Physiol. Res. 53: 115-117, 2004

RAPID COMMUNICATION

Somatostatin: Beneficial Effects on Remission in Young Adult Patients with Newly Diagnosed Diabetes Mellitus Type 1

K. VONDRA, M. VOBORSKÁ, M. KVAPIL[1], P. WEBER[2], H. DVOŘÁKOVÁ, S. STANICKÁ, V. ZAMRAZIL

Institute of Endocrinology, Prague, [1]Second Faculty of Medicine, Charles University, Prague, [2]Geriatrics Clinic, Brno-Bohunice, Czech Republic

Received June 5, 2003
Accepted July 16, 2003

Summary

To assess a possible influence of short-term administration of somatostatin on remission development in adult patients with newly diagnosed diabetes mellitus type 1, the somatostatin analog octreotide was given for two weeks after the establishment of the diagnosis at the daily dose of 150 μg subcutaneously in addition to the regular insulin and metabolic therapy. When compared to the control group, the remission was achieved earlier in the octreotide group (6±4 weeks vs. 11±12 weeks in the control group, $p<0.05$) and its duration was longer (99±49 weeks vs. 49±31 weeks in the control group, $p<0.05$). Moreover, remission also appeared in patients from the octreotide group with lower endogenous residual secretion of insulin (basal C peptide at the time of diagnosis in patients who later entered remission was 0.23±0.16 nmol/l vs. 0.34±0.18 nmol/l in the control group, $p<0.05$). The increase of 24-h urine excretion of C-peptide after the therapy with octreotide was predictive for remission development. It can thus be concluded that octreotide administration in adults with newly diagnosed diabetes mellitus type 1 positively influences both the onset and duration of remission.

Key words

Diabetes mellitus type 1 • Somatostatin • Octreotide • Remission

As was shown by Grunt *et al.* (1994), the administration of somatostatin in the early stages after diabetes mellitus type 1 (Type 1 DM) diagnosis can be an interesting approach to significantly prolonging the functional capacity of β-cells and thus to improve the course of the disease. Surprisingly, this observation has not been further systematically studied. The goal of this study was to assess the possible effect of somatostatin analogue (octreotide) on the onset and duration of remission in newly diagnosed young adults with diabetes mellitus type 1. More details about the patients studied are given in Table 1. The octreotide group received octreotide (Sandostatin – Novartis, 50 μg TID in subcutaneous injections during hospitalization at the Metabolic Care Unit of the Internal Department of the Second Faculty of Medicine of the Charles University, Prague) for two weeks after the establishment of the diagnosis of Type 1 DM in addition to the regular insulin and metabolic therapy. Criteria for remission complied with Scholin *et al.* 1999 (remission defined as

maintenance of HbA1c under 6.5 % and an insulin dosage under 0.4 U/kg/day^{-1} for a minimum of one month). In comparison with the control group, the therapy with octreotide was associated with beneficial effects on the remission (Table 2). Remission tended to be more frequent, appeared significantly earlier, and its duration was significantly longer. Moreover, the remission was observed in patients from the octreotide group with lower endogenous residual secretion of insulin (Table 1). In patients who later entered remission, the 24-h urine C-peptide excretion increased after the therapy with octreotide (before administration of octreotide 13.8±8.22 nmol/l/day, immediately after finishing octreotide administration 21.9±13.5 nmol/l/day, $p<0.0003$, 3 months after the end of therapy 18.3±9.8 nmol/l/day, $p<0.001$). The 24-h urine C-peptide excretion in patients who did not enter the remission stayed, after the therapy with octreotide, at the pretreatment basal levels. Using the dose of octreotide of 150 μg/day no hypoglycemia <2.8 mmol was noted. The most frequent adverse effect was a moderate abdominal discomfort (22 %), associated with diarrhea in some patients (17 %), but there was no need to terminate the therapy in any patients. The beneficial effect of octreotide can be explained by the ability of octreotide to block endogenous insulin secretion, induce "β-cell arrest" and thus contribute to the reparation of β-cells (Schloot and Eisenbarth 1995). In addition, liver and peripheral insulin sensitivity is also favorably influenced by the blockade of growth hormone secretion and by decreasing of non-esterified fatty acid levels (Wurzburger *et al.* 1992, Orskov *et al.* 1996). It is also important to take into account the direct effect of somatostatin on glucose metabolism in human muscles as was shown by Møller *et al.* (1995). Recent achievements in the therapy of endocrine orbitopathy using somatostatin analogues even suggest an important immunomodulatory effect of octreotide (Krassas 1998). The question about the detailed mechanism of the beneficial effect of octreotide on the remission development gives an interesting opportunity for further research.

