Outcomes of Treatment of Phenylketonuria During Pregnancy


Study Overview

Objective. To determine whether dietary treatment during pregnancy of women with phenylketonuria (PKU) has an impact on the developmental outcomes of their offspring.

Design. Longitudinal prospective study.

Setting and participants. A total of 253 children of women with PKU (n = 149), untreated mild hyperphenylalanemia (n = 33), or no known metabolic problems (n = 71) were followed up to age 4 years. The women were seen in 78 metabolic clinics or obstetrical offices in the United States, Canada, and Germany and were enrolled in the Maternal PKU Collaborative Study, ongoing since 1984.

Intervention. Women with PKU were offered a low-phenylalanine diet prior to or during pregnancy with the aim of maintaining metabolic control (plasma phenylalanine level ≤ 10 mg/dL). Women with mild hyperphenylalanemia (plasma phenylalanine level ≤ 1 mg/dL) on a normal diet were not treated.

Main outcome measures. Children’s scores on cognitive and behavioral assessments (McCarthy Scales of Children’s Abilities, Test of Language Development, Achenbach Child Behavior Checklist, Vineland Adaptive Behavior Scales, and Home Observation for Measurement of the Environment), compared by maternal metabolic status at 0 to 10 weeks’, 10 to 20 weeks’, and after 20 weeks’ gestation. The McCarthy Scales include a General Cognitive Index (GCI) and indices for verbal, perceptual performance, quantitative, memory, and motor skills [1,2].

Main results. Scores on the McCarthy GCI decreased in a clear linear fashion as weeks to metabolic control increased (r = –0.58; P < 0.001). The percentage of children attaining scores 1 and 2 standard deviations (SDs) below the mean increased as metabolic control decreased, and scores on each of the McCarthy subscales followed a similar pattern. Children of women who had metabolic control prior to pregnancy had a mean score of 99 (SD, 13).

Forty-seven percent of children whose mothers did not have metabolic control by 20 weeks’ gestation had a GCI score 2 SDs below the norm. Overall, 30% of children born to mothers with PKU had social and behavioral problems.

Conclusion

Delayed development in children of women with PKU is associated with lack of maternal metabolic control prior to or early in pregnancy; treatment any time during pregnancy may reduce the severity of the delayed development.

Commentary

Untreated maternal PKU increases the risk for cognitive impairment and developmental delay in children. Although maternal dietary therapy reduced such risks at various stages of pregnancy, it did not eliminate them. This study provides further evidence that children are best protected from elevated maternal phenylalanine levels when the mother attains metabolic control prior to pregnancy.

Applications for Clinical Practice

Further research should explore ways to reduce the developmental delays in children of women with PKU, and clinicians should continue to emphasize the importance of attaining metabolic control prior to pregnancy.

References