



COMMENTARY

Vitamin B12 and Circadian Rhythm Sleep Disorders: Patient Treatments vs. Controlled Studies

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Despite earlier reports of success, controlled studies have not confirmed the effectiveness of vitamin B12 in treating circadian rhythm sleep disorders. We try to explain why these two types of studies do not produce similar results.

The objective of a recent study [1] was described as follows:

“Individuals with circadian rhythm sleep disorder suffer from recurrent patterns of disrupted sleep that can significantly affect their daily functioning. Evidence suggests that vitamin B12 supplements may have a beneficial effect on sleep patterns. However, research on the effects of vitamin B12 supplements on sleep is limited. This study will determine the effects of vitamin B12 supplements on circadian rhythms and sleep-wake regulation”.

However, the results of the study were not published.

Most of the confusion regarding the effectiveness of B12 on sleep-wake circadian rhythm originates in the discrepancy between the results of studies involving many (group) patients conducted over short periods and the results of studies involving few patients over long periods. The former is usually “controlled” study comparing B12 against placebo. Here, we try to find out what might account for this discrepancy. We look at the results of two controlled studies.

Okawa, et al. [2] describes a controlled study involving 50 patients with delayed sleep phase syndrome (DSPS) and concludes that 3 mg methylcobalamin (MB12) administered over 4 weeks is not an effective treat-

ment. Takahashi K, et al. [3] describes a controlled study involving 45 DSPS patients and 6 N24 (non-24-hour sleep-wake syndrome) patients and concludes that 6 mg MB12 leads to a significant improvement of the sleep-wake rhythm parameters at the end of the 4th week, but not at the end of the 8th week of administration. There is no inconsistency between these studies at 4 weeks. The picture becomes unclear during the last 4 weeks [3] as the improvement is not sustained, and that subjects’ circadian rhythms lose consistency. This raises a question: Is too much B12 unhelpful? Can it counteract?

B12 aside, most people, on a given day, have experienced the occurrence of waking up too early, i.e. without obtaining enough sleep. That is, the wake up time does not necessarily coincide with the readiness to get up. We do not know how B12 works, not even for those that it works. They wake up earlier, but do they feel rested every morning? Indeed Mayer G, et al. [4] reports that sleep time was reduced significantly in normal subjects taking 1 mg of MB12 daily for 14 days. Similar reports may be found in [5]. That is, B12 can wake people up earlier.

It may be the case that B12 advances sleep onset or rising time without necessarily allowing enough sleep, in particular when large doses of B12 are taken every day. After initially waking up without feeling rested, the patient (on B12) may decide to get more sleep, but could do that only after a long delay; the patient eventually gets up rested but not earlier (this may also explain the reported inconsistency over the last 4 weeks [3]). If so, the problem can be corrected

by a period of no B12 or a reduction in the dosage. In fact, the patient [5], enjoying nearly 4 decades of relief, has had this experience many times. That is, following occasions when he wakes up early but not adequately rested, he skips B12 for a few days.

Furthermore, the control group [3] was not given placebo, but (very) small dose of B12. At the end of 8 weeks, this group had taken a total of 1.68 mg of MB12. Kamgar-Parsi B, et al. [5], the patient noticed improvement after taking 0.1 mg of cyanocobalamin for 20 days, a total of 2 mg. These two levels are comparable, especially given that MB12 is more active. Therefore, at 8 weeks, while the test group was not doing as well as it did at 4 weeks, the control group was positively affected by B12 (as reported in [3]), leading to a further reduced improvement difference between the two groups.

In [6], for the two patients, blind N24 girl, and DSPS man, who were monitored for a long time and who were treated satisfactorily the dosage was 1.5 mg a day. In [7] patients with both conditions were treated successfully with 3 mg a day. Different patients require different dosages, but the first question is whether B12 can help a given patient. A high dose of 6 mg may be the right dose to answer this first question quickly. If the response is positive, the dosage should probably be reduced significantly. Eventually, the patient herself should be able to determine how much or how often to take.

Takahashi K, et al. [3] reports moderate improvement for about 25%, and slight improvement for about 14% of patients at 4 weeks therapy though it does not quantify levels of improvement. In fact, a mere sleep onset advance of 2 minutes per day (on the average) amounts to 1 hour advance in a month or 3 hours advance in 3 months, e.g. shifting DSPS patients bedtime from 2 am to 11 pm. Based on [3], nearly 40% of patients showed improvement at 4 weeks which is quite encouraging.

So far, controlled studies have concluded in a short period of one to two months, whereas studies involving only few patients last much longer allowing us to observe what matters most: The long term well-being of the patients. Perhaps, a controlled study which would last many months, while observing the response of individual patients and allowing dosage readjustment for each individual will significantly increase our understanding of the effectiveness of vitamin B12 on circadian rhythm sleep disorder.

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