheless, the use of driving simulators is still recommended as a research tool given the absence of a standardisation that is the prerequisite for use in clinical practice.

Finally, crash risk is a multifactorial entity. Even if it is highly influenced by sleepiness, individual behaviours have a prominent effect in letting sleepiness determine a car accident. We emphasise that educational programmes, potentially involving driving simulators in different settings, remain the key instrument for risk management of sleepiness-related car accidents.

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Funding Ministry of Education, University and Research, Italy; PRIN 2006.

Competing interests None.

Contributors FP: study design, data collection and analysis, data interpretation, manuscript writing; SC: study design, data collection and analysis, data interpretation, manuscript writing; SM: study design, data interpretation; FC: study design, data interpretation, manuscript writing.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 29 July 2010
Published Online First 23 September 2010
doi:10.1136/thx.2010.140988

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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 (PaO2) <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 (QTc), and this may underlie the occurrence of potentially life-threatening cardiac arrhythmias2—4; however, few data exist about the cardiac response to hypoxia in patients with respiratory disease.

To establish whether hypoxia prolongs the QTc, 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 Po2 decreased from 10.56±0.14 kPa to 6.82±0.09 kPa (p<0.001) and mean arterial oxygen saturation (SaO2) 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 (557.8±4.08 ms to 348.5±3.49 ms; p<0.001). However, ECG frontal axis and QT, did not change (415.2±2.57 ms to 417.0±2.59 ms; p=0.50). There was no correlation between changes in QTc and PaO2, SaO2. 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 QTc. 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 QTc among patients with chronic respiratory disease, in contrast to the QTc prolongation seen in healthy subjects at altitude.2 4 5 The absence of response might be due to hypoxic preconditioning6 7 or drug effects upon autonomic effenter response (eg, salmeterol, ipratropium) or through other means (eg, renin-angiotensin system antagonists).8 Given the association between prolonged QTc and sudden death in COPD,2 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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JS drafted the manuscript and all authors have significantly contributed to, read and approved the final manuscript.

These data were orally presented in part at the British Thoracic Society Winter Meeting 2009 and have been published in abstract form in Thorax 2009;64: Supplement IV.

Funding This work was supported by the NIHR Respiratory Disease Biomedical Research Unit at the Royal Brompton and Harefield NHS Foundation Trust and Imperial College London.

Competing interests None.

Provenance and peer review Not commissioned; not externally peer reviewed.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>N</th>
<th>SD</th>
<th>SE mean</th>
<th>95% CI lower</th>
<th>95% CI upper</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>H+ (21%)</td>
<td>36.58 mmol/l</td>
<td>65</td>
<td>2.35</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H+ (15%)</td>
<td>36.06 mmol/l</td>
<td>65</td>
<td>2.41</td>
<td>0.30</td>
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<tr>
<td>ΔH+ (21–15%)</td>
<td>0.52 mmol/l</td>
<td>65</td>
<td>2.80</td>
<td>0.32</td>
<td>−0.1282</td>
<td>1.1590</td>
<td>0.12</td>
</tr>
<tr>
<td>PaCO2 (21%)</td>
<td>10.56 kPa</td>
<td>65</td>
<td>1.17</td>
<td>0.14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaCO2 (15%)</td>
<td>8.62 kPa</td>
<td>65</td>
<td>0.77</td>
<td>0.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔPaCO2 (21–15%)</td>
<td>1.94 kPa</td>
<td>65</td>
<td>0.40</td>
<td>0.05</td>
<td>0.14904</td>
<td>0.34942</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ΔPaO2 (21–15%)</td>
<td>3.75 kPa</td>
<td>65</td>
<td>1.06</td>
<td>0.13</td>
<td>3.48188</td>
<td>4.00920</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HCO3 (21%)</td>
<td>24.64 mmol/l</td>
<td>65</td>
<td>2.33</td>
<td>0.29</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HCO3 (15%)</td>
<td>11.56 mmol/l</td>
<td>65</td>
<td>1.7378</td>
<td>0.22</td>
<td>−0.0814</td>
<td>0.7798</td>
<td>0.11</td>
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<tr>
<td>ΔHCO3 (21–15%)</td>
<td>1.16 mmol/l</td>
<td>65</td>
<td>4.15</td>
<td>0.51</td>
<td>0.1310</td>
<td>2.1860</td>
<td>0.03</td>
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<tr>
<td>PR (21%)</td>
<td>161.23 ms</td>
<td>96</td>
<td>16.09</td>
<td>1.64</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PR (15%)</td>
<td>158.01 ms</td>
<td>96</td>
<td>20.31</td>
<td>2.07</td>
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<td></td>
<td></td>
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<tr>
<td>ΔPR (21–15%)</td>
<td>3.22 ms</td>
<td>96</td>
<td>12.63</td>
<td>0.660</td>
<td>5.778</td>
<td>1.29</td>
<td>0.01</td>
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<tr>
<td>QRSD (21%)</td>
<td>91.93 ms</td>
<td>101</td>
<td>15.97</td>
<td>1.59</td>
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<td></td>
<td></td>
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<tr>
<td>QRSD (15%)</td>
<td>90.27 ms</td>
<td>101</td>
<td>15.92</td>
<td>1.58</td>
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<td></td>
<td></td>
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<tr>
<td>ΔQRSD (21–15%)</td>
<td>1.66 ms</td>
<td>101</td>
<td>9.13</td>
<td>−0.138</td>
<td>3.465</td>
<td>0.91</td>
<td>0.07</td>
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<tr>
<td>QT (21%)</td>
<td>357.75 ms</td>
<td>101</td>
<td>40.97</td>
<td>4.08</td>
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<td></td>
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<tr>
<td>QT (15%)</td>
<td>348.83 ms</td>
<td>101</td>
<td>35.03</td>
<td>3.49</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ΔQT (21–15%)</td>
<td>8.92 ms</td>
<td>101</td>
<td>24.05</td>
<td>4.173</td>
<td>13.669</td>
<td>2.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QTc (21%)</td>
<td>415.16 ms</td>
<td>101</td>
<td>25.86</td>
<td>2.57</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QTc (15%)</td>
<td>416.95 ms</td>
<td>101</td>
<td>24.02</td>
<td>2.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔQTc (21–15%)</td>
<td>1.78 ms</td>
<td>101</td>
<td>26.70</td>
<td>−0.062</td>
<td>3.478</td>
<td>2.66</td>
<td>0.50</td>
</tr>
</tbody>
</table>

