

## Folic acid supplementation for epilepsy - A systematic review

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**Objective:** To examine whether use of folic acid in persons with epilepsy improves seizure control or reduces the adverse effects of antiepileptic drugs (AEDs) or improves the quality of life (QOL).

**Methods:** We searched the Medline on OVID from 1966 to 2003, The Cochrane epilepsy group trials register, the Cochrane Controlled Trials Register (The Cochrane Library Issue 3, 2004), and Cross references from identified studies. The selection criteria were randomized or quasirandomized studies investigating the effects of folic acid given alone or as add-on to AEDs among persons of all ages and both genders with any type of epilepsy. Both reviewers assessed the trials for inclusion and extracted the data. The outcomes assessed included 50% or more reduction in the seizure frequency, QOL by validated scales, side effects of AEDs such as gingival hyperplasia, neuropsychological effects, IQ scores, general well being, hemogram, neuropathy and serum levels of AEDs. Primary analyses were by intention to treat.

**Results:** Twelve studies with 359 subjects analysed met the inclusion criteria. All of them had weak methods, the randomization methods were not stated and enrolled small number of participants. Among 9 studies analysing 331 subjects, only two studies (75 patients) had data on 50% reduction in seizure frequency. 9/39 responded in each group (OR 0.96; 95% CI 0.32, 2.9). Other studies also reported no significant change in seizure frequency but did not give actual values. No data available regarding QOL in any of the twelve studies.

Folic acid treatment was not associated with any significant change in any of the measures of gingival health. These poorly and variably defined measures of gingival health are *Gingival hyperplasia* as measured by projected Kodachrome slides & study casts, *Hyperplasia index* which is the degree of extent of gingival hyperplasia ranging from 0 – 4, *Pocket depth* as assessed by probing, *Plaque index* which is the thickness of plaque in the dental surfaces measured using a disclosing solution and *Gingival index* is the inflammation of gingiva as measured by colour, edema, bleeding and ulceration (Data from 5 studies, 110 subjects).

Folic acid treatment was not associated with any significant change in intelligence, behavior, mental health or personality (data from 7 studies, 302 subjects) or on hemoglobin content, hematocrit, Mean Corpuscular Volume or Mean Corpuscular Hemoglobin Concentration (two studies, 62 subjects). Folic acid administration was not associated with any consistent changes in serum phenytoin levels (seven studies, 235 subjects) or in serum phenobarbitone levels (3 studies, 137 subjects) or improvement in the mean motor conduction velocities (1 study, 12 patients with neuropathy).

**Conclusions:** In view of methodological deficiencies and limited number of individuals studied, we have found no reliable evidence to support the use of folic acid in patients with epilepsy, perhaps except in pregnancy.