**Clinical Study**

**Impact of Orlistat-Induced Weight Loss on Diastolic Function and Heart Rate Variability in Severely Obese Subjects with Diabetes**

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Received 20 May 2010; Accepted 21 November 2010

Academic Editor: Luc F. Van Gaal

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**Objective.** Determine the impact of Orlistat-induced weight loss on metabolic profile and cardiovascular function in severely obese patients with type 2 diabetes.

**Methods.** Twenty-nine patients were randomized either to a nonplacebo control group or to a treatment group with Orlistat thrice a day. Metabolic profile, anthropometric parameters, heart rate variability indices, and echocardiographic variables were measured before and after a 12-week treatment period. **Results.** Treatment with Orlistat induced a modest but significant weight loss compared to controls (3.3 ± 3.0 versus 0.5 ± 2.2 kg, resp.; *P* = 0.003). There was significant decrease in fasting glycemia (7.9 ± 3.0 versus 6.7 ± 2.2 mmol/L; *P* = 0.03) and significant improvements in left ventricular diastolic function (*P* = 0.03) and in the sympathovagal balance (LF/HF ratio) (*P* = 0.04) in the Orlistat group. **Conclusion.** These results suggest that a modest weight loss improves fasting glycemia, left ventricular diastolic function, and sympathovagal balance in severely obese patients with type 2 diabetes.

1. **Introduction**

Severe obesity is defined as a body mass index (BMI) >40 kg/m² which is associated with comorbidities such as insulin resistance, diabetes mellitus, systemic hypertension, dyslipidemia, and cancer. Obesity is an independent risk factor for increased cardiovascular morbidity and mortality [1]. Furthermore, severely obese subjects have an increased total mortality with a concomitant increased risk of sudden death, which may be caused by fatal arrhythmias [1].

Heart rate variability (HRV) which is the fluctuation of heart rate around mean heart rate that may be assessed with a 24-hour cardiac Holter monitoring provides valuable information on the activity of the cardiac autonomic nervous system (ANS). The ANS is an important contributor to the regulation of both the cardiovascular system and energy expenditure and it is assumed to play a role in the pathophysiology of obesity and related complications [1, 2]. In obese subjects, many studies have observed abnormalities in the sympathetic and the parasympathetic ANS activity, which could partly explain the relation between obesity, comorbidities, sudden death, and arrhythmias [1, 3]. Available data regarding the metabolic and ANS impacts of weight loss in severely obese subjects by other methods than gastric bypass [4, 5] and hypocaloric diet [3, 6–9] are sparse. Excess body fat also directly influences heart function [1]. Obesity is associated with decreased left ventricular (LV) systolic function and impaired LV diastolic function [1, 10]. Whereas some studies using surgical procedures have reported that substantial weight loss induces significant improvements in LV diastolic function [10–14], the effect of modest weight loss on LV diastolic dysfunction in obese subjects has been less extensively investigated but has never been reported in severe obesity. Diet and exercise programs are associated with disappointing long-term results on weight loss in severely obese subjects [15]. Weight loss medication is recommended for subjects with a BMI >30 kg/m² or with a BMI >27 kg/m² associated with ≥1 risk factor of cardiovascular disease [16]. Orlistat is a gastrointestinal lipase inhibitor, reducing fat absorption, which may result in weight loss of approximately 5%–10% of the initial weight after one year [17]. It may be relevant to investigate the...
impact of modest weight loss on LV diastolic function and on HRV since these parameters may be associated with increased cardiovascular risk [18, 19]. This pilot study aimed to determine the impact of weight loss induced by Orlistat on HRV and on LV diastolic function in severely obese patients with type 2 diabetes.

2. Methods

2.1. Subjects. A total of 38 severely obese patients with type 2 diabetes were recruited from the waiting list of bariatric surgery in our Institution. The experimental protocol was approved by the ethics committee of IUCPQ and we certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. All the subjects gave their written informed consent. Subjects 18 years or older and treated with antidiabetic medication and/or insulin were included. Subjects were excluded if they used medication known to influence HRV or if they had documented chronic heart failure and/or kidney failure. Subjects were randomized to a control group or to a treatment group, which consisted of 120 mg of Orlistat (Xenical Roche, Nutley, NJ, USA) thrice a day, 30 minutes before meal, for 12 weeks. The medication was provided at no cost. For both treated and control groups, no reinforced specific nutritional intervention was recommended during this study other than the usual nutritional advice regarding the medication, reflecting a real clinical context. Follow-up was systematically conducted by phone for all subjects at 4 and 8 weeks into the study, in order to ensure subject’s compliance with the medication and to note any significant changes in lifestyle. Nine subjects did not complete the study. In the control group, (1) one underwent bariatric surgery, (2) one had medication change within follow-up period, and (3) five did not attend their follow-up visit. In the treated group, (1) one had clinically significant side effects on the medication, and (2) one did not attend the follow-up visit.