21%, baseline measurement while breathing room air; 15%, test measurement after breathing 15% O2 hypoxic mixture for 15 min; BE, base excess; ΔBE, change in base excess between 21% and 15% O2; HCO3, bicarbonate ion concentration; ΔHCO3, change in hydrogen ion concentration between 21% and 15% O2; PaCO2, partial pressure of CO2; ΔPaCO2, change in partial pressure of CO2 between 21% and 15% O2; PaO2, partial pressure of O2; ΔPaO2, change in partial pressure of O2 between 21% and 15% O2; PR, electrocardiographic PR interval; ΔPR, change in PR interval between 21% and 15% O2; PtcCO2, transcutaneous CO2; ΔPtcCO2, change in transcutaneous CO2 between 21% and 15% O2; QRSD, electrocardiographic QRSD interval; ΔQRSD, change in QRSD interval between 21% and 15% O2; QT, electrocardiographic QT interval; ΔQT, change in QT interval between 21% and 15% O2; QTc, oxygen saturation; ΔQTc, change in oxygen saturations between 21% and 15% O2.

A new potential biomarker for childhood tuberculosis

One of the major research areas for tuberculosis (TB) focuses not only on diagnostics but also on biomarkers that can provide prognostic data about the disease course and response to treatment. Although progress has been made, improved tests for paediatric TB are especially needed. Young children are at increased risk of progressing to TB after exposure, and may suffer from disseminated forms of the disease. Due to the paucibacillary nature of paediatric disease, the current armamentarium and future pipeline of TB diagnostics that largely rely on microbial growth and/or molecular detection are unlikely to demonstrate performance equivalent to that in adults. Thus, an accurate surrogate marker of disease may be crucial to improving the diagnosis of paediatric TB. We have tested and evaluated a novel B-cell assay called the antibodies in lymphocyte supernatant, or ALS, which has performed very well in diagnosing TB disease both in Asia and Africa (manuscript in preparation). Here, we report the performance of ALS as a biomarker in children with culture-confirmed TB.

The ALS assay is based on a principle similar to that of the enzyme-linked immunosorbent spot assay, measuring antibody-secreting cells in cultures of peripheral blood mononuclear cells (PBMCs). The ALS assay detects antibody secretion from in vivo activated plasma B cells that migrate throughout the peripheral circulation in response to TB antigens that are present during active disease but not latent TB infection. The ALS methodology for children includes phlebotomy of 3.5 ml of blood in order to isolate 5 million PBMCs; these cells are incubated in tissue culture plates without stimulation for 48–72 h. The supernatant is collected, placed into BCG-coated microtitre plates and IgG responses to...
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Thorax 2011 66: 726-727 originally published online October 22, 2010
doi: 10.1136/thx.2010.151712

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