Respiratory Physiology & Neurobiology 239 (2017) 81–86

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

# Respiratory load perception in overweight and asthmatic children

Victoria MacBean[a,*], Lorna Wheatley[b], Alan C. Lunt[a], Gerrard F. Rafferty[a]

[a] Division of Asthma, Allergy & Lung Biology, King's College London Department of Respiratory Medicine, Bessemer Road, London SE5 9PJ, United Kingdom
[b] Chest Unit, King's College Hospital NHS Foundation Trust, Denmark Hill, London SE5 9RS, United Kingdom

ARTICLE INFO

*Article history:*
Received 1 December 2016
Received in revised form 10 February 2017
Accepted 12 February 2017

*Keywords:*
Obesity
Asthma
Child
Breathlessness perception

ABSTRACT

Overweight asthmatic children report greater symptoms than normal weight asthmatics, despite comparable airflow obstruction. This has been widely assumed to be due to heightened perception of respiratory effort.

Three groups of children (healthy weight controls, healthy weight asthmatics, overweight asthmatics) rated perceived respiratory effort throughout an inspiratory resistive loading protocol. Parasternal intercostal electromyogram was used as an objective marker of respiratory load; this was expressed relative to tidal volume and reported as a ratio of the baseline value (neuroventilatory activity ratio (NVEAR)).

Significant increases in perception scores ($p < 0.0001$), and decreases in NVEAR ($p < 0.0001$) were observed from lowest to highest resistive load. Higher BMI increased overall perception scores, with no influence of asthma or BMI-for-age percentile on the resistance-perception relationships.

These data, indicating elevated overall respiratory effort in overweight asthmatic children but comparable responses to dynamic changes in load, suggest that the greater disease burden in overweight asthmatic children may be due to altered respiratory mechanics associated with increased body mass.



## 1. Introduction

Asthma is one of the most common chronic conditions of childhood, with a lifetime prevalence of 27.7% in 6–7 year olds and 19.9% in 13–14 year olds in English-speaking countries worldwide (Lai et al., 2009). A strong incident link between excess weight and asthma is well recognised, though the mechanisms underlying this connection remain poorly understood (Rasmussen and Hancox, 2014; Dixon and Poynter, 2016). The prevalence of both overweight and asthma have increased markedly in recent decades (Wang and Lobstein, 2006), and while rates of asthma may have reached a plateau in Western societies (Toelle and Marks, 2005), overweight and obesity is expected to continue to rise. Clinical management of concomitant asthma and overweight is therefore likely to continue to present a significant burden to clinicians.

Despite no differences in objective measures of lung disease severity, coexistent asthma and obesity is associated with higher asthma symptom scores (Sah et al., 2013), greater use of short-acting bronchodilators (Belamarich et al., 2000), increased healthcare utilisation (Carroll et al., 2007) and poorer health-related quality of life (Van Gent et al., 2007). Obese children with asthma report higher levels of non-specific breathlessness (Sah et al., 2013) and tend to overestimate the magnitude of airflow obstruction (Kopel et al., 2010). It could be hypothesised, therefore, that overweight or obese children with asthma have heightened perception of respiratory symptoms, although the elastic (resulting from reduced chest wall compliance) and threshold (from elevated intra-abdominal pressure, distal gas trapping and intrinsic positive end expiratory pressure) loads imposed on the respiratory system by obesity itself may contribute to the greater disease burden in obese and overweight children with asthma.

Differences in respiratory load perception have been studied previously in children by investigating subjects' rating of breathlessness or respiratory effort during the application of extrinsic or intrinsic loads (Davenport and Kifle, 2001; Julius et al., 2002). Using an objective marker of response to respiratory load against which to compare subjective scores allows further evaluation of the perception of changing respiratory effort. Measurement of respiratory muscle activity via the parasternal intercostal electromyogram (EMGpara) has been shown to be a valid marker of changing respiratory load in adults (Reilly et al., 2013; Steier et al., 2009) and both healthy and wheezy children (MacBean et al., 2016a). Measurement of EMGpara alongside subjective reports of perceived load

* Corresponding author at: Department of Respiratory Medicine, King's College London, Bessemer Road, London SE5 9PJ, United Kingdom.
*E-mail addresses:* victoria.macbean@kcl.ac.uk (V. MacBean), lorna.wheatley@nhs.net (L. Wheatley), alan.lunt@nhs.net (A.C. Lunt), gerrard.rafferty@kcl.ac.uk (G.F. Rafferty).