2.2. Anthropometric Measurements. Total body mass, lean and fat mass, height, and BMI have been determined with an electrical bioimpedance balance (Tanita TBF-350, Tokyo, Japan). Waist circumference was measured using standardized method with an inelastic tape. Blood pressure and resting heart rate were measured following a 30-minute resting period while subjects were lying on their side during the echocardiogram study. Blood pressure was measured using an adapted size blood pressure cuff and an electronic sphygmomanometer (Welch-Allyn, 5200 series, Arden, NC, USA).

2.3. Biochemistry. Blood sample was taken after a 12-hour fast. Glycemia was determined using an enzymatic method (Hitachi, 717 Auto analyzer; Roche, Laval, Canada) and glycated hemoglobin (HbA1c) was measured by binding affinity (Abbott IMX, Mississauga, Canada). Plasma cholesterol and triglycerides concentrations were measured using previously described methods (Hitachi, 717 Auto analyzer; Roche, Laval, Canada) [20, 21]. Serum HDL-cholesterol was analysed with an enzymatic precipitation of LDL-cholesterol and VLDL-cholesterol, using phosphotungstic acid and MgCl2. LDL-cholesterol concentration was calculated with Friedewald’s formula [22].

2.4. Echocardiography. Echocardiographic measures were performed with a commercial ultrasound system (Sonos 5500; Hewlet Packard, Andover, Massachusetts). Standard parasternal, short-axis, and apical views were performed in accordance with the recommendations of the American Society of Echocardiography and the same observer, who was blinded to randomisation, obtained all recordings and measurements. Left ventricular diastolic dysfunction (LVDD), using transmitral and pulmonary veins recordings, was evaluated using well-standardized criteria as previously reported [20, 21]. Tissue Doppler was not performed.

Left ventricular mass (LVM) was calculated according to the following formula [23]: LVM (g) = 0.8 × 1.04[(LVEDD + IVST + PWT)3 − (LVEDD)3] + 0.6, where LVEDD represents the left ventricle end diastolic dimension, IVST the interventricular septal thickness, and PWT the posterior wall thickness.

2.5. Heart Rate Variability. Heart rate variability (HRV) was derived from a 24-hour Holter monitoring system (Marquette Electronics Inc., Milwaukee, WI) in all subjects during normal daily life activity [21]. Numerous indices in the frequency and the time domains were determined [7, 21]: mean value of all RR intervals (mean NN), standard deviation of the RR intervals (SDNN), standard deviation of the mean NN intervals for each 5 minutes period (SDANN), square root of the mean squared difference of successive RR intervals (RMSSD), percentage of differences between adjacent normal RR intervals exceeding 50 milliseconds (pNN50), high frequency (HF), and low frequency (LF). Within the 24-hour evaluation, three periods were assessed: (1) 24 hours, (2) daytime period defined as 8:00 AM to 8:00 PM, and (3) night time period defined as 12:00 AM to 6:00 AM. The separation into daytime and night time was arbitrary [7].

2.6. Statistical Analysis. Data are presented as mean ± standard deviation unless otherwise specified. Comparisons between normal, spontaneous, and pseudonormal pattern of LV filling pre and posttreatment were conducted with a mixed ANOVA design. This analysis allowed us to first compare groups (treatment versus control) in regards to baseline data and to determine the treatment effect as well as interactions between groups and treatment. The factor with random effect was linked to subjects. The dependent variable associated to LV diastolic function was analyzed using a cumulative multinomial distribution with an independent covariance structure. Thereafter, if significant differences occurred, a posteriori Tukey’s comparison technique was performed to determine differences. Relationships among variables were measured using Pearson’s correlation coefficients. In order to test the normality distribution of the data,
There were no significant statistical differences of patients in both groups before and after treatment. Table 1 presents clinical parameters.