Table 1. Characteristic of patients in octreotide and control group at the time of diagnosis of Type I diabetes mellitus (before starting octreotide administration).

	Octreotide group	**Control group**	**p**
n	18	40	ns
Age (years)	26±7	25±5	ns
Body mass index (kg/m^2)	21.4±3.9	21.2±2.7	ns
Weight loss during the symptomatic period (%)	11.6±5.7	11.2±5.8	ns
HbA1c (%) (Abbot IMX set)	12.3±3.2	10.2±3.9	ns
Basal C-peptide (nmol/l)			
a) in patients who later entered remission	0.23±0.16	0.34±0.18	<0.001
b) in patients who did not enter remission	0.11±0.07	0.26±0.12	<0.01
Prevalence of antiGAD (%) (CIS, RIA)	69	76	ns

Data are given as means ± S.D. C peptide was measured by IRMA (Immunotech Prague, Czech Republic).

Table 2. Prevalence, onset, and duration of remission in the octreotide and control groups.

	Octreotide group	**Control group**	**p**
Prevalence (%)	72	60	ns
*Onset (weeks)**	6±4	11±12	<0.05
Duration (weeks)	99±49	49±31	<0.05

* after diagnosis of diabetes mellitus. Data are given as means ± SD.

Acknowledgements

This work was supported by the grant #00000023761 of the Ministry of Health of the Czech Republic.

References

GRUNT JA, HASAN AH, WILLOUGHBY L, HOWARD P: A randomized trial of a somatostatin analog for preserving beta cell. *J Pediatr Endocrinol* **7**: 331-334, 1994.

KRASSAS GE: Somatostatin analogues in the treatment of thyroid eye disease. *Thyroid* **8**: 443-5, 1998.

MØLLLER N, BAGGER JP, SCHMITZ O, JØRGENSEN JOL: Somatostatin enhances insulin stimulated glucose uptake in the perfused human forearm. *J Clin Endocrinol Metab* **80**: 1789 –1793, 1995.

ORSKOV L, MØLLER N, BAK JF, PORKSEN N, SCHMITZ O: Effect of the somatostatin analog, octreotide on glucose metabolism and insulin sensitivity in insulin-dependent diabetes mellitus. *Metabolism* **45**: 211-217, 1996.

SCHLOOT N, EISENBARTH GS: Isohormonal therapy of endocrine autoimunity. *Imunol Today* **16**: 289-293, 1996.

SCHOLIN A, BERNE C, SCHVARCZ E, KARLSSON FA, BJORK E: Factors predicting clinical remission in adult patients with type 1 diabetes. *J Intern Med* **245**: 155-62, 1999.

WURZBURGER MI, PRELEVIC GM, SONKSEN PH, BALINT-PERIC LA: The effect of the somatostatin analogue octreotide on growth hormone secretion in insulin-dependent diabetics without residual insulin secretion. *Horm Metab Res* **24**: 329-332, 1992.

Reprint requests

Dr. Karel Vondra, Institute of Endocrinology, Národní 8, 116 94 Prague 1, Czech Republic. E-mail: kvondra@endo.cz