



Short communication

Comparative effects of short-term and long-term insulin-induced hypoglycemia on glucose production in the perfused livers of weaned rats

Romir Rodrigues¹, Kassia P. S. Feitosa², Antonio M. Felisberto-Junior³, Helenton C. Barrena², Rui Curi⁴, Roberto B. Bazotte²

¹Department of Pharmacy, UNIPAR, 87706-490, Paranavaí, PR, Brazil

²Department of Pharmacology and Therapeutics, State University of Maringá, Maringá, PR, 87020-900, Brazil

³Department of Biology, UNINGA, Maringá, PR, Brazil

⁴Department of Physiology and Biophysics, University of São Paulo, 05508-900, São Paulo, SP, Brazil

Correspondence: Roberto B. Bazotte, e-mail: rbbazotte@uem.br

Abstract:

The liver glucose production (LGP) levels of 15-h overnight fasted weaned rats submitted to short-term insulin-induced hypoglycemia (ST-IIH) and long-term IIH (LT-IIH) were compared. Experiments to characterize ST-IIH or LT-IIH that followed an intraperitoneal (*ip*) injection (1.0 U/kg) of regular (ST-IIH) or insulin detemir (LT-IIH) were performed and glycemia were measured 0 (normoglycemic control), 0.5 h (ST-IIH), 4 h and 6 h (LT-IIH) later. The values of glycemia (mg/dl) were 77.8 ± 7.2 (normoglycemic control), 26.2 ± 6.1 (ST-IIH 0.5 h), 21.2 ± 7.6 (LT-IIH 4 h) and 35.3 ± 14.5 (LT-IIH 6.0). The LGP levels were measured in the rats submitted to ST-IIH (0.5 h) and LT-IIH (4 h or 6 h). The rats that received *ip* saline were used as the normoglycemic control group (COG). The livers from the COG and IIH groups (ST-IIH or LT-IIH) were perfused *in situ* with infusion of L-alanine (5 mM), L-glutamine (10 mM), glutamine dipeptide (5 mM), L-lactate (2 mM) or glycerol (2 mM). The ST-IIH rats showed a higher LGP level than COG group following the L-glutamine infusion ($p < 0.05$), but the LGP levels that were measured following the L-lactate, L-alanine, glutamine dipeptide (5 mM), L-lactate (2 mM) or glycerol infusion remained unchanged. Moreover, if the period of IIH was expanded to 4 h following insulin injection, the LGP levels induced by L-alanine, glutamine dipeptide or glycerol infusion also increased ($p < 0.05$, LT-IIH vs. COG). However, the LGP from the L-lactate infusion remained unchanged until 6 h after insulin injection. In conclusion, these results suggest that the intensification of liver gluconeogenesis during ST-IIH and LT-IIH in weaned rats is not a synchronous "all or nothing" process; instead, this process integrated in a temporal manner and is specific for each gluconeogenic substrate.

Key words:

hypoglycemia, liver gluconeogenesis, weaned rats, insulin detemir
