

Dear Dave

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Is there an association between the use of the combined oral contraceptive and reduced Vitamin B₁₂ deficiency

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The reduction in serum Vitamin B₁₂ in women using the combined oral contraceptive is not usually clinically significant as vitamin metabolism and stores are normal. Further investigations are warranted if there are signs and symptoms suggestive of deficiency or other factors such as diet.

An association between use of the combined oral contraceptive and reduced Vitamin B₁₂ serum concentrations has been noted since 1969¹, but the clinical significance of this is debated.

Mean serum B₁₂ concentrations may be 33–40% lower in women using the combined oral contraceptive compared to non-users^{2,3}. One study of 71 women using low dose (20 micrograms ethinyl estradiol) oral contraception vs. 170 control non-users found that 13% of combined oral contraceptive users had Vitamin B₁₂ concentrations less than 130 pmol/L compared to none in the control group; 15% had subnormal Vitamin B₁₂ concentrations (130–170 pmol/L) compared to 4% in the non-users; and 72% had normal Vitamin B₁₂ concentrations compared to 92% of the non-users.⁴ Another study found 50% of combined oral contraceptive users have serum B₁₂ concentrations less than normal (< 170 pmol/L) and 15% were clearly deficient (< 70 pmol/L).

Despite apparent low serum B₁₂ concentrations in some users of the combined oral contraceptive, clinical symptoms and macrocytosis are rare and tend only to be reported as case studies.⁵ An early study of 201 cases of megaloblastic anaemia found only one case to be associated with oral contraceptive use.⁶

It is now accepted that the reduced serum B₁₂ concentrations observed in OC users do not usually represent a true deficiency as absorption, excretion and stores of Vitamin B₁₂ are usually normal. In addition, metabolic markers for deficiency (methylmalonic acid and homocysteine) remain unchanged and clinical symptoms are rare.⁶

It is postulated that the low serum B₁₂ is due to a reduction in Vitamin B₁₂ binding proteins in serum. In particular it may be due to reduced haptocorrin, the major binding protein for Vitamin B₁₂, although the mechanism is still unknown and under investigation.⁶

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References

1. Hjelt K, Brynskov J, Hippe E, Lundstrom P, Munck O. Oral contraceptives and cobalamin (Vitamin B₁₂) metabolism. *Acta Obstet et Gynecol Scand.* 1985;64:59-63
2. Green T, Houghton L, Donovan U, Gibson R, O'Connor D. Oral contraceptives did not affect biochemical folate indexes and homocysteine concentrations in adolescent females. *J Am Diet Assoc.* 1998;98:49-55
3. Wynn V. Vitamins and oral contraceptive use. *Lancet.* 1975; 1(7906):561-4
4. Sutterlin M, Bussen S, Rieger L, Dietl J, Steck T. Serum folate and Vitamin B₁₂ levels in women using modern oral contraceptives (OC) containing 20 micrograms ethinyl estradiol. *Eur J Obstet Gynecol Reprod Biol.* 2003;107:57-61
5. Kornberg A, Segal R, Theitler J et al. Folic acid deficiency, megaloblastic anaemia and peripheral polyneuropathy due to oral contraceptives. *Isr J Med Sci.* 1989;23:142-5
6. Bor M. Do we have any good reason to suggest restricting the use of oral contraceptives in women with pre-existing Vitamin B₁₂ deficiency? *Eur J Obstet Gynecol Reprod Biol.* 2004;115:240-1