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Insulin-Induced Relative Hypoglycemia on Hemodynamics and Metabolic Insulin Sensitivity in Adults with Obesity

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Relative hypoglycemia (RH) is linked to stress hormones that alter autonomic function. While the clinical risks of RH have been investigated, less is known about the induction of RH on hemodynamics or metabolic insulin sensitivity in adults with obesity. **PURPOSE:** To determine if RH alters aortic waveforms and metabolic insulin sensitivity to a greater extent in those with chronic hyperglycemia (HG) versus normoglycemia (NG). **METHODS:** Seventy-one adults with obesity (55.02 ± 0.9 y; 36.2 ± 0.6 kg/m²) were classified using ADA criteria of HbA1c > 5.7% as HG (n=34, 28F; HbA1c=6.02±0.1%) or NG (n=36, 30F; HbA1c=5.4±0.0%). A 2-hr OGTT was also used to depict glucose tolerance status. A 120min hyperinsulinemic-euglycemic clamp (40mU/m²/min, 90 mg/dl) was used to determine metabolic insulin sensitivity (glucose infusion rate (GIR)). Pulse wave analysis (applanation tonometry) was used to assess augmentation index (AIx75), brachial (bBP) and central (cBP) blood pressure, as well as waveform components (forward pressure (Pf), backward pressure (Pb), and reflection magnitude (RM)) at 0 and 120min of the clamp. Plasma nitrate and nitrite were measured as surrogates of nitric oxide. RH was defined as the percent drop in glucose from fasting to steady state (90-120min) periods of the clamp, and symptoms were noted if any. **RESULTS:** There were no differences in age, weight, VO₂max, or fasting aortic waveforms between groups. HG had higher HbA1c (P<0.01), fasting glucose (P=0.04), 2-hr OGTT glucose (P<0.01), and had a greater drop in glucose in response to insulin (-16.5 ± 2.8 vs. -10.7 ± 2.0 %; P=0.03), whereas GIR was lower than NG (P=0.03). Despite no hypoglycemic symptoms being reported, heart rate (HR) increased in NG compared to HG (5.9 ± 1.4 vs. -0.61 ± 1.8 %; P<0.01), while Pf decreased in HG (-6.9 ± 3.5 vs. 3.0 ± 3.1 %; P=0.04). However, insulin lowered AIx75, AP, Pb and RM as well as plasma nitrate and nitrite similarly between NG and HG (P≤0.05). Insulin-mediated decreases in HR associated with lower Pf (r=0.34, P<0.01). **CONCLUSION:** Insulin-induced RH was higher in HG compared to NG. This corresponded with a blunted rise in HR and drop in Pf during insulin infusion. These data suggest RH may relate to altered vascular and/or autonomic function in adults with HG.

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