Short report

Intensifying glycaemic control with insulin reduces adiponectin and its HMW isoform moderately in type 2, but not in type 1, diabetes

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Abstract

Introduction. – As the impact of diabetes control was not tested on adiponectin (ADPN) levels, this study was designed to assess whether or not controlling hyperglycaemia can affect ADPN.

Patients and methods. – A total of 15 T1D and 48 T2D patients with HbA\textsubscript{1c} greater than 10% were studied at the time of hospitalization for uncontrolled diabetes. Total, and high-, medium- and low-molecular-weight (HMW, MMW, LMW) ADPN were measured at the time of study inclusion, on days 1 and 8, and at 1, 3 and 6 months after insulin treatment.

Results. – While diabetes control improved, total and HMW ADPN decreased on days 1 and 8, but remained steady thereafter in T2D patients. In T1D patients, ADPN levels remained unchanged throughout the study.

Conclusion. – Glycaemic control with insulin reduces ADPN in T2D patients in the short-term, but was ineffective in T1D.

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Keywords: Adiponectin; Type 1 diabetes mellitus; Type 2 diabetes mellitus; Glycaemic control

Résumé

Intensifier le contrôle glycémique par l’insuline réduit modérément l’adiponectine totale et sa forme de haut poids moléculaire chez les seuls diabétiques de type 2.

Introduction. – L’effet de l’équilibre glycémique du diabète sur les concentrations plasmatiques d’adiponectine (ADPN) n’est pas connu. Nous avons étudié si la réduction de l’hyperglycémie par insulinothérapie modifie celles-ci.

Patients et méthodes. – Quinze diabétiques de type 1 (DT1) et 48 diabétiques de type 2 (DT2) hospitalisés pour déséquilibre du diabète (HbA\textsubscript{1c} > 10\%) ont été inclus. L’ADPN totale et ses isomères de poids moléculaires haut, moyen et bas (HMW, MMW, LMW) ont été mesurés à l’inclusion, à j1 et à j8 puis à un, trois et six mois d’un traitement par insuline.

Résultats. – Chez les DT2, l’ADPN totale et son isomère HMW ont diminué à j1 et à j8, puis sont restés stables malgré un contrôle glycémique nettement amélioré. Chez les DT1, les concentrations sont restées inchangées.

Conclusion. – Le traitement du diabète par insuline réduit l’ADPN à court terme dans le DT2, mais pas dans le DT1.

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Mots clés : Adiponectine ; Diabète de type 1 ; Diabète de type 2 ; Équilibre glycémique

In both type 1 and type 2 diabetes (T1D and T2D), high adiponectin (ADPN) levels are associated with microvascular complications, especially nephropathy [1,2]. However, these studies did not evaluate whether or not controlling diabetes
would affect circulating ADPN. For this reason, this study was carried out to determine whether or not improving glycaemic control [3,4] would alter circulating ADPN.

1. Research design and methods

A total of 63 patients with diabetes, aged 18 years or over, were consecutively studied, comprising 15 T1D [seven men and eight women, aged 29 ± (SEM) 7 years, diabetes duration 4 ± 6 years] and 48 T2D (34 men and 14 women, aged 54 ± 11 years, diabetes duration 10 ± 9 years) admitted to our diabetes department at the Paris Bichat Hospital for uncontrolled diabetes (HbA1c > 10%). All patients were given insulin intravenously, then subcutaneously, using a basal–bolus regimen. Other drugs, including lipid- and blood-pressure-lowering agents, were left unchanged. Also measured were total, and high-, medium- and low-molecular-weight (HMW, MMW, LMW) ADPN levels, using an Elisa kit (ALPCO Diagnostics, Salem, NC, USA) at the time of study inclusion (ADPN0), on day 1 (ADPN1) and day 8 (ADPN8) of hospitalization, then at 1 (ADPN1m), 3 (ADPN3m) and 6 months (ADPN6m) after discharge. Blood pressure, eye funduscopy, urinary albumin excretion (UAE) and glomerular filtration rate (GFR; MDRD equation) were recorded on inclusion.

Immediate glycaemia, mean 2-week glycaemia (OneTouch® Ultra® monitoring system), body mass index (BMI), abdominal circumference and body mass composition by impedancemetry (BC-418MA, Tanita, Arlington Heights, IL, USA) were recorded every time ADPN was measured.

The study protocol was approved by the local ethics committee, and all patients gave written informed consent to participate. Data are given as mean values ± SEM. The values of ADPN and its isoforms had a skewed distribution and were, therefore, log-transformed for comparisons. Repeated-measures Anova was used to test the effect of time on selected variables; otherwise, non-parametric tests were used (Spearman’s rank test for correlation and Mann–Whitney test for intergroup comparisons). All data were analyzed using StatView V software (SAS Institute, Cary, NC, USA).

