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Adiponectin Secretion by Primary Human Adipocytes in Patients With Remission of Type 2 Diabetes Mellitus after Bariatric Surgery

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Abstract:

Introduction. The remission of type 2 Diabetes Mellitus (t2DM) after bariatric surgery has been associated with the secretion of several adipokines, where adiponectin plays a key role. Adipocyte´s production of adiponectin may be a mechanism participating in t2DM remission. This study aimed to explore whether adiponectin secretion by cultured primary human adipocytes were related to remission of t2DM after bariatric surgery

Methods. Observational, longitudinal study. Candidates for bariatric surgery were included. Clinical and biochemical data, as well as plasma adiponectin (ELISA), were recorded at recruitment and after 6 months from bariatric surgery. Clinical follow up was performed in order to document remission of t2DM. During bariatric surgery, primary human adipocytes were derived from omental fat, and adiponectin production was evaluated at control and niacin-stimulated culture conditions.

Results. Fifteen patients were included, and 8 (53%) of them showed t2DM remission. Higher (p=0.002) plasma adiponectin was observed in patients with t2DM remission after 6 months from surgery. Besides, significant difference (p=0.04) was documented in primary human adipocytes after niacin stimulation.

Conclusion. Plasma adiponectin and stimulated adipocyte's response of adiponectin secretion may be predictive of t2DM remission after bariatric surgery.

INTRODUCTION

The remission of type 2 Diabetes Mellitus (t2DM) after bariatric surgery has been related with the secretion of several cytokines, being adiponectin one of the focused adipokine (1). Adipocytes are largely responsible for adiponectin production (2); however, adipocyte´s basal production of adiponectin or their stimulated production have not been explored during t2DM remission. This study aimed to characterize adiponectin secretion by cultured primary human adipocytes in patients with and without remission of t2DM after bariatric surgery.

METHODS

Design. Observational, longitudinal study.

Study population. Fifteen patients with morbid obesity, t2DM and candidates for bariatric surgery, were included.

Biochemical assays and human primary adipocytes assay. Clinical and biochemical data, as well as plasma adiponectin (ELISA), were recorded at recruitment and after 6 months from bariatric surgery. During bariatric surgery, primary human adipocytes were derived from omental fat. Standardization assays allowed determining the number of cells and concentration of Niacin to be used for the stimulation tests and the collection time of the culture medium. Statistically significant difference in adiponectin concentration in culture medium was observed when using 500,000 cells / milliliter per well in culture plate. On the other hand, a significant difference was observed when stimulating adiponectin secretion with 15nM Niacin with collection of culture medium after 30 minutes.

t2DM remission. Clinical follow up was performed in order to document remission of t2DM, as defined by Hb_{a1c} <6.0% and fasting glucose <100 mg/dL (3).

Statistical analysis. Quantitative data were resumed as mean±SD and qualitative data as n(%). Statistical inferences were performed by two-way T-test. Statistical significance was considered if p<0.05.

RESULTS

Fifteen patients were included, 67% males, aged 47.6±6.4 years old. Mean BMI 47.9±9.8 kg/m^2, fasting glucose 119.0±23.6 mg/dL, Hb_{a1c} 6.9±1.4%, HDL cholesterol 36.3±8.0 mg/dL, LDL cholesterol 98.6±23.2 mg/dL and triglycerides 107.2±41.8 mg/dL.

After 6 months from bariatric surgery, 8 (53%) patients showed t2DM remission, and their baseline characteristics are shown in Table 1.

Table 1. *Clinical-Demographic Characteristics and t2DM Remission (n=15)*

	T2DM W/O REMISSION (n=7)	T2DM WITH REMISSION (n=8)	p
Age (y-o)	51.2 ± 4.6	44.2 ± 6.4	0.054
Male sex	5 (71.4)	5 (62.5)	0.18
Baseline BMI (kg/m^2)	50.4 ± 10.4	45.4 ± 9.4	0.41
Fasting glucose (mg/dL) 0 months 6 months	 119.3 ± 30.2 107.7 ± 27.5	 118.7 ± 17.8 78.7 ± 4.3	 0.96 **0.02**
Hb_{a1c} 0 months 6 months	 6.9 ± 0.9 6.1 ± 0.7	 6.9 ± 1.8 5.2 ± 0.1	 0.92 **0.01**
HDL cholesterol 0 months 6 months	 40.6 ± 6.1 39.3 ± 7.0	 41.9 ± 4.5 49.5 ± 4.3	 0.10 **0.03**
LDL cholesterol 0 months 6 months	91.2 ± 22.1 104.2 ± 26.8	105.9 ± 23.9 103.5 ± 17.1	0.29 0.96
Triglycerides 0 months 6 months	 149.3 ± 70.3 118.8 ± 14.3	 137 ± 39.6 102.67 ± 29.6	 0.71 **0.02**
Characteristics of the study population divided by t2DM remission. Quantitative data are shown as mean with standard deviation. Measurements are presented at baseline and 6 months after bariatric surgery.			