### Table 1: Baseline characteristics of type 2 diabetic severely obese subjects before and after treatment.

|                  | Control group |  | Treatment group |  |
|------------------|---------------|---|-----------------|---|
|                  | Pre           | Post | Pre            | Post |
| N                | 13            | 13  | 16             | 16   |
| Age (years)      | 48 ± 11       | —   | 47 ± 9         | —    |
| Duration of diabetes (years) | 4.8 ± 4.6 | —   | 7.2 ± 6.1      | —    |
| Men/Women (number) | 7/6           | 7/6 | 7/9            | 7/9  |
| Weight (kg)      | 142.6 ± 34.6  | 142.1 ± 35.0 | 129.6 ± 17.4   | 125.9 ± 17.5*1 |
| BMI (kg/m²)      | 51.2 ± 9.2    | 51.2 ± 9.0  | 45.9 ± 7.3     | 44.8 ± 7.5*1 |
| Waist circumference (cm) | 145.8 ± 20.8 | 144.3 ± 20.6 | 138.4 ± 14.7   | 133.9 ± 17.0* |
| Fat percentage (%) | 48.5 ± 5.4    | 48.8 ± 4.1  | 45.7 ± 8.3     | 45.6 ± 8.7  |
| Fat mass (kg)    | 67.3 ± 13.6   | 66.2 ± 13.8 | 59.1 ± 13.1    | 57.4 ± 13.5 |
| Fat free mass (kg) | 72.3 ± 18.9  | 70.0 ± 17.8 | 70.4 ± 15.4    | 68.5 ± 15.2* |
| Resting HR (beat/min) | 83 ± 7          | 84 ± 12      | 80 ± 12        | 78 ± 11   |
| SBP (mmHg)       | 127 ± 20      | 126 ± 15     | 137 ± 18       | 127 ± 13  |
| DBP (mmHg)       | 71 ± 10       | 70 ± 9       | 74 ± 12        | 70 ± 11   |
| Fasting glycemia (mmol/L) | 8.0 ± 2.5     | 8.1 ± 2.5    | 7.9 ± 3.0      | 6.7 ± 2.2* |
| HbA1c (%)        | 7.3 ± 1.1     | 6.7 ± 0.9*   | 7.3 ± 2.1      | 6.6 ± 1.3* |
| Total cholesterol | 4.8 ± 0.8     | 4.7 ± 0.7    | 4.5 ± 0.7      | 4.3 ± 0.8  |
| HDL-cholesterol (mmol/L) | 1.3 ± 0.2     | 1.2 ± 0.3    | 1.2 ± 0.3      | 1.2 ± 0.3  |
| LDL-cholesterol (mmol/L) | 2.7 ± 0.8     | 2.5 ± 0.7*   | 2.5 ± 0.6      | 2.2 ± 0.8* |
| Triglyceride (mmol/L) | 1.8 ± 0.5     | 2.0 ± 0.7    | 1.7 ± 0.6      | 1.9 ± 0.8  |

Mean ± standard deviation; *P < .05: pre versus post; †P < .05: control versus treatment; BMI: Body mass index; DBP: Diastolic blood pressure; HR: Heart rate; MBP: Mean blood pressure; SBP: Systolic blood pressure.

1One subject missing in the control group.
2Two subjects missing in the control group.
3One subject missing in the treatment group.
4Two subjects missing in the treatment group.

The Shapiro-Wilk test was performed. Brown and Forsythe’s variation of Levene’s statistics test was used to verify the homogeneity of variances. A P value inferior to .05 was considered statistically significant. Data were analysed using the statistical packages Sigma Stat (Chicago, IL, USA) and SAS (SAS Institute Inc., Cary, NC, USA).

### 3. Results

#### 3.1. Clinical Parameters

Table 1 presents clinical characteristics of patients in both groups before and after treatment. There were no significant statistical differences between the two groups for all parameters at the beginning of the study (Table 1). After 3 months of treatment with Orlistat, there was a significant reduction in body weight (P < .001), BMI (P = .003), and waist circumference (P = .005). When compared to the control group, mean weight loss (3.7 ± 3.0 versus 0.5 ± 2.2 kg; P = .003), corresponding to a percentage of weight loss of 2.9 ± 2.5 versus 0.3 ± 1.5% (P = .003), was statistically different. Weight loss in the treatment group was associated with improvements in fasting glycemia, which decreased only in the group treated with Orlistat (P = .03). However, there was a significant decrease in HbA1c (controls: P < .001 and treated: P = .02) as well as in the LDL-cholesterol levels in both groups (controls: P = .05 and treated: P = .03). In the treatment group, fat-free mass decreased significantly (P = .03). No significant difference was observed between the two groups after treatment for the other anthropometric and metabolic parameters (Table 1).

