INTRANASAL CO-ADMINISTRATION OF INSULIN AND C-PEPTIDE RESTORES METABOLIC AND HORMONAL INDICES IN RATS WITH NORMOINSULINEMIC, BUT NOT WITH HYPERINSULINEMIC, TYPE 2 DIABETES

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Introduction

In type 2 diabetes mellitus (T2DM), the functions of the brain insulin system are impaired, which is associated with a decrease in insulin transport across the blood-brain barrier due to insulin resistance. To restore insulin deficiency in the brain, intranasally administered insulin (II) can be used, and its effect can be enhanced by intranasal administration of C-peptide (ICP).

Objective

The aim of this work is to study the effect of ten-day treatment of male Wistar rats with hyperinsulinemic and normoinsulinemic T2DM with II (20 μg/rat/day), ICP (36 μg/rat/day) or II+ICP on metabolic and hormonal parameters.

Methods and Materials

- The study was conducted on Wistar male rats.
- Hyperinsulinemic T2DM was induced by a 3-month high-fat diet (HFD) and low-dose streptozotocin treatment (15 μg/kg) of adult rats.
- Normoinsulinemic T2DM was induced by high-dose streptozotocin treatment (75 μg/kg) of 5-day-old rats.
- For both models of T2DM, 5 groups were formed (n=5): control, which received intranasal saline (C1, C2), diabetes without treatment (HI-D, NI-D), diabetes treated for 9 days with ICP at a dose of 36 μg/ rat/day (HI-DC, NI-DC), II at a dose of 20 μg/rat/day (HI-DI, NI-DI) and their combinations at the same doses (HI-DCI, NI-DCI).
- OGTT test was performed at the end of experiment.
- Blood samples were obtained from the tail vein. The blood levels of glucose, insulin, leptin, tT4, tT3, fT3, and fT4 were measured using ELISA kits.
- The statistical analyses were performed using the software IBM SPSS Statistics 23.0.0.0 (“IBM”, New York, NY, USA).

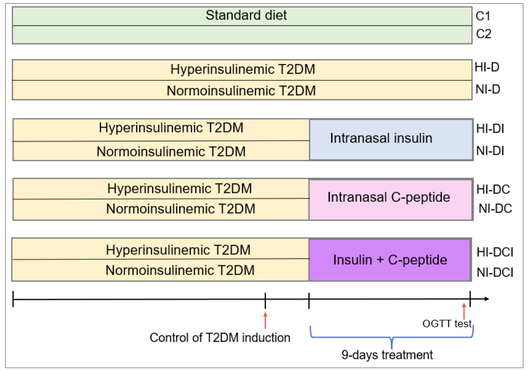
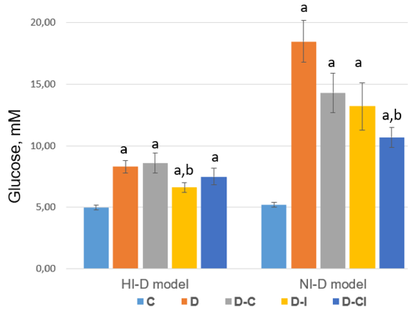


Figure 1.
The design of the experiments

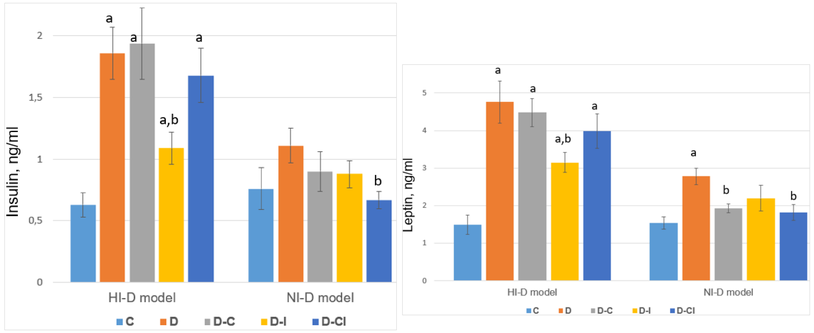
Results

Figure 2. Glucose levels 2 hours later after glucose loading during OGTT in the studied groups at the end of experiment.



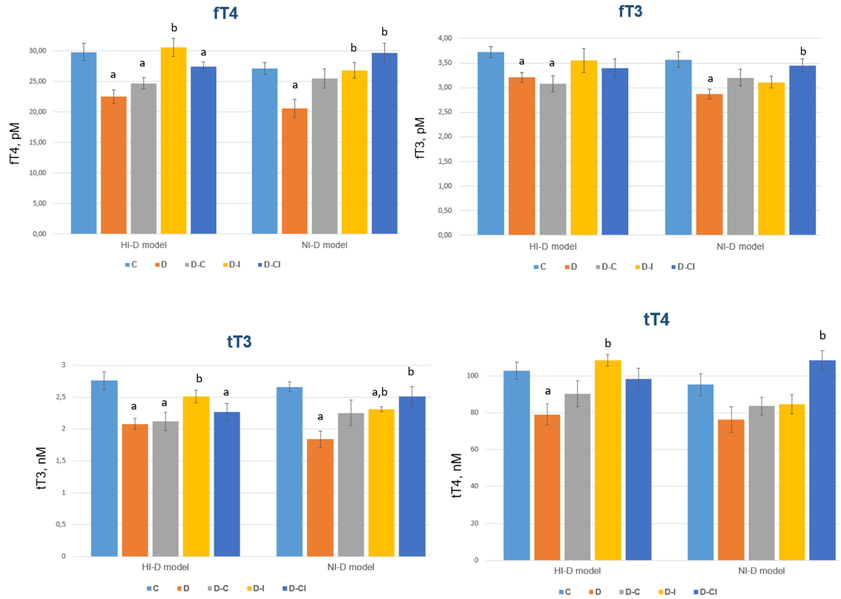
The difference between C (a) and D (b) is significant at P < 0.05. M ± SEM. N=5

Figure 3. Glucose-stimulated plasma levels of insulin and leptin in OGTT in the studied groups at the end of experiment.



The difference between C (a) and D (b) is significant at P < 0.05. M ± SEM. N=5

Figure 4. The effect of C-peptide and intranasally administered insulin on the levels of thyroid hormones in the blood of male rats with T2DM.



The difference between C (a) and D (b) is significant at P < 0.05. M ± SEM. N=5

Conclusions

In normoinsulinemic T2DM, ICP improved thyroid hormone deficiency and enhanced the restorative effects of II on glucose, insulin, and leptin sensitivity. In hyperinsulinemic T2DM, ICP was ineffective, and in combination with II weakened the restorative effects of II.

Thus, the data indicate that ICP and its combination with II are effective in restoring metabolic and hormonal parameters in normoinsulinemic, but not hyperinsulinemic, T2DM.

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