Exposure to Glucocorticoids in the First Part of Fetal Life is Associated with Insulin Secretory Defect in Adult Humans

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Abstract

Objective

High glucocorticoid levels in rodents inhibit development of beta cells during fetal life and lead to insulin deficiency in adulthood. To test whether similar phenomena occur in humans, we compared beta-cell function in adults who were exposed to glucocorticoids during the first part of fetal life with that of nonexposed subjects.

Research Design and Methods

The study was conducted in 16 adult participants exposed to glucocorticoids during the first part of fetal life and in 16 nonexposed healthy participants with normal glucose tolerance who were matched for age, sex, and body mass index (BMI). Exposed participants had been born to mothers who were treated with dexamethasone 1 to 1.5 mg/day from the sixth gestational week (GW) to prevent genital virilization in children at risk of 21-hydroxylase deficiency. We selected offspring of mothers who stopped dexamethasone before the 18th GW following negative genotyping of the fetus. Insulin and glucagon secretion were measured during an oral glucose tolerance test (OGTT) and graded intravenous (IV) glucose and arginine tests. Insulin sensitivity was measured by hyperinsulinemic-euglycemic-clamp.

Results

Age, BMI, and anthropometric characteristics were similar in the 2 groups. Insulinogenic index during OGTT and insulin sensitivity

during the clamp were similar in the 2 groups. In exposed subjects, insulin secretion during graded IV glucose infusion and after arginine administration decreased by 17% (P = 0.02) and 22% (P = 0.002), respectively, while glucagon secretion after arginine increased.

Conclusion

Overexposure to glucocorticoids during the first part of fetal life is associated with lower insulin secretion at adult age, which may lead to abnormal glucose tolerance later in life.

Keywords: glucocorticoids, insulin secretion, fetal programming