Effect of leucovorin (folinic acid) on the developmental quotient of children with Down’s syndrome (trisomy 21) and influence of thyroid status.

Blehaut H, Mircher C, Ravel A, Conte M, de Portzamparc V, Poret G, de Kermadec FH, Rethore MO, Sturtz FG.

Institut Jerome Lejeune, Paris, France.

BACKGROUND: Seven genes involved in folate metabolism are located on chromosome 21. Previous studies have shown that folate deficiency may contribute to mental retardation in Down’s syndrome (DS).

METHODOLOGY: We investigated the effect of oral folate supplementation (daily dose of 1.0+/-.0.3 mg/kg) on cognitive functions in DS children, aged from 3 to 30 months. They received 1 mg/kg leucovorin or placebo daily, for 12 months, in a single-centre, randomised, double-blind study. Folinic acid (leucovorin, LV) was preferred to folic acid as its bioavailability is higher. The developmental age (DA) of the patients was assessed on the Brunet-Lezine scale, from baseline to the end of treatment.

RESULTS: The intent-to-treat analysis (113 patients) did not show a positive effect of leucovorin treatment. However, it identified important factors influencing treatment effect, such as age, sex, and concomitant treatments, including thyroid treatment in particular. A per protocol analysis was carried out on patients evaluated by the same examiner at the beginning and end of the treatment period. This analysis of 87 patients (43 LV-treated vs. 44 patients on placebo) revealed a positive effect of leucovorin on developmental age (DA). DA was 53.1% the normal value with leucovorin and only 44.1% with placebo (p<0.05). This positive effect of leucovorin was particularly strong in patients receiving concomitant thyroxin treatment (59.5% vs. 41.8%, p<0.05). No adverse event related to leucovorin was observed.

CONCLUSION: These results suggest that leucovorin improves the psychomotor development of children with Down’s syndrome, at least in some subgroups of the DS population, particularly those on thyroxin treatment.

TRIAL REGISTRATION: ClinicalTrials.gov, NCT00294593.

PMID: 20084109

FREE FULL TEXT