

Use of Glargine Insulin in Pregnant Women with Type 1 Diabetes

The Case

A 35 yo woman presented to Endocrine Clinic for management of her DM I. She had had 2 children and was managed on NPH and Novolog. Her control was suboptimal with lots of high and low blood sugars. We discussed switching her to glargine for basal control and surmised that she was on NPH vs. glargine because of her previous pregnancies (glargine is not yet widely used in diabetic women during pregnancy).

The Search

PubMed: "lantus in pregnancy" (limited to human studies with free full text available in English on human studies)

The Paper

Imbergamo MP, Amato MC, Sciortino G, et al. Use of glargine in pregnant women with type 1 diabetes mellitus: a case control study. *Clin Ther.* 2008 June;30(8):1476-84.

The Study

Case-control study done at the Diabetes and Pregnancy Outpatient Clinic at the University of Palermo in Palermo, Italy 2004-2007

Clinical question:

Population: In pregnant women with type 1 diabetes mellitus

Intervention: does use of glargine insulin for basal blood glucose control,

Comparison: as opposed to use of NPH,

Outcome: lead to increased complications during pregnancy either for the mother (eg, preeclampsia, progression of diabetes, hypoglycemia, ketosis) or for the fetus (eg, congenital anomalies, spontaneous abortion, neonatal hypoglycemia, decreased weight/length/head circumference, etc)?

Relevance:

Studies have shown an increased prevalence of congenital anomalies and spontaneous abortion in diabetic women who have poor glycemic. Glargine is associated with effective glycemic control and reduced frequency of hypoglycemic episodes, but its clinical utility during pregnancy has not been established. Concerns linger regarding its mitogenic action due to modification of the C-terminal site of the insulin B chain, which enhances insulin's affinity for the insulin growth factor 1 (IGF-1) receptor.

Methods:

Pregnant women, both type 1 diabetics and non-diabetic women, were followed throughout the course of their pregnancy at an outpatient clinic. Patients who transferred care to other hospitals, who had 1st trimester spontaneous miscarriages, or who had been on glargine prior to pregnancy but chose to switch to NPH during the pregnancy were excluded. In all there were 43 non-diabetic women and 30 diabetic women in this study. 15 diabetic women took glargine with aspart or lispro QID AC/HS, the other 15 diabetic women took NPH with aspart or lispro QID AC/HS.

All women (diabetic and non-diabetic) were evaluated for age, mode of delivery, weight gain during pregnancy, whether they had htn before pregnancy, whether they became hypertensive during pregnancy, and whether they had 3rd trimester preeclampsia. Diabetic women were also evaluated for duration of diabetes, complications of diabetes (retinopathy, nephropathy, micro- or macroalbuminuria) and their progression during pregnancy, rate of mild or severe hypoglycemia, rate of ketosis, A1c, fasting and postprandial blood glucose, and total insulin requirement.

Neonatal weight and length, head circumference, and abdominal circumference and femoral length in the 2nd and 3rd trimesters were measured in all patients. Congenital anomalies, neonatal

hypoglycemia, neonatal respiratory adaptation, respiratory distress syndrome, neonatal hypocalcemia, and neonatal jaundice were also evaluated. Children of diabetic mothers were also evaluated for interventricular septal thickness by echocardiography at 20 and 32 weeks.

Validity:

This was a retrospective case-control study. As such, there was no randomization or concealment. Its largest limitation is probably its small patient cohort (only 15 diabetic patients on glargine, 73 patients in the study total). All groups appeared to start with similar prognostic factors, though they were not evaluated for some factors which affect pregnancy (eg, alcohol use, other medical conditions, etc). Patients who had 1st trimester spontaneous abortions were also excluded from the study leading to curiosity about the possible affect of glargine on this risk. There is no obvious bias in this study.

Results:

In general:

- No significant difference between the glargine vs. NPH women with regard to age, duration of disease, week and mode of delivery, weight gain during pregnancy, or complication rates
- No cases of perinatal deaths or congenital anomalies
- Significantly shorter duration of pregnancy in diabetic vs. non-diabetic women
- Significantly higher rates of C-sections in the diabetic group vs. the non-diabetic group

Among the women:

- No significant difference in the glargine vs. NPH groups with regard to rates of maternal complications of diabetes
- Glargine group used significantly less lispro or aspart insulin compared to the NPH group, but no difference between the glargine and NPH groups with regard to total insulin requirement during pregnancy
- Glargine group had significantly lower A1cs at the end of the 1st trimester and lower fasting and postprandial blood glucose in the 1st and 2nd trimesters

Among the neonates:

- Compared to the non-diabetic patients, neonates of diabetic women significantly more likely to be large for gestational age (LGA), but no significant difference between glargine and NPH groups
- No significant difference in 2nd and 3rd trimester head circumference and abdominal circumference between any of the groups
- Unexpectedly, a significantly higher frequency of neonates in the <50th percentile for femoral length in the 2nd trimester in the glargine vs. the non-diabetic group (though not between the glargine and NPH group or the NPH group and the non-diabetic group)
- No significant difference in interventricular septal thickness between the glargine and NPH groups
- No significant difference between any of the groups with regard to Apgar scores or fetal/neonatal complications.

Potential application to our patient:

Our patient used NPH during both of her pregnancies. She was not interested in having additional children. The findings in this study would be applicable in a type 1 diabetic woman interested in pregnancy who is of average child-bearing age (avg. age in the glargine and NPH groups was 27 and 30 respectively) and weight (avg. pregravidic weight in the glargine and NPH groups was 60 and 61 respectively).

Conclusion:

Preliminary studies of pregnant type 1 diabetic women who use glargine have not shown it to increase the likelihood maternal or fetal complications. Compared to NPH, it may even lead to tighter blood glucose control in the first and 1st and 2nd trimesters as seen in this study. However, larger prospective studies are needed to confirm these findings. I will likely continue to recommend NPH for diabetic women for the time being.