

# Oral Versus Intramuscular Cobalamin Treatment in Megaloblastic Anemia: A Single-Center, Prospective, Randomized, Open-Label Study

Zahit Bolaman, MD, Gurhan Kadikoylu, MD, Vahit Yukselen, MD, Irfan Yavasoglu, MD, Sabri Barutca, MD, and Taskin Senturk, MD

Presented By: Tiara Bianco and John Wironen



## Introduction

The prevalence of Vitamin B12 deficiency is between 8 and 16% in adults between the ages of 24 and 64 years and higher in the elderly.<sup>2</sup> The serious clinical sequelae of long-term vitamin B deficiency, include neurocognitive changes,<sup>3</sup> paresthesia, numbness and gait problems.<sup>4</sup> If the deficiency continues for an extended period of time, these changes can be permanent and debilitating.<sup>5</sup> Given these serious consequences, it is essential that practitioners effectively treat patients with this deficiency.

The standard of care for vitamin B12 deficiency is to provide monthly intramuscular injections of cobalamin.<sup>6</sup> However, this method has several drawbacks, including requiring clinic appointments, travel by the patient, time commitments, and associated expenses. An alternative treatment that allowed home care could provide the dual benefits of improved cost-effectiveness and greater convenience.

In this single-center, prospective, randomized, open-labeled study, the cheapest and most effective treatment for megaloblastic anemia resulting from a cobalamin deficiency was investigated. This article compared the use of intramuscular injections to the oral administration of cyanocobalamin in 70 patients over 90 days, comparing both effectiveness and cost. From this the authors concluded that oral cobalamin treatment was equally effective at treating vitamin B12 deficiency as intramuscular injections. They also concluded that oral therapy was less expensive and better tolerated.

## Purpose

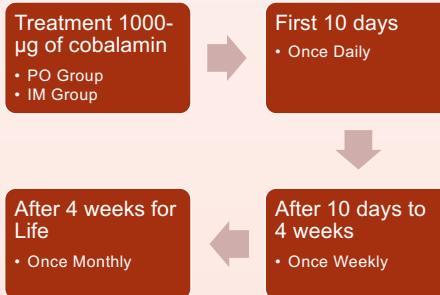
The purpose of this study was to compare the treatments of PO versus IM cobalamin for patients with megaloblastic anemia due to a cobalamin deficiency in terms of cost and effectiveness.

## Methods

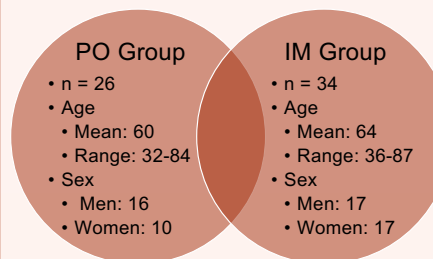
Sixty patients over the age of 16 with a serum cobalamin concentration less than 160 pg/mL, megaloblastic anemia due to a cobalamin deficiency, and a mean corpuscular volume greater than 94 fL participated in a 90 day, prospective, randomized, open-labeled study at the Division of Hematology, Department of Internal Medicine, Adnan Menderes University Research and Practice Hospital in Aydin, Turkey.

