CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

Obesity-hypoventilation syndrome (Pickwickian syndrome) in children

PROTOCOLS

Principal investigator

Raphael (Ralph) Folman, MD, FRCPC, Trillium Health Centre, 100 Queensway W, Mississauga ON L5B 1B8; tel.: 905-848-7100; ralph.folman@utoronto.ca

Co-investigators

Catherine Birken, MD, University of Toronto
Paolo Campisi, MD, University of Toronto
Minh T. Do, MSc, PhD, Ottawa University (Public Health Agency of Canada Representative)
Vito Forte, MD, University of Toronto
Ian MacLusky, MD, Ottawa University
Brian McCrindle, MD, University of Toronto
Indra Narang, MD, University of Toronto
Manisha Witmans, MD, Stollery Children's Hospital, Edmonton

Background

The obesity-hypoventilation syndrome (OHS), also known as the cardiopulmonary syndrome, has rarely been recognized or reported in the paediatric age group (<18 years). It is also known as the Pickwickian syndrome, referring to "Joe" in Charles Dicken's "Pickwick Papers", who was "a wonderfully fat boy... standing upright... with his eyes closed." It is characterized by a combination of morbid obesity and sleep-disordered breathing, resulting in both daytime hypersomnolence and chronic hypoventilation.[1,2]

The majority of cases are a consequence of simple morbid obesity, although a small subpopulation is associated with an intrinsic disorder of hypothalamic function, with associated sleep disturbance, hyperphagia, and primary hypoventilation.[3] Children with OHS experience sleep-disordered breathing (sleep apnea, usually obstructive) and nocturnal hypoventilation. The resulting sleep fragmentation causes excessive daytime drowsiness, with the attending adverse sequelae on intellectual function.

Polysomnography documents decreased tidal and expiratory reserve volumes, alveolar hypoventilation, hypoxia, and hypercapnia. If untreated, these cases can progress to polycythemia, cor pulmonale, and congestive heart failure.

Treatment consists of mainly weight reduction, plus non-invasive ventilation support, such as CPAP or BiPAP. Occasionally, tracheostomy and invasive night-time ventilation are needed to reverse the hypoxia and hypercapnia.

While other significant morbidities related to paediatric obesity have been extensively documented, the OHS is not well recognized by paediatric healthcare providers, in spite of the serious consequences of non-treatment, and the presence of an "obesity epidemic" in the entire developed world. In the adult literature, however, the combination of obesity, sleep disturbance, and sleep-disordered breathing has well described adverse health effects,[2] with decreased intellectual functioning affecting learning ability and causing an increased risk of motor-vehicle accidents in adolescent drivers, as well as type 2 diabetes mellitus and cardiovascular events.

The incidence of paediatric OHS is not well documented. A study of obese children in Belgium found 17% with central sleep apnea, and 19% with mild to severe obstructive sleep apnea.[4] However, this study did not mention daytime hypersomnolence. In Canadian tertiary paediatric sleep clinics, the incidence observed of referred patients was four or five cases per year (personal communication: Drs.Witmans, Narang, MacLusky).With about seven large tertiary centres, and three smaller centres in Canada, the total number of cases diagnosed annually would be 40 to 50. We suspect that there are many more unrecognized cases that are not referred.

Methods

The CPSP methodology is the optimal way to collect data on these reportedly rare cases, as well as having the important benefit of raising awareness of this condition among practicing paediatricians. In view of the increasing prevalence of childhood obesity, there is the potential for increased recognition of a disorder that is almost certainly under-diagnosed. Each reported case will be further assessed by means of a detailed questionnaire.

Case definition

Report any new patient less than 18 years of age with the following clinical features:

- Weight: >95th percentile for age
- BMI: >95th percentile for age, or >30 kg/m^2
- Nocturnal: sleep apnea, i.e., snoring, restless sleep, mouth-breathing
- Excessive daytime drowsiness: falling asleep in class, or at other inappropriate times.

plus at least two of the following:

- Hypercapnia: serum bicarb >27 meq/L
- $PaCO_2$: >45 mm Hg (arterial or capillary gases, obtained in daytime)
- Oxygen saturation: <92%, in awake state, and room air

Exclusion criteria

- Primary lung diseases, e.g., cystic fibrosis, bronchiectasis. (Asthma is not an exclusion.)
- Hypothyroidism
- Cushing's syndrome
- Prader-Willi syndrome
- Primary cardiac diseases, congenital or acquired (e.g., viral myocarditis)
- Congenital craniofacial abnormalities (e.g., Alpert, Cohen, Carpenter, Crouzon syndromes)
- Pseudohypoparathyroidism (Albright hereditary osteodystrophy)
- Laurence-Moon-Biedl syndrome
- Central hypoventilation syndrome (Ondine's disease)

Obesity-hypoventilation syndrome (Pickwickian syndrome) in children (continued)

Objectives

1) To determine the incidence of OHS in the paediatric population
2) To document the burden of illness on all aspects of the patient's life

Duration

April 2012 to March 2014

Expected number of cases

The total number of expected cases is 50-100 cases per year.

Ethical approval

Research Ethics Board of the Credit Valley Hospital and Trillium Health Centre, Mississauga, Ontario

Analysis and publication

Analysis will be done at one or more of the centres where co-investigators are affiliated. The research team will submit final results at national and possibly international paediatric conferences and to peer-reviewed journals.

References

1. Piper AJ,Grunstein RR. Obesity hypoventilation syndrome – mechanisms and management. *Am J Resp Crit Care Med* 2011;183(3):292-8.
2. Mokhlesi B. Obesity hypoventilation syndrome: a state-of-the-art review. *Respir Care* 2010;55(10):1347-62.
3. Carroll MS, Patwari PP, Weese-Mayer DE. Carbon dioxide chemoreception and hypoventilation syndromes with autonomic dysregulation. *J Appl Physiol* 2010;108(4): 979-88.
4. Verhulst SL, Schrauwen N, Haentjens D et al. Sleep-disordered breathing in overweight and obese children and adolescents: prevalence, characteristics and the role of fat distribution. *Arch Dis Child* 2007;92:205-8.