The putative satiety hormone PYY is raised in cardiac cachexia associated with primary pulmonary hypertension

C W le Roux, M A Ghatel, J S R Gibbs, S R Bloom


W eight loss greater than 6% independently correlates with reduced survival in patients with congestive heart failure (CHF).¹ Cardiac cachexia is a gradual and graded process, with wasting affecting muscle, bone, adipose tissue and the heart.² Reduced appetite has been proposed as a important factor for weight loss caused by cardiac cachexia.²

The mechanism of cardiac cachexia remains largely unclear. Gastric myoneural inhibition and gastrointestinal hypomotility with delayed gastric emptying is commonly observed, and gut hormones may also play a role, because the anorexia is often characterised by a premature feeling of fullness and loss of hunger.³ The gut hormone ghrelin stimulates hunger, increases food consumption, and was previously shown to be raised in patients with cardiac cachexia and CHF.³ Ghrelin is produced from the stomach and usually rises in anticipation of a meal and then falls after the ingestion of nutrients.

The gut hormone PYY3–36, acting as a terminator of hunger, is produced by the L cells in the distal gastrointestinal tract; it reduces appetite and 24 hour food intake by binding to the neuropeptide Y Y2 receptor in the hypothalamic arcuate nucleus.⁴

Severe pulmonary hypertension results in a low cardiac output and neurohumoral activation. Patients frequently report loss of appetite and weight, and since it occurs in a young population they have little co-morbid disease, which itself might affect appetite. This study aimed to evaluate dynamic PYY and ghrelin responses to a standard meal in control subjects and patients with cardiac cachexia associated with pulmonary hypertension.

METHODS

Patients with primary pulmonary hypertension and cardiac cachexia, as defined by weight loss of more than 6%, underwent diagnostic work up to determine aetiology and severity of pulmonary hypertension according to the World Health Organization and British Cardiac Society criteria. The patients in this study were in WHO functional class III or above, the time since onset of disease was 4.9 (2.1) years, and the shuttle walking test distance was 211.3 (98.5) m. They had a systolic pulmonary artery pressure of 93 (12.1) mm Hg, pulmonary artery oxygen saturation of 52.6 (13.1%), Fick cardiac index of 2.3 (1.5) l/min/m², and the pulmonary vasculature resistance was 1667 (1103) dynes/cm⁵/s. Patients involved in the study were taking the following medication: warfarin (nine patients), bosentan (five patients), digoxin (four patients), spironolactone (three patients), treflurin (three patients), frusmeide (two patients) and amlovidine, candesartin, ramipril, montelukast, and iloprost, each being taken by one of the patients. Sodium, creatinine, albumin, and protein were within the reference range in all patients. The study was performed in accordance with the Declaration of Helsinki and informed consent was obtained.

Table 1 demonstrates the demographics of the nine patients and nine control subjects (recruited through local advertising) who received a 720 kcal standard breakfast between 7–8 am following an overnight fast. Blood samples were obtained every 30 minutes starting 30 minutes before the meal and ending 120 minutes after the meal. Samples were immediately centrifuged, plasma separated and stored at −80°C until analysis using established in-house assays.⁴ Parametric statistical analysis was done using Sigmasstat v2.0 (SPSS Science, Chicago, Illinois, USA). The PYY, ghrelin, and body mass index (BMI) data were normally distributed and statistical comparisons were made using an unpaired t test. Linear regression was used to evaluate the correlation between BMI, fasting ghrelin, and peak PYY. A probability level of p < 0.05 (5%) was considered significant.

RESULTS

There were no differences in age, sex, and BMI between control subjects and patients (table 1). PYY was 60% higher in the patients post-meal at 30 minutes (p = 0.01), 49% higher at 60 minutes (p = 0.02), and 46% higher at 90 minutes (p = 0.04) when compared with the control subjects (fig 1). There was no difference in fasting PYY concentrations (p = 0.42).

Both groups showed the expected pattern of reduction in ghrelin post-meal. The fasting ghrelin concentrations for the patients and control subjects were 704.1 (423) pmol/l and 484.6 (204) pmol/l, respectively (p = 0.13), while the 90

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<th>Table 1 Demographics of patients and control subjects</th>
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<td>Cardiac cachexia</td>
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<td>Subjects (female)</td>
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<td>Age (years)</td>
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<td>BMI (kg/m²)</td>
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Figure 1 PYY response following standard meal in cardiac cachexia associated with pulmonary hypertension and control subjects (solid circles, patients with cardiac cachexia; open circles, control subjects)
A 28 year old man sustained an isolated stab injury to the left third intercostal space in the mid clavicular line. The weapon was reported to be a kitchen knife 12 cm in length. A transthoracic echocardiogram revealed a pericardial effusion. He was transferred to our department and was taken to theatre for emergency surgery. A median sternotomy was performed. An entry wound was found over the anterior aspect of the right ventricular outflow tract, and an exit wound on the inferior surface of the right ventricle near the atrioventricular groove (panel A). Cardiopulmonary bypass was instituted because of haemodynamic instability. Both ventricular tears were repaired with interrupted 4/0 polypropylene sutures. An intraoperative transoesophageal echocardiogram was performed following weaning from bypass to assess intracardiac structures. This revealed severe regurgitation through the anterior leaflet of the tricuspid valve (panels B and C).

Bypass was re-instituted with bicaval cannulation. The right atrium was opened directly on beating heart and a defect confirmed in the tricuspid leaflet. This was repaired with interrupted 5/0 polypropylene sutures. The patient made an uneventful recovery and was discharged home.

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Severe tricuspid regurgitation following a stab to the heart

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