Association of serum leptin with hypoventilation in human obesity

P R Phipps, E Starritt, I Caterson, R R Grunstein

INTRODUCTION

Obesity is rapidly increasing in prevalence with a major impact on ill health and health costs.1 Sleep disordered breathing, usually manifest by obstructive sleep apnoea (OSA), is common in obesity. However, some patients with obesity and OSA develop daytime hypercapnia (obesity hypoventilation syndrome, OHS).2

Leptin is a protein hormone produced by mammalian adipocytes. It acts within the hypothalamus via a specific receptor to reduce appetite and increase energy expenditure.3 Serum levels correlate positively with total body fat mass. In obesity there may be a failure of central feedback mechanisms leading to leptin resistance.4 There is evidence, for example, that obese humans have a relative deficiency of CNS leptin (obesity hypoventilation syndrome, OHS).4

We further characterised this relationship by measuring leptin levels and arterial blood gas tensions in patients with various degrees of obesity and sleep disordered breathing, including patients with awake hypercapnia.

METHODS

Consecutive patients undergoing diagnostic sleep studies at Royal Prince Alfred Hospital between July and December 1999 were studied. Anthropometric measurements, spirometric tests, and arterial blood gas sampling were performed in the afternoon before a nocturnal sleep study. The following morning venous blood was drawn for measurement of fasting serum leptin (Radioimmunoassay, Linco Research Inc, Missouri, USA). The reproducibility of the assay was ±25% and the accuracy was ±0.5 ng/ml. Daytime hypercapnia was defined as arterial carbon dioxide tension (PaCO₂) of >6.0 kPa (in the absence of metabolic and acute respiratory alkalosis) and hypoxaemia as arterial oxygen tension (PaO₂) of <10.7 kPa in patients aged <60 years and <10.0 kPa in those aged >60 years. Obesity was defined as a body mass index (BMI) of >28 kg/m².5

Results are expressed as mean (SD). A total of 56 patients were studied (16 women) with a mean age of 46 years (range 22–80). Forty four patients were eucapnic (PaCO₂ 5.5 (0.4) kPa) and 12 were hypercapnic (PaCO₂ 6.5 (1.1) kPa). Twenty patients were obese and hypoxic (PaO₂ 8.8 (1.6) kPa). As expected, fasting serum leptin levels were closely related to % body fat in the entire patient group (r=0.77). In the obese group (n=39) hypercapnic patients had significantly higher fasting serum leptin levels than eucapnic patients, with leptin levels of 39.1 (17.9) and 21.4 (11.4) ng/ml, respectively (p<0.005, fig 1). There was no difference in degree of body fat among eucapnic and hypercapnic patients, with leptin and % body fat as explanatory variables (SPSS for Windows 10.0, SPSS Inc, USA). Odds ratios with 95% confidence intervals were calculated for both variables. Statistical significance was taken at the 5% level.

RESULTS

Results are expressed as mean (SD). A total of 56 patients were studied (16 women) with a mean age of 46 years (range 22–80). Forty four patients were eucapnic (PaCO₂ 5.5 (0.4) kPa) and 12 were hypercapnic (PaCO₂ 6.5 (1.1) kPa). Twenty patients were obese and hypoxic (PaO₂ 8.8 (1.6) kPa). As expected, fasting serum leptin levels were closely related to % body fat in the entire patient group (r=0.77). In the obese group (n=39) hypercapnic patients had significantly higher fasting serum leptin levels than eucapnic patients, with leptin levels of 39.1 (17.9) and 21.4 (11.4) ng/ml, respectively (p<0.005, fig 1). There was no difference in degree of body fat
in patients with obesity. Examining both serum leptin levels and the presence of OHS disordered breathing, a higher leptin level predisposes to the OHS. This suggests that, in patients with obesity and sleep % body fat for the presence of hypercapnia in patients with

We have observed that serum leptin is a better predictor than

DISCUSSION

between the hypercapnic (% body fat 43.8 (6.0)%) and eucapnic (% body fat 40.8 (6.2)%) patients (p>0.4). Serum leptin (b=0.113, SE(b)=0.044, p=0.01, OR 1.12 (95% CI 1.03 to1.22)) but not % body fat (b=-0.087, SE(b)=0.094, p=0.4, OR 0.92 (95% CI 0.76 to 1.1)) was a predictor for the presence of hypercapnia. The results were similar in the obese hypoxic group of patients (fig 2). There was no difference in the apnoea-hypopnoea index (AHI) between the two groups (mean 47/hour for eucapnic patients and 37/hour for hypercapnic patients, p>0.2).

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Authors’ affiliations

P R Phipps, E Starritt, R R Grunstein, Centre for Respiratory Failure and Sleep Disorders, Royal Prince Alfred Hospital, Sydney, NSW 2050 and Institute of Respiratory Medicine, University of Sydney, NSW 2006, Australia
I Caterson, Human Nutrition Unit, Department of Biochemistry, University of Sydney, Sydney, NSW 2006, Australia

REFERENCES