http://dx.doi.org/10.1016/j.resp.2017.02.007
1569-9048/

**Table 1**
Subject characteristics. All data are shown as median (IQR).

| | Controls (n = 9) | Normal weight asthma (n = 9) | Overweight asthma (n = 9) | p value |
|---|---|---|---|---|
| Age | 10.92 (10.77–12.13) | 10.77 (9.00–13.58) | 12.13 (10.98–13.17) | 0.667 |
| Sex (male: female) | 3: 6 | 3: 6 | 3: 6 | 1.00 |
| Height (cm) | 152.7 (142.7–163.1) | 147.7 (129.1–164.0) | 156.7 (155.8–161.1) | 0.327 |
| Weight (kg) | 32.8 (31.5–45.1) | 35.7 (30.1–52.1) | 55.4 (52.2–68.1) | 0.008[a,b] |
| BMI-for-age percentile (%) | 39.0 (21.0–51.5) | 61.1 (32.0–73.8) | 97.0 (94.0–97.9) | <0.001[a,b] |
| $FEV_1$ (z score) | 0.51 (0.10–0.75) | 0.88 (0.39–1.27) | −0.98 (−1.2–−0.44) | 0.016[a,b] |
| FVC (z score) | 0.57 (0.14–0.67) | 1.27 (0.56–1.62) | 0.01 (−0.87–1.09) | 0.076 |
| $FEV_1$/FVC ratio (z score) | 0.53 (0.19–0.61) | −0.31 (−1.08–0.17) | −1.18 (−1.27–−1.02) | 0.015[a,b] |
| TLC (z score) | 0.04 (−0.65–0.48) | 0.56 (0.25–1.83) | −1.29 (−1.66–−0.54) | 0.055 |
| IC (z score) | −0.28 (−2.05–−0.01) | −0.17 (−1.43–0.38) | −0.19 (−0.49–0.27) | 0.518 |
| FRC (z score) | 0.18 (−0.33–0.38) | 0.00 (−0.58–0.49) | −1.72 (−2.44–−0.82) | 0.017[a,b] |
| RV (z score) | −0.43 (−1.02–−0.29) | −0.10 (−0.25–0.00) | −0.79 (−1.24–0.51) | 0.643 |
| RV/TLC ratio (z score) | −0.09 (−0.85–0.30) | −0.17 (−0.67–0.17) | 0.13 (−0.82–0.44) | 0.883 |

[a] Significant difference between control and overweight asthmatic subjects.
[b] Significant difference between healthy weight asthmatics and overweight asthmatics.

allows any hyper-perception to be differentiated from physiological responses to respiratory load.

The purpose of the current study was, therefore, to investigate any differences in respiratory load perception between overweight children with asthma and healthy weight asthmatic and non-asthmatic counterparts, with additional validation of any differences, or lack thereof, quantified by objective measurement of respiratory load via EMGpara.

These data have been previously presented in the form of an abstract (MacBean et al., 2016b).

## 2. Methods

### 2.1. Ethical approval

The study was granted ethical approval by the National Research Ethics Committee London – Dulwich and conformed to the principles of the Declaration of Helsinki. Parents/guardians of all participants gave informed written consent and assent was obtained from children.

### 2.2. Participant identification and classification

Children were recruited from databases of previous research participants and from respiratory clinics operating at King's College Hospital. Children were classed as asthmatic if they had a physician diagnosis of asthma and were being prescribed preventative medication (inhaled corticosteroids and/or leukotriene receptor antagonists). Classification of normal weight or overweight was based on World Health Organisation (WHO) BMI-for-age percentiles using WHO Anthro Plus software using the data of De Onis et al. (2007), with overweight classified as a BMI-for-age above the 85th percentile and normal weight as BMI-for-age between 2nd-85th percentile. All children had to be free of any additional cardiac, respiratory or neurological disorder, or recent respiratory illness (within the preceding six weeks). No *a priori* sample size calculation was undertaken due to the exploratory nature of the study.

### 2.3. Pulmonary function tests

Spirometry and body plethysmography was undertaken in accordance with international criteria. Values for forced expiratory volume in one second ($FEV_1$), forced vital capacity (FVC), total lung capacity (TLC), inspiratory capacity (IC), functional residual capacity (FRC), residual volume (RV) and RV/TLC ratio were compared against reference values (Quanjer et al., 2012; Rosenthal et al., 1993; Zapletal et al., 1977) and expressed as standardised residuals (z-scores).

**Table 2**
Changes in perception scores and neural respiratory drive from lowest to highest resistance in 27 children undergoing inspiratory resistive loading. VAS: visual analogue scale; PCERT: Pictorial Children's Effort Rating Table; NVEAR: neuroventilatory efficiency activity ratio.

| | Lowest resistance level | Highest resistance level | p value |
|---|---|---|---|
| VAS (mm) | 8.55 (4.0–19.0) | 73.21 (44.63–80.88) | <0.0001 |
| PCERT (AU) | 1.59 (1.42–2.75) | 7.25 (5.25–8.5) | <0.0001 |
| NVEAR (AU) | 0.89 (0.71–1.09) | 0.50 (0.44–0.59) | <0.0001 |

### 2.4. Inspiratory resistive loading

Inspiratory resistive loads were applied using a MicroMedical Respiratory Muscle Analyser (MicroRMA, MicroMedical, UK). The device was pre-programmed to provide seven levels of inspiratory resistance: 1.0, 1.5, 2.3, 3.0, 4.0. 5.5 and 7.0 kiloPascals per litre per second (kPa/l/s). Each resistance was applied for ten breaths and repeated at least three times. Resistances were applied in a pre-determined order that differed between sets to prevent pattern recognition.

### 2.5. Load perception

Perception of inspiratory effort was assessed using a 100 mm visual analogue scale (VAS) with anchor points at 0 cm ("no difficulty at all") and 100 mm ("impossible"), and the Pictorial Children's Effort Rating Table (PCERT), (Yelling et al., 2002). Children were asked the question "how difficult was it to breathe?", and asked to rate their perception of respiratory effort first by drawing a line on the VAS then pointing to a step on the PCERT.

### 2.6. Respiratory flow, tidal volume and airway pressure

Respiratory flow was recorded using a pneumotachograph (Hans Rudolph Inc, Kansas City, USA) attached proximally to a flanged mouthpiece and distally to the MicroRMA device. The pressure drop across the pneumotachograph was measured using a differential pressure transducer (Spirometer, ADInstruments, Sydney, Australia). Mouth pressure was recorded from a side arm incorporated into the pneumotachograph and detected using a differential pressure transducer (MP45, Validyne, Northridge, CA, USA) and associated carrier-demodulator amplifier (CD280, Validyne, Northridge, CA, USA). Pressure and flow were recorded throughout the inspiratory loading using LabChart software (ver-