#### 3.2. Heart Rate Variability

##### 3.2.1. Time Domain

In the 24-hour HRV indices, there was a significant increase in rMSSD (P = .02) as well as in pNN50 (P = .03) in the treated group following weight loss (Table 2). While there was no significant change in the HRV daytime indices, night time measures showed a significant improvement in rMSSD in the treated group only (P = .023).

##### 3.2.2. Spectral domain

Following weight loss, high-frequency (HF) power measured during the 24-hour period increased significantly (daytime: P = .056 and night time: P = .01) (Table 2). The LF/HF ratio decreased significantly in the treated group in the 24-hour assessment (P = .038) as well as during daytime (P = .006).

#### 3.3. Echocardiography

Echocardiographic parameters measured in both groups as well as normal values are shown in Table 3. There were no statistically significant differences in heart dimensions or parameters of LV diastolic function between the control group and the Orlistat-treated group at
the beginning of the study. Despite normal baseline values, we observed a nonstatistical increment in ejection fraction after treatment with Orlistat ($P = .054$), the values after treatment being also significantly greater than the ejection fraction values of the control group ($P = .04$). There were 11 out of 16 subjects with impaired LV diastolic function (7 spontaneous and 4 pseudonormal LVDD) in the treatment group while there were 7 out of 13 subjects (5 spontaneous and 2 pseudonormal LVDD) in the control group (Figure 1). Isovolumetric relaxation time, A wave velocity, E/A ratio, deceleration time, as well as the A wave duration were not statistically different following treatment. However, E wave velocity significantly increased in the treatment group ($P = .046$). During the Valsalva manoeuvre, we observed a significant decrease of the A wave velocity in the treatment group ($P = .007$), concomitant to a significant increase in the E/A ratio ($P = .024$). This increment was statistically different to the effect observed in the control group ($P = .027$). Accordingly, for the patients with a pseudonormal diastolic function, using the E/A value assessed during the

| Table 2: Heart rate variability indices in severely obese subjects with type 2 diabetes before and after treatment. |
|---|---|---|---|---|
| | Control group | | Treatment group | |
| | Pre | Post | Pre | Post |
| N | 13 | 12 | 16 | 16 |
| Mean NN (ms) | 768 ± 86 | 786 ± 111 | 775 ± 102 | 796 ± 101 |
| SDNN (ms) | 106 ± 34 | 106 ± 30 | 102 ± 25 | 112 ± 23 |
| SDANN (ms) | 93 ± 38 | 91 ± 35 | 88 ± 22 | 97 ± 22 |
| rMSSD (ms) | 26 ± 15 | 28 ± 16 | 24 ± 10 | 30 ± 10* |
| pNN50 (%) | 7 ± 10 | 8 ± 10 | 6 ± 7 | 9 ± 8* |
| HF (ln) | 4.4 ± 1.0 | 4.6 ± 0.9 | 4.5 ± 0.9 | 4.9 ± 0.7* |
| LF (ln) | 5.6 ± 0.9 | 5.7 ± 0.7 | 5.7 ± 1.0 | 5.9 ± 0.7 |
| LF/HF ratio | 3.7 ± 1.9 | 3.4 ± 1.7 | 3.3 ± 1.1 | 2.8 ± 1.3* |

(b) Daytime

| | Control group | | Treatment group | |
| | Pre | Post | Pre | Post |
| N | 13 | 12 | 16 | 16 |
| Mean NN (ms) | 733 ± 100 | 762 ± 133 | 734 ± 104 | 742 ± 105 |
| SDNN (ms) | 80 ± 29 | 85 ± 30 | 80 ± 22 | 84 ± 22 |
| SDANN (ms) | 68 ± 23 | 69 ± 26 | 63 ± 18 | 66 ± 21 |
| rMSSD (ms) | 21 ± 18 | 26 ± 20 | 21 ± 8 | 25 ± 9 |
| pNN50 (%) | 5 ± 13 | 7 ± 13 | 4 ± 5 | 6 ± 7 |
| HF (ln) | 3.8 ± 1.2 | 4.3 ± 1.2 | 4.1 ± 1.0 | 4.6 ± 0.8 |
| LF (ln) | 4.9 ± 0.9 | 5.4 ± 0.8 | 5.5 ± 1.0 | 5.7 ± 0.7 |
| LF/HF ratio | 3.8 ± 2.4 | 3.7 ± 2.5 | 4.0 ± 1.8 | 3.2 ± 1.2* |