2. Results

In patients with T1D, glycaemia was 14.1 ± 6.4 mmol/L on admission, and fell to 8.4 ± 3.9 mmol/L on day 1 and to 7.9 ± 5.2 mmol/L on day 8. Baseline HbA1c was 11.7 ± 2.9%, which was reduced to 9.8 ± 2.4% after 1 month, to 8.2 ± 2.7% after 3 months and to 8.1 ± 2.5% after 6 months. Baseline BMI (24.8 ± 6.5 kg/m²), total body fat percentage (31.2 ± 10.3%) and abdominal circumference (103 ± 15 cm) progressively increased during the follow-up (data not shown). Total ADPN on day 0 (5.04 ± 2.9 μg/L) decreased to 4.73 ± 2.7 μg/L on day 1 (P = 0.031) and to 4.51 ± 2.9 μg/L on day 8 (P = 0.012 versus ADPN0). A time effect was observed on the global evolution of total ADPN from inclusion to the end of the study (P = 0.024), but no further decreases were observed between day 8 and 1, 3 and 6 months (Fig. 1). The decrease in total ADPN was mainly due to a decrease in the HMW isoform from 2.13 ± 2 μg/L on admission to 1.83 ± 1.7 μg/L on day 1 (P = 0.009) and 1.69 ± 1.8 μg/L on day 8 (P = 0.007 versus HMW at day 0), whereas the other two isoforms were almost unchanged (data not shown). The reduction in total ADPN was independent of age (P = 0.29), gender (P = 0.4), diabetes duration (P = 0.91), HbA1c (P = 0.27), GFR (P = 0.21), BMI (P = 0.83), body fat composition (P = 0.27), and the presence or absence of retinopathy (P = 0.69) and nephropathy (P = 0.52). Moreover, baseline total ADPN levels did not differ between patients with and without severe retinopathy (P = 0.28), and in patients with UAE greater than 300 mg/24 h versus normoalbuminuric patients (P = 0.004).

In patients with T2D, glycaemia was 15.6 ± 10.5 mmol/L on admission, 8.7 ± 3.6 mmol/L on day 1 and 7.5 ± 3.6 mmol/L on day 8. HbA1c decreased from 12.6 ± 2.9% at inclusion at 9.3 ± 1.6% at 1 month, 8.2 ± 2.7% at 3 months and 8.1 ± 2.3% at 6 months. Baseline BMI (28.5 ± 6.5 kg/m²), total body fat percentage (31.2 ± 10.3%) and abdominal circumference (93 ± 15 cm) progressively increased during the follow-up (data not shown). Total ADPN on day 0 (5.04 ± 2.9 μg/L) decreased to 4.73 ± 2.7 μg/L on day 1 (P = 0.031) and to 4.51 ± 2.9 μg/L on day 8 (P = 0.012 versus ADPN0). A time effect was observed on the global evolution of total ADPN from inclusion to the end of the study (P = 0.024), but no further decreases were observed between day 8 and 1, 3 and 6 months (Fig. 1). The decrease in total ADPN was mainly due to a decrease in the HMW isoform from 2.13 ± 2 μg/L on admission to 1.83 ± 1.7 μg/L on day 1 (P = 0.009) and 1.69 ± 1.8 μg/L on day 8 (P = 0.007 versus HMW at day 0), whereas the other two isoforms were almost unchanged (data not shown). The reduction in total ADPN was independent of age (P = 0.29), gender (P = 0.4), diabetes duration (P = 0.91), HbA1c (P = 0.27), GFR (P = 0.21), BMI (P = 0.83), body fat composition (P = 0.27), and the presence or absence of retinopathy (P = 0.69) and nephropathy (P = 0.52). Moreover, baseline total ADPN levels did not differ between patients with and without severe retinopathy (P = 0.28), and in patients with UAE greater than 300 mg/24 h compared with normoalbuminuric patients (P = 0.47). There was no correlation between ADPN and its HMW isoform with HbA1c at either the time of study inclusion (r = 0.01, P = 0.97 and r = −0.02, P = 0.93, respectively) or at 6 months (r = 0.02, P = 0.95 and r = −0.009, P = 0.97, respectively) in neither T1D nor T2D patients (r = 0.13, P = 0.29 and r = 0.10, P = 0.42, respectively, at inclusion; r = 0.12, P = 0.53 and r = −0.005, P = 0.98 at 6 months, respectively). In addition, there was no correlation between ADPN and immediate or mean 2-week glycaemia at any time during the study in either T1D or T2D patients (data not shown).
3. Conclusion

In T1D, baseline ADPN levels were markedly elevated in patients with microangiopathy, a fact that has been reported previously [1,5]. However, reduction of hyperglycaemia did not influence ADPN, a finding consistent with reports of patients with recently diagnosed T1D [6] and in those undergoing pancreas transplantation [7].

In T2D patients, acute insulin treatment for improving glycaemic control resulted in a modest, but statistically significant, decrease in ADPN in the short-term. However, it is not clear whether this ADPN decline was due to reducing glycaemia or to the insulin treatment. The present results are consistent with previous data showing that exogenous insulin lowers plasma ADPN in healthy subjects during hyperinsulinaemic–euglycaemic clamp tests [8,9]. In addition, in T2D patients, total ADPN levels were also reported to fall under hyperinsulinaemic conditions primarily due to a reduction in the HMW isofrom [10].

Previous reports of the relationship between ADPN and glycaemia are conflicting. While Fernández-Real et al. [11] showed that both fasting plasma glucose and HbA1c correlated negatively with ADPN in patients with T2D or glucose intolerance, Owecki et al. [12] did not find a link between ADPN and glycaemic control in obese patients with T2D. In our study, immediate glycaemia, mean 2-week glycaemia and HbA1c were not linked to ADPN. These results are consistent with a previous report that hypoadiponectinaemia in T2D is more closely related to insulin sensitivity than to glycaemia, and that it is mostly attributable to insulin resistance and/or hyperinsulinaemia [13]. Furthermore, no additional decrease in ADPN was observed during the 6-month follow-up, although HbA1c progressively decreased during that time.

In summary, these data suggest that ADPN levels are regulated by factors other than glycaemic control.

Conflict of interest statement

None.

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References