Effects of long-term combined treatment with somatostatin analogs and pegvisomant on cardiac structure and performance in acromegaly

Renata S. Auriemma, Ludovica F.S. Grasso, Mariano Galdiero, Claudia Pivonello, Ciro Salzano, Mariarosaria Negri, Cristina de Angelis, Annamaria Colao, Rosario Pivonello

Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Università Federico II di Napoli, Naples, Italy

OBJECTIVES

Somatostatin analogs (SA) are known to revert acromegalic cardiomyopathy mainly in young patients with short disease duration, whereas pegvisomant (PEG) reportedly improves cardiac structure and performance in patients resistant to SA. To date, no data are available on the effects of long-term combined treatment with SA and PEG on cardiovascular complications. The current study aimed at investigating the effects of long-term SA+PEG on cardiac structure and performance in acromegaly.

METHODS

Thirty-six acromegalic patients (14 men, 22 women, aged 52.3±10.2 yrs) proven to be resistant to long-term high dose medical treatment with SA monotherapy entered the study. Resistance to SA monotherapy was defined as a serum IGFI level of greater than 1.8 times the ULN measured 28 days after the last SA injection. After long-term SA monotherapy (range 6-156 months) octreotide LA dose ranged 10-40 mg/28 days and later prolactin dose ranged 120-240 mg/28 days. In all patients PEG was added at the starting dose of 10 mg/day, with an overall weekly dose of 70 mg. Dose adjustment by 10 mg/day was carried out every 3 months on the basis of IGFI levels. Final PEG dose ranged 35-500 mg/week. Weight, body mass index (BMI), systolic (SBP) and diastolic (DBP) blood pressure, IGFI, fasting glucose (FG), fasting insulin (FI), HOMA-IR, glycated haemoglobin (HbA1c), and lipid fractions were evaluated at diagnosis (T0), after long-term (median 36 months) SA (T1), and after 12 (T2) and 60 (T60) months of combined treatment with SA and PEG, with last follow up (FU) being performed after a median time of 78 months (range 60-144 months). At each time point all patients underwent echocardiography to evaluate ejection fraction (EF), left ventricular mass index (LVMi), early (E) to late or atrial (A) peak velocities ratio (E/A) and isovolumic relaxation time (IVRT). Left ventricular (LV) hypertrophy was defined as LVMi>135 g/m² in men and >110 g/m² in women. LV diastolic dysfunction was defined as E/A lower than 1 or 0.5 for patients younger or older than 50 yr, respectively, and/or as IVRT longer than 0.22 (10 yr or age), 10 (30-50 yr of age), or 15 msec (>50 yr of age). LV systolic dysfunction was defined as ejection fraction (EF) lower than 50%.

RESULTS

At T1, SA induced a slight, but not significant decrease in IGFI (p=0.077, Fig. 1), whereas FI (p=0.004, Fig. 2), HOMA-IR (p=0.013, Fig. 2), EF (p=0.013, Fig. 3), E/A (p=0.001, Fig. 3) and IVRT (p=0.000, Fig. 3) significantly improved. At T2, IGFI (p=0.001, Fig. 2), FI (p=0.001, Fig. 2), HOMA-IR (p=0.000, Fig. 2), HDL (p=0.05, Fig. 4), EF (p=0.002, Fig. 3), LVMI (p=0.000, Fig. 3), E/A (p=0.006, Fig. 3) and IVRT (p=0.000, Fig. 3) significantly improved compared to T0, with FI (p=0.001, Fig. 2), HOMA-IR (p=0.000, Fig. 2), LVMI (p=0.000, Fig. 3) and E/A (p=0.006, Fig. 3) further improving compared to T1. At T60, IGFI (p=0.000, Fig. 1), FI (p=0.001, Fig. 2), HOMA-IR (p=0.000, Fig. 2), HDL (p=0.018, Fig. 3), LVMI (p=0.002, Fig. 3), E/A (p=0.049, Fig. 3) and IVRT (p=0.014, Fig. 3) significantly ameliorated compared to T0, with IGFI (p=0.000, Fig. 1), FI (p=0.027, Fig. 2), HOMA-IR (p=0.009, Fig. 3), LVMI (p=0.049, Fig. 3) and E/A (p=0.005, Fig. 3) further improving compared to T1. MetS prevalence significantly reduced as compared to T1 (p=0.034). At T60, LVMi normalized in 83.3% of patients (p=0.000, Fig. 1), FI (p=0.000, Fig. 2), HOMA-IR (p=0.000, Fig. 2), HDL (p=0.031, Fig. 4), EF (p=0.035), LVMI (p=0.000, Fig. 3), E/A (p=0.02, Fig. 3) and IVRT (p=0.001, Fig. 3) significantly improved compared to T0, with IGFI (p=0.000, Fig. 1), FI (p=0.000, Fig. 2), HOMA-IR (p=0.000, Fig. 2), LVMI (p=0.000, Fig. 3) and E/A (p=0.005, Fig. 3) further ameliorating as compared to T1. MetS prevalence significantly reduced as compared to T1 (p=0.034). PEG dose significantly correlated with LVMi (r=0.57, p=0.000), FI (p=0.45, Fig. 3), HDL (p=0.36, p=0.03), EF (p=0.43, p=0.03) and IVRT (p=0.50, p=0.001). PEG dose was the best predictive factor of LVMI (r=2.8, p=0.001) at T12, and of EF (r=2.59, p=0.02) and of ΔLVMI (r=2.79, p=0.01) at T60.

CONCLUSIONS

The results of the current study demonstrate that long-term PEG addition to SA improves cardiac structure and performance, particularly diastolic dysfunction, in acromegalic patients resistant to SA, therefore representing a valid therapeutic strategy in acromegalic patients with left ventricular hypertrophy and diastolic dysfunction.

References