

## Investigation of biomarker responses to depletion/repletion with vitamin B<sub>12</sub>

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Despite dietary intakes well above current recommendations, low biomarker status of vitamin B<sub>12</sub> is a common problem in older adults, largely as a result of malabsorption of food-bound vitamin B<sub>12</sub>. This arises mainly from atrophic gastritis which leads to reduced gastric acid production (hypochlorhydria). Hydrochloric acid is essential for the absorption of food-bound vitamin B<sub>12</sub>, and thus vitamin B<sub>12</sub> absorption is reduced in states of hypochlorhydria, although in theory free vitamin B<sub>12</sub> (from supplements or fortified) should still be absorbed. Gastric acid suppressant medications, such as proton pump inhibitors (PPI) drugs induce hypochlorhydria and therefore a state similar to atrophic gastritis. The aim of the present study is to investigate the effect of hypochlorhydria on absorption of food-bound vitamin B<sub>12</sub> and to determine whether low-dose supplemental vitamin B<sub>12</sub> would overcome any vitamin B<sub>12</sub> malabsorption. Forty-one healthy males, aged 18–45, participated in a vitamin B<sub>12</sub> depletion/repletion trial. During the depletion phase (week 0–6) all subjects were administered with a PPI (omeprazole, 20 mg/d); after which they were randomised (by vitamin B<sub>12</sub> status as measured by serum holotranscobalamin; holoTC; the metabolically active fraction of total circulating vitamin B<sub>12</sub>) into one of the two treatment groups to receive; omeprazole (20 mg/d) plus supplemental vitamin B<sub>12</sub> (10 µg/d) or omeprazole (20 mg/d) plus placebo for the repletion phase of the study (week 7–12).

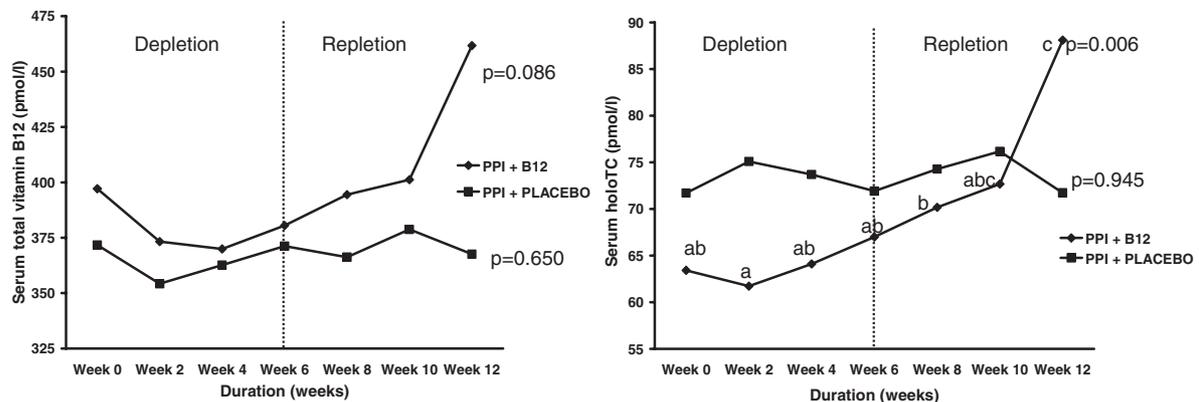


Fig. 1. Serum total B<sub>12</sub> and holoTC responses to vitamin B<sub>12</sub> depletion/repletion were compared by repeated measures ANOVA on log transformed data.

Contrary to expectations, no significant change in vitamin B<sub>12</sub> status (as assessed by either total vitamin B<sub>12</sub> or holoTC) was observed during the depletion phase of the study. During the repletion phase of the study, an increase in vitamin B<sub>12</sub> status was observed in the treatment group, but this was significant ( $P = 0.006$ ) only using the biomarker holoTC, with the response for total vitamin B<sub>12</sub> failing to reach significance. In conclusion, these results supports the emerging view that holoTC (compared with the traditional biomarker of status, serum total vitamin B<sub>12</sub>) is a more sensitive biomarker in detecting small changes in vitamin B<sub>12</sub> intake. Although the acute administration of PPI drugs did not significantly suppress vitamin B<sub>12</sub>, repletion with 10 µg/d of supplemental vitamin B<sub>12</sub> was sufficient to significantly increase biomarker status within just 4 weeks. The consequence of long-term PPI therapy on vitamin B<sub>12</sub> status is still to be determined.