

# RANDOMIZED TRIAL OF THE EFFECT OF SUPPLEMENTATION ON THE COGNITIVE FUNCTION OF OLDER PEOPLE WITH SUBNORMAL COBALAMIN LEVELS

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## SUMMARY

**Background.** Low serum cobalamin levels are often found in apparently normal older subjects. A major worry of leaving cobalamin deficiency untreated is that it may lead to subtle deterioration in cognitive function.

**Objectives.** To investigate the effect of supplementation on the cognitive function of older people with cobalamin deficiency by a randomized trial.

**Methods.** Fifty Chinese subjects more than 60 years old with serum cobalamin level <120 pmol/l were randomized into supplement and control groups. Fasting serum methylmalonic acid levels (MMA) were measured. A battery of neuropsychological tests was administered. The supplement group received intramuscular cyanocobalamin injections, while the control group received no intervention. They were followed up at around 4 months.

**Results.** 78% of the subjects had raised MMA, indicating metabolic cobalamin deficiency. Supplemented subjects improved in performance IQ, but the amount of improvement was not significantly more than that of control subjects. Moreover, the supplement group fared worse than the control group at follow-up in some motor function scores. Three out of seven demented subjects had improvement in Mini-Mental State Examination scores, but there was no consistent improvement in other neuropsychological scores.

**Conclusions.** This study suggested that cobalamin deficiency did not invariably cause cognitive impairment in older people. There remain the possibilities that cobalamin deficiency causes cognitive impairment or exacerbates coexisting dementia in some older people. © 1998 John Wiley & Sons, Ltd.

KEY WORDS—cobalamin; vitamin B12; supplementation; cognitive; elderly

Many studies have shown a high prevalence of subnormal serum cobalamin levels in apparently normal older people (Waters *et al.*, 1971; Garry *et al.*, 1984; Pennypacker *et al.*, 1990). The majority of older people with low serum cobalamin levels, however, have no clinical evidence of cobalamin deficiency (Matchar *et al.*, 1994), even though more than half of them have evidence of metabolic deficiency, ie elevated methylmalonic acid level (MMA) (Lindenbaum *et al.*, 1994; Pennypacker

*et al.*, 1990). On the other hand, it has been suggested that subtle cobalamin deficiency might have mild neurological complications (Carmel, 1996). There is, therefore, a worry that leaving cobalamin deficiency untreated in asymptomatic older people may lead to a subtle deterioration in cognitive function which may become irreversible (Martin *et al.*, 1992).

There has been much debate about the association between cobalamin deficiency and dementia. Many studies have shown an association between cobalamin deficiency and Alzheimer's disease (McCaddon and Kelly, 1994). However, the benefit of cobalamin supplementation in deficient people with dementia was based on case studies and not

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