(c) Night time

| | Control group | | Treatment group | |
| | Pre | Post | Pre | Post |
| N | 13 | 12 | 16 | 16 |
| Mean NN (ms) | 840 ± 86 | 827 ± 96 | 851 ± 112 | 890 ± 105 |
| SDNN (ms) | 88 ± 45 | 86 ± 30 | 83 ± 25 | 85 ± 23 |
| SDANN (ms) | 57 ± 39 | 60 ± 31 | 57 ± 18 | 53 ± 16 |
| rMSSD (ms) | 32 ± 17 | 30 ± 11 | 31 ± 15 | 36 ± 16* |
| pNN50 (%) | 10 ± 12 | 10 ± 10 | 11 ± 12 | 15 ± 14 |
| HF (ln) | 5.1 ± 1.1 | 4.9 ± 0.9 | 5.0 ± 1.0 | 5.4 ± 1.0 |
| LF (ln) | 6.2 ± 1.1 | 5.9 ± 0.9 | 6.0 ± 1.0 | 6.2 ± 0.9* |
| LF/HF ratio | 3.7 ± 2.6 | 3.2 ± 2.0 | 2.9 ± 1.4 | 2.6 ± 1.7 |

Mean ± standard deviation; *$P < .05$: pre versus post; †$P < .05$: control versus treatment; ln: logarithmic transformation; HF: High frequency; LF: Low frequency; Mean NN: Mean value of all RR intervals; pNN50: Percentage of intervals differing of ≥50 ms than the preceding interval; rMSSD: square root of the mean squared difference of successive RR intervals; SDANN: Standard deviation of the mean NN intervals for each 5 minutes period; SDNN: Standard deviation of the RR intervals.
was no improvement (P = .001). Changes in 24-hour and daytime also showed correlations (r = 0.487, P = .014, resp.).

3.3.1. Correlations. As expected, a positive correlation was found between body weight and BMI and LV mass (r = 0.68 and r = 0.44, resp.; both P < .001). An inverse correlation was also observed between body weight, BMI, and LV ejection fraction (r = −0.48 and r = −0.52, resp.; both P < .001). There was positive correlation between E/A ratio and 24-hour measurement of HF (r = 0.361; P < .001), rMSSD (r = 0.456; P < .001), and pNN50 (r = 0.458; P < .001). Changes in E/A ratio and delta LF/HF ratio during 24-hour and daytime also showed correlations (r = 0.377; P = .048 and r = 0.458; P = .014, resp.).

4. Discussion

We observed that modest Orlistat-induced weight loss enhances sympathovagal balance and cardiac function in severely obese patients with type 2 diabetes. After a 3-month treatment period with Orlistat, subjects lost significantly more weight than subjects in the control group.

Akehi et al. reported that very-low calorie diet-induced weight loss in moderately obese subjects improved NN, SDNN, SDANN, rMSSD, HF, and LF/HF ratio values [6]. This was interpreted as an improvement in the sympathovagal balance. Similarly, Poirier et al. [7] reported that a 10% diet-induced weight loss in 8 severely obese subjects was associated with significant improvement in autonomic cardiovascular modulation through enhancement of parasympathetic modulation which translates clinically into decreased heart rate and increased HRV. In our study, rMSSD, pNN50, and HF values of the 24-hour HRV were significantly improved in the treated group. All these indices are considered to reflect the parasympathetic system and being protective from a cardiovascular disease viewpoint [25]. Furthermore, another significant improvement was the decrease in the LF/HF ratio assessed during 24 hours and during daytime in the treatment group. Accordingly, Poirier et al. observed that the improvement in HRV after weight loss occurred mainly during the daytime period [7]. Our results show similar improvement in the parasympathetic modulation and in the sympathovagal balance, particularly during daytime. Studies [10, 14, 26] reported that, following bariatric surgery which induced important weight loss in severely obese subjects, LV mass was significantly reduced. In our study, weight loss in the treatment group was accompanied with a significant decrease in the posterior wall thickness and in LV mass as also reported by others [27–29].

