OBSERVATIONS

Birth Weight: Genetic and Intrauterine Environment in Normal Pregnancy

Recent meta-analysis (1) and systematic review (2) show that high and low birth weight are related in a U-shaped manner to later risk of type 2 diabetes. It is also interesting to denote the positive birth weight/type 2 diabetes associations within the normal weight range. It is now widely accepted that both genetic and environmental factors are engaged in intrauterine growth, glucose tolerance, and development of type 2 diabetes in later life. The polymorphisms of the insulin receptor substrate (IRS)-1 (3) and β3-adrenergic receptor (β3-AR) genes (4) are genetic risk factors that are associated with insulin resistance and predisposition to type 2 diabetes. In the same way the intrauterine hormonal environment has shown strong influences on birth weight, this—together with early postnatal hormonal environment—increases the risk of obesity and type 2 diabetes in later life.

The purpose of our study was to determine whether both IRS-1 and β3-AR polymorphisms, as well as serum C-peptide and leptin values, were associated with birth weight in a large newborn population of normal pregnancies. Anonymous cord blood samples of newborns arising from 762 uncomplicated consecutive pregnancies (gestational age 38–42 weeks; mothers had no documented gestational diabetes, type 2 diabetes, impaired glucose tolerance, or hypertension, were not cigarette smokers, and were not obese before pregnancy) were evaluated for IRS-1/Gly972Arg, ADR-β3/Trp64Arg by methods previously reported (5). C-peptide (Biochem Immuno System; Italia SpA, Bologna, Italy) and leptin (Linco Research, St. Charles, MO) were assayed by commercial kits. Grouped birth weights and the prevalence of both IRS-1 [(hetero + homozygote/total, percent) 2.5–3.0 kg (16/126, 12.7%), 3.0–3.5 kg (52/327, 15.9%), 3.5–4.0 kg (46/254, 18.1%), >4.0 kg (12/45, 26.7%)] and β3-AR [2.5–3.0 kg (7/130, 5.4%), 3.0–3.5 kg (35/331, 10.6%), 3.5–4.0 kg (30/255, 11.8%), >4.0 kg (8/46, 17.4%)] gene polymorphisms were significantly correlated ($P = 0.036$ and $P = 0.019$, respectively, χ^2 for trend). A more significant correlation (ANOVA) was found between the grouped birth weights for C-peptide [(ng/ml value, number) 2.5–3.0 kg (1.2 ± 0.06, 121), 3.0–3.5 kg (1.4 ± 0.04, 297), 3.5–4.0 kg (1.4 ± 0.05/231), >4.0 kg (1.6 ± 0.14, 42), $P = 0.009$] and leptin [2.5–3.0 kg (6.0 ± 0.39, 128), 3.0–3.5 kg (8.6 ± 0.40, 323), 3.5–4.0 kg (11.0 ± 0.47, 243), >4.0 kg (15.6 ± 1.4, 45), $P < 0.0001$] plasma cord blood.

Our results indicate that both genetic and hormonal intrauterine environmental factors are engaged in determining the birth weight within the normal range although with different impact. In fact, the grouped normal range of birth weight was significantly related to both IRS-1 and β3-AR polymorphisms as well as to greater serum C-peptide and leptin values. As obesity and type 2 diabetes are major public health problems that are increasing in all regions of the world, it is necessary to develop primary prevention strategies by creating a very proactive attitude toward a healthy lifestyle before and during pregnancy. This way we can modify the "intra-uterine environment" and prevent excessive weight gain during the pregnancy, thereby reducing the incidence of diabetes and the obesity epidemic in the next generations.

SARA FALLUCCA, PHD[1]
MARIO VASTA, MD[2]
ERNESTA SCIULLO, PHD[1]
STEFANO BALDUCCI, MD[1]
FRANCESCO FALLUCCA, MD[1]

From the [1]Department of Clinical Sciences, II Faculty "Sapienza" University, Rome, Italy; and the [2]Diabetes Unit, Urbino Hospital, Urbino, Italy.
Corresponding author: Stefano Balducci, sbalducci@esinet.it.
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