Inositol and folate resistant neural tube defects

P Cavalli, A J Copp

Highly folate resistant NTDs. NTDs in mice homozygous for such “folic acid resistant” NTDs. NTD recurrences were noted among 593 women (1%) who elected to undergo combined inositol and folic acid treatment (500 mg inositol and 2.5 mg folic acid daily), starting three months before conception. Amniotic fluid karyotype was normal in both NTD pregnancies. There were no known illneses in either family, nor was there a history of medication or drug usage, x ray exposure, infectious disease, alcohol intake, or smoking during the first two pregnancies. The mother had a normal blood glucose concentration two hours after a standard glucose load both before and during each pregnancy. Following the second affected pregnancy, both parents were tested for the C677T mutation in methylenetetrahydrofolate reductase (MTHFR), but only wild type alleles were found.

During extensive genetic counselling, the parents were informed that their previous affected pregnancies could be folate resistant and that a high recurrence risk of NTD (approximately 1 in 9 chance) was to be expected in a third pregnancy. The preventive effect of inositol in mouse studies, and the absence of significant side effects of inositol therapy (up to 12 g/day) in psychiatric patients, were discussed, as well as a possible adverse effect of inositol, in stimulating uterine contractions. The parents took the personal decision to undergo combined inositol and folic acid treatment (500 mg inositol and 2.5 mg folic acid daily), starting three months before conception and continuing until 60 days of pregnancy. Tablets were prepared by an external chemist, using FU inositol (Farmacopea Ufficiale, 98.60% purity).

During the third pregnancy, maternal serum and amniotic fluid alpha-fetoprotein measurements were within the normal range at the 15th week of pregnancy, while ultrasound examinations at 15, 20, and 22 weeks showed normal fetal and placental growth parameters. The pregnancy progressed uneventfully, with no particular episodes of uterine contractions, and a healthy baby boy weighing 3900 g was delivered spontaneously at 40+3 weeks. Apgar scores were 8 at one minute and 10 at five minutes. Length and head circumference were at the 50th centile. Clinical evaluation after birth was normal, routine blood and urine tests were in the normal range, and neurological assessment, performed two weeks after birth, showed normal psychomotor development.

In conclusion, inositol has been taken during pregnancy without toxicity for mother or fetus, and with no anomalous uterine contractions. Given the strong preventive effect of inositol in mice, this normal pregnancy outcome, despite the high recurrence risk of NTD, indicates the need for further evaluation of inositol as an adjunct therapy to folic acid for preventing folate resistant NTD.

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