To our knowledge, there are no data available in severely obese subjects investigating the impact of weight loss on the pseudonormal pattern of LV filling using the Valsalva manoeuvre. We observed an improvement of LV diastolic function in over half of the treated subjects compared to only one patient who had an improved LV diastolic function in the control group. Of note, the relations between HRV and echocardiographic parameters revealed that rMSSD and HF values correlate with E/A ratio. Interestingly, we also found a significant positive correlation between changes in E/A ratio and changes in LF/HF ratio during 24-hour and
daytime. These associations suggest that improvement in the parasympathetic function is related to improvement in the cardiac LV diastolic function parameters, as we previously reported in overweight subjects with diabetes [21]. Of note, there are only few reported studies using pharmacological approach in severely obese patients [30–32] and HRV and diastolic function has not been evaluated within the same study in this population.

The magnitude of weight loss induced by the medication is smaller (2.9 ± 2.5%) but may be comparable to findings previously reported, accounting for the time-treatment period. Sjöström et al. have reported a 10% weight lost (10 kg) after a year of treatment with Orlistat in a cohort of overweight to severely obese subjects [33]. Other studies using Orlistat for a longer period (12 to 24 months) have also reported similar results [34–39]. Taking into account that our study only lasted three months, we may speculate that subjects of our study could have possibly lost comparable amount of weight if had our study lasted 12 months. Indubitably, the definitive treatment in this obesity category is bariatric surgery, but clinicians aim at a 5%–10% weight loss in order to achieve better metabolic profile in obese subjects [1, 15]. Fasting glycemia significantly decreased in the treated group in contrast to the control group. Accordingly, Fujioka et al. [40] reported that every 4.5 kg reduction in weight should result in a 1.1 mmol/L decrement in fasting glycemia and to a 0.5% reduction in HbA1c. Accordingly, HbA1c values have significantly decreased in the treated group. However, we also observed a significant decrease in HbA1c in the control group, which was not different to the decrease observed in the treated group. We also observed a significant decrease in LDL cholesterol in the treated group as well as in the control group. This is not unusual and it is often encountered in placebo groups of weight loss studies. Indeed, similar results have been reported in obese subjects after a 4-week run-in period before treatment with Orlistat [34, 35]. Studies [38, 39] in overweight to obese type 2 diabetic patients with longer treatment duration (6 to 12 months) resulting to greater weight loss report greater changes in metabolic profiles, leading after 12 months to significant differences between Orlistat-treated group and control group.

We acknowledge that this study included a small number of subjects. Therefore, it should be considered as a pilot study. However, weight loss was significant in the treated group whereas it was not in the control group. Also, a
few echocardiographic veins assessment, were not adequately recorded because of technical reasons due to the corpulence of the subjects. Mitral inflow velocities are known to be load-dependent. Other indices of LV diastolic function, such as tissue Doppler-derived indices, may be less load-dependent. However, Dumesnil et al. [41] reported that tissue Doppler-derived indices are not totally preload independent and should be interpreted in light of the other Doppler parameters and the use of Valsalva’s manoeuvre.

5. Summary

The aim of this study was to determine the impact of Orlistat-induced weight loss on the metabolic profile and cardiovascular function in severely obese type 2 diabetes patients. Twenty-nine severely obese patients with type 2 diabetes were randomized either to a nonplacebo control group or to a treatment group with Orlistat thrice a day. Metabolic profile, anthropometric parameters, heart rate variability indices, and echocardiographic variables were measured before and after a 12-week treatment period. Our results suggest that a modest weight loss improves fasting glycemia, diastolic function, and sympathovagal balance in severely obese patients with type 2 diabetes.

6. Conclusions

Despite modest but significant weight loss, we observed that subjects treated with Orlistat showed improvements in fasting glycemia. We also observed improvements in HRV as well as in the LV diastolic function. The improvement in the cardiac parasympathetic ANS modulation was associated with enhancement in LV diastolic function. Our results emphasize the benefit of even modest weight loss in severely obese patients with diabetes.

Disclosures

Roche Company had no role in the design, collection, analysis, or interpretation of the data nor in the decision to submit the study for publication.

Acknowledgments

The authors are grateful to their volunteers whose availability made this work possible. J. Martin is a recipient of a graduate scholarship from the CIHR Training program in Obesity/Healthy Body Weight Research. P. Poirier is a clinical scientist from the Fond de Recherche en Santé du Québec (FRSQ).

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