Decreased Insulin Requirements In Type 1 Diabetic Pregnant Females Decrease In The Post-Partum Period

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A. Rationale

Diabetes carries a major burden of disease. According to the CDC the prevalence of diabetes, both diagnosed and undiagnosed, was estimated to be 18.2 million or 6.3% of U.S. population in 2002. Diabetes carries with it an increased risk of heart disease and stroke and is known to be the leading cause of new blindness between age 20-74 and the leading cause of end stage renal disease in the U.S. The underlying mechanism of both type 1 and type 2 diabetes involves an element of pancreatic beta-cell failure. Based on findings from the Diabetes Complications and Control Trial a subset of type 1 diabetics with residual Beta-cell function as measured by C-peptide were found to have decreased complications from diabetes and its treatment including reduced retinopathy, nephropathy, hypoglycemia. Therefore recovery of endogenous beta-cell function may help reduce complications of diabetes and mechanisms to promote beta-cell recovery should be investigated. There is an observation the insulin requirements in Type 1 diabetic pregnant females decrease in the post-partum period. A case report by Singer et al identifies a patient whose insulin requirements decreased in the post-partum period concomitantly with an increase of C-peptide (a measurement of endogenous insulin production and hence pancreatic beta-cell function). This study will attempt to answer the question of whether the observed decreased insulin requirements in this population are due to a recovery of beta-cell function as measured by C-peptide. If this is true the mechanism behind recovery of beta-cell function in this population can be investigated.

B. Study Design

This will be a cohort observational study of 74 subjects with each subject serving as her control. The sample size was determined for 80% power using 0.3 as the effect size of change in C-peptide at diagnosis compared to post-partum and 0.86 as the estimated standard deviation of C-peptide measurements in a paired t-test analysis. The effect size was estimated using observational values of the natural history of C-peptide at diagnosis of type 1 diabetes. In those diagnosed pre-puberty C-peptide was <0.6 ng/ml. In those diagnosed a puberty or adulthood C-peptide was 0.9-2.7 ng/ml. The desired increase of C-peptide in the post-partum period compared to diagnosis is 1.5-fold. Given this and the observed values, the smallest absolute effect size was calculated as [(0.6* 1.5)- 0.6]= 0.3. The standard deviation was estimated using one-fourth of the largest range of expected values which was determined to be [(4.05-0.60/4]=0.86. The sample size was adjusted to include a 10% attrition rate to account for possible planned or spontaneous terminations of pregnancy.

C. Study Procedure

In this study, phlebotomy will be required for measurement of C-peptide at post-partum day one, 6 weeks post-partum, and 12 weeks post-partum. The phlebotomy will require minutes and may cause discomfort to the patient during the procedure. This will be in addition to routine pre-natal care as C-peptide measurements are not routinely done in the pre-natal or post-partum period. The subjects will also undergo measurement of HgbA1C as determined by routine pre-natal care. The study will take 5 years so that an adequate number of patients can be recruited and followed assuming we can recruit 30 subjects per year. Each subject will participate in the study for approximately one year.

D. Study Drugs

There are no study drugs.

E. Medical Devices

There are no medical devices.

F. Study Questionnaires

Each participant will be asked to complete a food diary upon enrollment and every week throughout the course of the study to determine diet composition. These questionnaires will be reviewed monthly to ensure maintenance of diet composition. The subject will also be asked to track daily insulin requirements during the course of the study.

G. Study subjects

Type one diabetic pregnant women of all ethnicities presenting at less than or equal to 12 weeks gestation. Women who have been diagnosed with type one diabetes within the past year prior to enrollment in the study and women who do not have C-peptide value at diagnosis will be excluded.

H. Recruitment of Subjects

Recruitment will occur in conjunction with endocrinologists and obstetricians for women meeting the inclusion and exclusion criteria.

I. Confidentiality

Data will be collected and analyzed in a confidential manner with each participant receiving a study code.

J. Conflict of Interest

There is no conflict of interest as there is no study drug/device and no association with manufacturers of C-peptide assay.

K. Location of Study

Columbia University Medical Center, Naomi Berri Diabetes Center, Department of Medicine, Division of Endocrinology, Department of Obstetrics/Gynecology.

L. Potential Risks

Risk from phlebotomy being discomfort, bleeding, bruising.

M. Potential Benefits

Patients may benefit from improved pre-natal follow-up with resultant improved glycemic control.

N. Alternative Therapies

There are no alternative therapies.

O. Compensation to Subjects

Coverage of transportation costs.

P. Costs to Subjects

There are no costs to subjects.

Q. Minors as Research Subjects

N/A

R. Radiation or Radioactive Substances

N/A

S. References

Palmer et al. C-peptide Is the Appropriate Outcome Measure for Type 1 Diabetes Clinical Trials to Preserve Beta-Cell Function. Diabetes 2004, Vol 53: 250-264.

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Effect of Intensive Therapy on Residual Beta-Cell function in Patients with Type 1 Diabetes in the Diabetes Control and Complications Trial. Annals of Internal Medicine 1998, Vol 128 (7):517-523.