## Methods (Cont.)

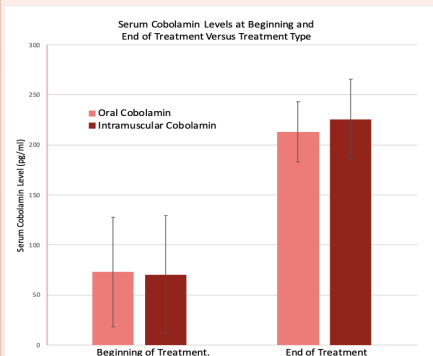
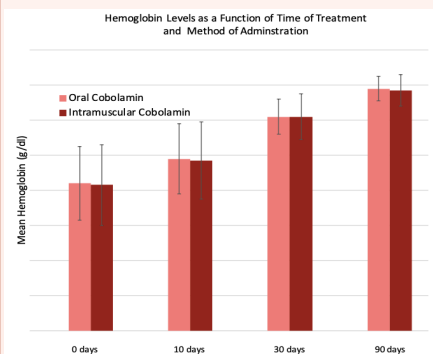
Patients were excluded from this study if they were vomiting and/or had diarrhea, alcohol use greater than 40 g/d, inability to provide informed consent, history of malignancy, folate deficiency, inability to ingest oral medication, pregnant or breastfeeding, and using a medication that would interfere with folate metabolism such as methotrexate or colchicine. The patients were assigned using block randomized study to be a part of the PO group or IM group receiving 1000-µg cobalamin once daily for the first ten days, followed by once weekly for four weeks, and then once monthly for life. To ensure the success of the treatment the patients were assessed for reticulocytosis until it was detected between days five and ten of treatment. In order to determine therapeutic effectiveness, on days 0, 10, 30, and 90 hematologic parameters were measured as well as serum vitamin B<sub>12</sub> concentrations on days 0 and 90. Laboratory tests of serum potassium levels and eosinophilia blood smears as well as patient interviews were conducted by Hematologists on days 0, 30, and 90 to determine tolerability of both treatment options. The authors compared the cost of the study drug and of the injections. Wilcoxon and Mann-Whitney *U* statistical analysis tests were used to compare the oral and parenteral treatment arms. 2-paired *t* test were used to compare pretreatment and posttreatment values. Lastly, the nominal variables were compared using the Yates chi-square test and the *p* values were considered to be statistically significant at <0.05. Funding source not stated in article.



## Patient Demographics



## Results



## Conclusions

From these results it can be concluded that PO cobalamin treatment is as effective as IM cobalamin treatment when treating patients with metaplastic anemia due to a cobalamin deficiency. It was also determined that the PO treatment was more tolerated and less expensive in comparison to the IM treatment costing \$80 oppose \$220, respectively. Within this study there were many strengths including that it was done simply to investigate the possibility of administering B12 orally, the authors, as a result, present as being unbiased. Another strength of this article was its design employed block randomization and had statistically similar control and test groups, making the outcomes, as far as statistically possible, reliable. The study also had many weaknesses including is limited sample size (60 people) with 30 or fewer in the control and treatment groups. Additionally, due to lack of available standardized dosage forms, liquid vitamin B12 was mixed with fruit juice to administer the PO dosage, which may have skewed the results of this study. Future studies should be performed and focus on using commercially available preparations of B12 that can be standardized and easily administered in a multi-center clinical trial. Also, the number of patients enrolled needs to be much larger than any of the previous studies have been able to muster.

## References

- Bolaman, Z., Kadikoylu, G., Yukselen, V., Yavasoglu, I., Barutca, S., & Senturk, T. (2003). Oral versus intramuscular cobalamin treatment in megaloblastic anemia: a single-center, prospective, randomized, open-label study. *Clinical therapeutics*, 25(12), 3124–3134. doi:10.1016/s0149-2918(03)90096-8
- Metaxas, C., Mathis, D., Jeger, C., Hersberger, K. E., Arnet, I., & Walter, P. (2017). Early biomarker response and patient preferences to oral and intramuscular vitamin B12 substitution in primary care: a randomised parallel-group trial. *Swiss medical weekly*, 147, w14421. doi:10.4414/smw.2017.14421
- Kelly G. S. (1998). Foliates: supplemental forms and therapeutic applications. *Alternative medicine review: a journal of clinical therapeutics*, 3(3), 208–220.
- Stabler S. P. (2013). Clinical practice. Vitamin B12 deficiency. *The New England journal of medicine*, 368(2), 149–160. doi:10.1056/NEJMc1113996
- Green R. (2017). Vitamin B<sub>12</sub> deficiency from the perspective of a practicing hematologist. *Blood*, 129(19), 2603–2611. doi:10.1182/blood-2016-10-569186
- Sanz-Cuesta, T., González-Escobar, P., Riesgo-Fuertes, R., Garrido-Elustondo, S., del Cura-González, I., Martín-Fernández, J., ... OB12 Group (2012). Oral versus intramuscular administration of vitamin B12 for the treatment of patients with vitamin B12 deficiency: a pragmatic, randomised, multicentre, non-inferiority clinical trial undertaken in the primary healthcare setting (Project OB12). *BMC public health*, 12, 394. doi:10.1186/1471-2458-12-394