Increase in vitamin B-12 during highly active antiretroviral therapy

Dear Sir:

With great interest, we read the article by Remacha et al (1) in which they discussed a role for homocysteine as a marker for vitamin B-12 status in HIV-infected patients undergoing highly active antiretroviral therapy (HAART). Compared with patients not receiving such therapy, patients receiving HAART not only had higher CD4+ and CD8+ cell counts and leukocyte counts, they also had higher hemoglobin and vitamin B-12 concentrations and mean corpuscular volumes but lower homocysteine concentrations. With regard to cell counts and vitamin B-12, we obtained similar results in patients with HIV infection (2). In addition, antiretroviral therapy decreased concentrations of the immune system activation markers neopterin and soluble 75-kDa tumor necrosis factor receptor. Thus, treatment of patients with HAART not only improves blood cell counts and vitamin B-12 status, it also slows down immune system activation. Amelioration of hyperhomocysteinemia might be a consequence of this latter effect.

Low vitamin B-12 concentrations are often seen in HIV-infected persons, sometimes even despite vitamin supplementation. Data indicate that such patients have an increased demand for vitamins. Immune system activation leading to increased formation of reactive oxygen species could deplete antioxidants including oxidation-sensitive B vitamins (3). In particular, both vitamin B-12 and methyltetrahydrofolate, which are essential cofactors in homocysteine-methionine metabolism, are easily oxidized (3, 4). In line with this assumption, the coincidence of increased concentrations of immune system activation markers and of homocysteine has been observed in several diseases (3, 5). By decreasing virus load, HAART may down-regulate an overactivated immune system in patients, and antioxidant status may improve. Thus, vitamin B-12 might also increase, even without supplementation. In conclusion, elevated homocysteine concentrations characterize patients with decreased vitamin B-12 concentrations. However, these decreased vitamin B-12 concentrations are not necessarily due to insufficient dietary intake of B vitamins; they could also be a consequence of the oxidative stress associated with immune system activation.

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REFERENCES

Reply to D Fuchs et al

Dear Sir:

We thank Fuchs et al for their kind letter. Unfortunately, their recent work (1) was not available to us and thus could not be included in the article of ours to which they refer (2). Essentially, both works coincided in many respects, given the previous data in this field (3). The improvement in vitamin B-12 concentrations in HIV-infected patients after highly active antiretroviral therapy (HAART) was expected because of the relation of vitamin B-12 deficiency to hyperhomocysteinemia (4, 5). Moreover, there is some
evidence of antioxidant disturbances in HIV infection (6). Although the involvement of oxidative stress in neurologic disturbances due to vitamin B-12 deficiency arouses considerable interest, such involvement has yet to be shown. In this regard, other hypotheses have been proposed for the pathogenesis of cobalamin neuropathy, such as a decline in formate synthesis, disturbances in methylmalonic acid metabolism, and the action of inactive cobalamin analogues (7).

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REFERENCES

Erratum


In the third line in the left-hand column on page 207, the word milligram should be replaced with microgram. The sentence should read as follows: The slope for actual dose, as can be seen, was 0.70, which means that, for every microgram of the increment in cholecalciferol input per day, serum 25(OH)D₃ at equilibrium was higher by 0.70 nmol/L.

Erratum


On page 154, column 2, sentence 1 should read as follows: Greater maternal age and parity are associated with prolonged amenorrhea (8–10) as are various characteristics of breastfeeding, such as a high number of feedings per 24 h, nighttime feedings (11), and a long duration of breastfeeding per 24 h (10).

On page 154, column 2, sentence 3 should read as follows: The relation of lactational amenorrhea with maternal nutritional status has been subject to debate, but most recent studies report a longer duration of amenorrhea among more malnourished women (8, 14), even in affluent societies (11).