

## Comment on “Efficacy of Long-Term Oral Vitamin B<sub>12</sub> Supplementation after Total Gastrectomy: Results from a Prospective Study”

Jean-Pierre Rothen Kurt E. Hersberger Isabelle Arnet

Pharmaceutical Care Research Group, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland

### Keywords

Cobalamin · Oral supplementation · Adherence

**Comentário a “Efficacy of Long-Term Oral Vitamin B<sub>12</sub> Supplementation after Total Gastrectomy: Results from a Prospective Study”**

### Palavras Chave

Cobalamina · Suplementação oral · Aderência

Dear Editor,

We read with interest J. Moleiro and colleagues' recent article [1] published in this journal. The authors conducted a prospective study on long-term oral vitamin B<sub>12</sub> supplementation with 26 patients after total gastrectomy, which is one of the causes for the widespread cobalamin deficiency [2]. Some clear findings advocate for oral supplementation, such as its equivalence with intramuscular administration in cobalamin deficiency [3], its preference by patients compared to intramuscular injections [3, 4], and its lower costs [5].

While the authors must be acknowledged for their long observational period of 24 months, certain aspects of the methodology in this study lead to concern.

Firstly, there are some ambiguities around the cut-off value of 200 pg/mL selected by the authors [1] to define

vitamin B<sub>12</sub> deficiency. One uncertainty is the lack of a clear literature reference to support the value, as the cited reference number 10 does not mention threshold values. The second uncertainty is the missing name of the analytical method used by the authors [1]. Because substantial differences exist between the common analytical methods [6], this information is indispensable for the interpretation of the results. As an example, the expected range for 95% of healthy individuals is 187–883 pg/mL with Abbott assays and 126–505 pg/mL with Beckman-Coulter assays [6]. Thus, single values and threshold values need to be related to the analytical method in order to allow comparison.

Secondly, in the presented study [1], serum values of vitamin B<sub>12</sub> reach on average 867 pg/mL (range: 453–3,500 pg/mL) after 6 months and 1,078 pg/mL (395–3,920 pg/mL) after 24 months, which for some patients is up to 20-fold above the targeted value. Although cobalamin is considered non-toxic, the clinical reason is weak for the daily administration of 1 mg cobalamin that yields values massively exceeding the reference range for healthy people. A systematic literature search on the adequate dosage of vitamin B<sub>12</sub> supplementation after bariatric surgery suggests that daily quantities of 350 µg are sufficient [7].

Thirdly, the authors mention the term “large dose” to explain the presumed transport mechanism of cobalamin with an intrinsic factor-independent resorption [1]. Even without active resorption due to gastrectomy, a passive

resorption of approximately 1.2% cobalamin can be expected [8]. Thus, an absorption of 12 µg will result from the daily intake of 1 mg cobalamin, which exceeds the recommended dietary allowance of cobalamin of 3 µg. Consequently, we do not see the rationale for a daily administration of 1 mg cobalamin over 2 years.

Finally, even if patient's behavior directly influences blood values, non-adherence is mostly used in the context of therapies where patients are actively involved in treatment administration, such as oral treatment. Because intramuscular treatment is generally administered by a physician, it is unclear what the authors mean by "non-compliance with intramuscular supplementation" [1].

To conclude, we suggest supplementing vitamin B<sub>12</sub> orally at a daily dose of 350 µg [7] independent of the underlying reason for the deficiency. If higher dosages seem appropriate, the variation of the administration interval

might represent a practicable solution. The initiation of high doses of oral vitamin B<sub>12</sub> (1,000 µg) followed by weekly and then monthly administrations have been suggested in megaloblastic anemia [9]. Newer dosing regimens should be developed, taking the issue of patient's adherence into consideration.

The authors did not want to reply to these comments.

---

### Disclosure Statement

The authors have no conflicts of interest to declare.

---

### Funding Sources

None.

---

## References

- 1 Moleiro J, Mão de Ferro S, Ferreira S, Serrano M, Silveira M, Dias Pereira A. Efficacy of long-term oral vitamin B12 supplementation after total gastrectomy: results from a prospective study. *GE Port J Gastroenterol*. 2018 Apr;25(3):117–22.
- 2 Shipton MJ, Thachil J. Vitamin B12 deficiency - A 21st century perspective. *Clin Med (Lond)*. 2015 Apr;15(2):145–50.
- 3 Metaxas C, Mathis D, Jeger C, Hersberger KE, Arnet I, Walter P. Early biomarker response and patient preferences to oral and intramuscular vitamin B12 substitution in primary care: a randomised parallel-group trial. *Swiss Med Wkly*. 2017 Apr;147:w14421.
- 4 Nyholm E, Turpin P, Swain D, Cunningham B, Daly S, Nightingale P, et al. Oral vitamin B12 can change our practice. *Postgrad Med J*. 2003 Apr;79(930):218–20.
- 5 Kolber MR, Houle SK. Oral vitamin B12: a cost-effective alternative. *Can Fam Physician*. 2014 Feb;60(2):111–2.
- 6 İspir E, Serdar MA, Ozgurtas T, Gulbahar O, Akin KO, Yesildal F, et al. Comparison of four automated serum vitamin B12 assays. *Clin Chem Lab Med*. 2015 Jul;53(8):1205–13.
- 7 Smelt HJ, Pouwels S, Smulders JF. Different supplementation regimes to treat perioperative vitamin B12 deficiencies in bariatric surgery: a systematic review. *Obes Surg*. 2017 Jan;27(1):254–62.
- 8 Carmel R. How I treat cobalamin (vitamin B12) deficiency. *Blood*. 2008 Sep;112(6):2214–21.
- 9 Bolaman Z, Kadikoylu G, Yukselen V, Yavasoglu I, Barutca S, Senturk T. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: a single-center, prospective, randomized, open-label study. *Clin Ther*. 2003 Dec;25(12):3124–34.