Higher plasma adiponectin was observed in patients with t2DM remission after 6 months from surgery (Figure 1, p=0.002). Likewise, significant difference (Figure 2, p=0.04) was documented in niacin stimulated adiponectin production rate, measured in primary human adipocytes obtained at time 0, during bariatric surgery.

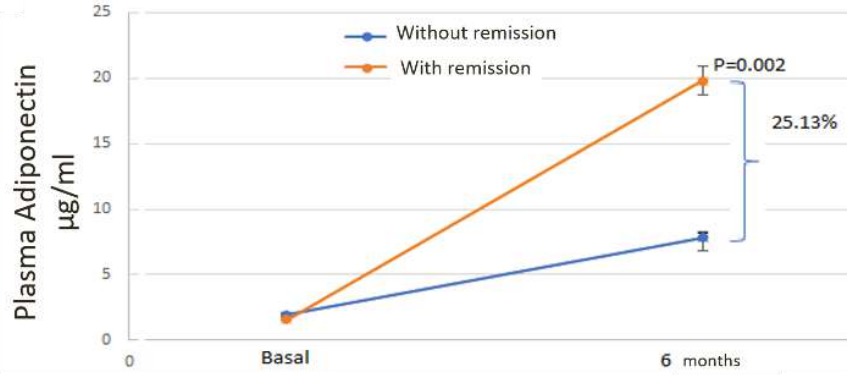

Figure 1. Plasma Adiponectin and t2DM remission. The figure shows the plasma concentration of adiponectin at 0 and 6 months after surgery.

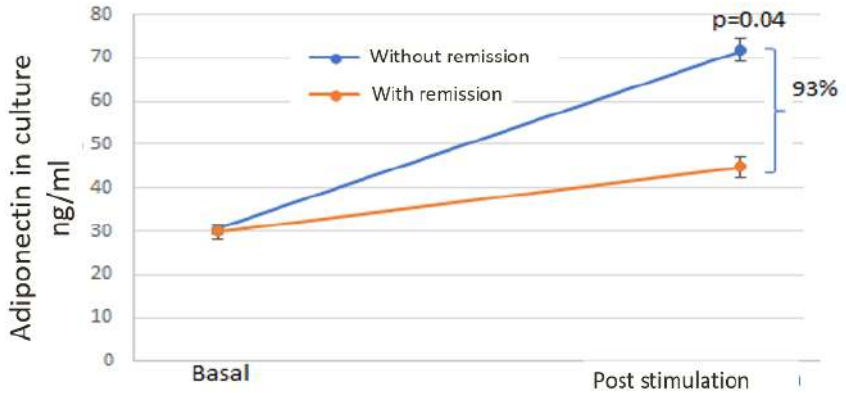

Figure 2. Adiponectin production rate in primary human adipocytes at time "0" and t2DM remission. The figure shows basal and stimulated **a**diponectin production rate by adipocytes obtained during bariatric surgery.

DISCUSSION

Mechanisms responsible for post-surgical remission of t2M and insulin sensitivity in morbid obesity remain unclear. To our knowledge, this is the first study evaluating markers like adiponectin secretion rate in human primary adipocytes in the preoperative period as a predictor of t2DM remission.

Interestingly, basal adiponectin secretion by adipocytes showed no differences between t2DM remission and non-remission groups; but stimulation of adiponectin secretion with niacin unmasked significant differences between groups, with a higher adiponectin production rate by adipocytes from those patients without t2DM, probably indicating an underlying adiponectin resistance condition. Data obtained by the present study design support the role of adiponectin and adipocyte's production rate in diabetes mellitus and obesity (4,5).

On the other hand, basal plasma adiponectin concentration was similar between patients with remission t2DM vs non-remission; however, a higher plasma adiponectin concentration was observed in the group of patients who achieved remission of t2DM, which is in agreement with that reported in the literature (6).

These observations suggest that there are differences in the adipocyte´s production pattern of adiponectin, which are related to glucose metabolism in obese patients after bariatric surgery.

In conclusion, increase in plasma adiponectin concentration as well as stimulated adipocyte's response of adiponectin secretion in culture, were related and predictive of t2DM remission after bariatric surgery.

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