Insulin Detemir Does Not Cross the Human Placenta

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Insulin detemir (IDet) is a relatively new long-acting insulin analog that offers improved absorption pharmacokinetics and slower tissue distribution due to high plasma protein binding (1). As IDet is increasingly used for treatment of insulin-requiring diabetes, including women with type 2 diabetes (who may conceive while being treated with IDet) as well as women with gestational diabetes mellitus, its transplacental pharmacokinetics warrants study (2). The placental transfer of IDet in humans has not been previously studied. The objective of this study was to determine whether IDet administered to pregnant women crosses the human placenta.

Sixteen pregnant women with either gestational diabetes mellitus (11 subjects) or type 2 diabetes (5 subjects) receiving IDet were enrolled in this institutional review board–approved study after giving informed consent. At delivery, 5 mL of maternal venous blood and umbilical cord blood were collected. Plasma was separated and frozen at −20°C until analyzed.

IDet and human insulin were measured using the Thermo Scientific Mass Spectrometric Immunoassay Insulin workflow. This workflow combines immunocapture of insulin analogs on a proprietary microfluidic column that is derivatized with an anti-insulin antibody and liquid chromatography-mass spectrometric detection.

The anti-insulin antibody targets a conserved region within insulin allowing for the simultaneous immunopurification of multiple insulin analogs, while the liquid chromatography-mass spectrometry enables the differentiation of each insulin analog based on its specific liquid chromatographic separation and mass spectrometric detection. Immunocaptured insulin analogs were separated on a 100 × 0.5-mm Thermo Scientific ProSwift column using a Thermo Scientific Dionex UltiMate 3000 RSLC system, and their intact detection was acquired on a Thermo Scientific Q Exactive mass spectrometer. Limits of detection were 50 pmol/L for IDet and 15 pmol/L for endogenous insulin.

Mean prepregnancy weight was 85.9 kg (range 52.2–135.5 kg) and weight at delivery was 100.5 kg (range 65.9–129 kg). BMI ranged between 21 and 52.4 kg/m^2 (mean 32.4). Daily doses of IDet ranged between 10 and 96 units (mean 57.7). Maternal IDet plasma concentrations at delivery ranged between 159 and 3,804 pmol/L, with a mean of 1,015. None of the umbilical cord plasma samples measured positive for IDet.

Mean maternal endogenous insulin levels were 101.6 pmol/L (range 10.8–184.8 pmol/L) and umbilical concentrations were 178 pmol/L (range 8–789).

Delivery occurred at a mean gestational age of 37.7 weeks (range 36.1–39.4) and mean birth weight was 3,490 grams (range 1,960–4,310). Apgar scores ranged between 4 and 9 at 1 min and 8 and 9 at 5 min. None of the 16 infants experienced neonatal hypoglycemia.

A recent randomized study in pregnant women with type 1 diabetes demonstrated that IDet was not inferior to NPH insulin in either effectiveness or safety (3). In the same study, treatment with IDet resulted in similar rates of early fetal loss and perinatal deaths and a more favorable gestational age at birth compared with NPH insulin (4).

The current study used a novel and highly specific method to detect IDet and distinguish it from endogenous insulin. Our study shows that while maternal IDet levels were in the expected range previously described in adults (5), the hormone was undetectable in the fetal circulation, indicating that IDet does not cross the human placenta.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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