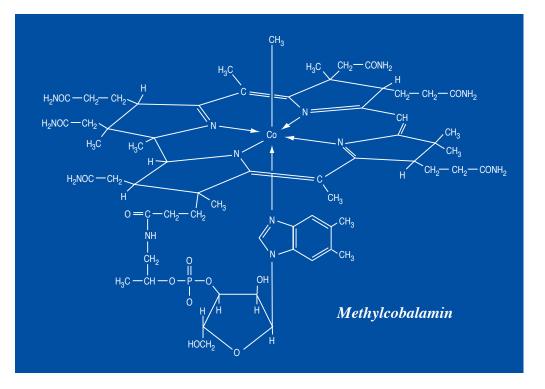
Methylcobalamin

Introduction

Methylcobalamin is one of the two coenzyme forms of vitamin B12 (the other being adenosylcobalamin). It is a cofactor in the enzyme methionine synthase, which functions to transfer methyl groups for the regeneration of methionine from homocysteine.

Pharmacokinetics

Evidence indicates methylcobalamin is utilized more efficiently than cyanocobalamin to increase levels of one of the coenzyme forms of vitamin B12. Experiments have demonstrated similar absorption of methylcobalamin following oral administration. The quantity of cobalamin detected following a small oral dose of methylcobalamin is similar to the amount following administration of cyanocobalamin; but significantly more cobalamin accumulates



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in liver tissue following administration of methylcobalamin. Human urinary excretion of methylcobalamin is about one-third that of a similar dose of cyanocobalamin, indicating substantially greater tissue retention.¹

Clinical Indications

Bell's Palsy

Evidence suggests methylcobalamin dramatically shortened the recovery time for facial nerve function in Bell's palsy.²

Cancer

Cell culture and *in vivo* experimental results indicated methylcobalamin can inhibit the proliferation of malignant cells.³ Methylcobalamin enhanced survival time and reduced tumor growth following inoculation of mice with Ehrlich ascites tumor cells.⁴ Methylcobalamin has been shown to increase survival time of leukemic mice. Under the same experimental conditions, cyanocobalamin was inactive.⁵ Although more research is required to verify findings, experimental evidence suggested methylcobalamin might enhance the efficacy of methotrex-ate.⁶

Diabetic Neuropathy

Oral administration of methylcobalamin (500 mcg three times daily for four months) resulted in subjective improvement in burning sensations, numbness, loss of sensation, and muscle cramps. An improvement in reflexes, vibration sense, lower motor neuron weakness, and sensitivity to pain was also observed.⁷

Eye Function

Experiments indicated chronic administration of methylcobalamin protected cultured retinal neurons against N-methyl-D-aspartate-receptor-mediated glutamate neurotoxicity.⁸ Deterioration of accommodation following visual work has also been shown to improve in individuals receiving methylcobalamin.⁹

Heart Rate Variability

Heart rate variability is a means of detecting the relative activity and balance of the sympathetic/parasympathetic nervous systems. Methylcobalamin produces improvements in several components of heart rate variability, suggesting a balancing effect on the nervous system.¹⁰

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HIV

Under experimental conditions, methylcobalamin inhibited HIV-1 infection of normal human blood monocytes and lymphocytes.¹¹

Homocysteinemia

Elevated levels of homocysteine can be a metabolic indication of decreased levels of the methylcobalamin form of vitamin B12. Therefore, it is not surprising that elevated homocysteine levels were reduced from a mean value of 14.7 to 10.2 nmol/ml following parenteral treatment with methylcobalamin.¹²

Male Infertility

In one study, methylcobalamin, at a dose of 6 mg per day for 16 weeks, improved sperm count by 37.5 percent.¹³ In a separate investigation, methylcobalamin, given at a dose of 1,500 micrograms per day for 4-24 weeks, resulted in sperm concentration increases in 38 percent of cases, total sperm count increases in 54 percent of cases, and sperm motility increases in 50 percent of cases.¹⁴

Sleep Disturbances

The use of methylcobalamin in the treatment of a variety of sleep-wake disorders is very promising. Although the exact mechanism of action is not yet elucidated, it is possible that methylcobalamin is needed for the synthesis of melatonin, since the biosynthetic formation of melatonin requires the donation of a methyl group. Supplementation appears to have a great deal of ability to modulate melatonin secretion, enhance light-sensitivity, normalize circadian rhythms, and normalize sleep-wake rhythm.¹⁵⁻²⁰

Side Effects and Toxicity

Methylcobalamin has excellent tolerability and no known toxicity.

Dosage

The dosage for clinical effect is 1,500-6,000 mcg per day. No significant therapeutic advantage appears to occur from dosages exceeding this maximum dose. Methylcobalamin has been administered orally, intramuscularly, and intravenously; however, positive clinical results have been reported irrespective of the method of administration. It is not clear whether any therapeutic advantage is gained from the non-oral methods of administration.

References

- Okuda K, Yashima K, Kitazaki T, Takara I. Intestinal absorption and concurrent chemical changes of methylcobalamin. J Lab Clin Med 1973;81:557-567.
- Jalaludin MA. Methylcobalamin treatment of Bell's palsy. *Methods Find Exp Clin Pharmacol* 1995;17:539-544.
- 3. Nishizawa Y, Yamamoto T, Terada N, et al. Effects of methylcobalamin on the proliferation of androgen-sensitive or estrogen-sensitive malignant cells in culture and *in vivo. Int J Vitam Nutr Res* 1997;67:164-170.
- Shimizu N, Hamazoe R, Kanayama H, et al. Experimental study of antitumor effect of methyl-B12. Oncology 1987;44:169-173.
- Tsao CS, Myashita K. Influence of cobalamin on the survival of mice bearing ascites tumor. *Pathology* 1993;61:104-108.
- Miasishcheva NV, Gerasimova GK, Il'ina NS, Sof'ina ZP. Effect of methylcobalamin on methotrexate transport in normal and tumorous tissues. *Biull Eksp Biol Med* 1985;99:736-738. [Article in Russian]
- Yaqub BA, Siddique A, Sulimani R. Effects of methylcobalamin on diabetic neuropathy. *Clin Neurol Neurosurg* 1992;94:105-111.
- 8. Kikuchi M, Kashii S, Honda Y, et al. Protective effects of methylcobalamin, a vitamin B12 analog, against glutamate-induced neurotoxicity in retinal cell culture. *Invest Ophthalmol Vis Sci* 1997;38:848-854.
- Iwasaki T, Kurimoto S. Effect of methylcobalamin in accommodative dysfunction of eye by visual load. Sangyo Ika Daigaku Zasshi 1987;9:127-132.
- Yoshioka K, Tanaka K. Effect of methylcobalamin on diabetic autonomic neuropathy as assessed by power spectral analysis of heart rate variations. *Horm Metab Res* 1995;27:43-44.
- 11. Weinberg JB, Sauls DL, Misukonis MA, Shugars DC. Inhibition of productive human immunodeficiency virus-1 infection by cobalamins. *Blood* 1995;86:1281-1287.
- Araki A, Sako Y, Ito H. Plasma homocysteine concentrations in Japanese patients with non-insulin-dependent diabetes mellitus: effect of parenteral methylcobalamin treatment. *Atherosclerosis* 1993;103:149-157.
- 13. Moriyama H, Nakamura K, Sanda N, et al. Studies on the usefulness of a long-term, high-dose treatment of methylcobalamin in patients with oligozoospermia. *Hinyokika Kiyo* 1987;33:151-156.
- Isoyama R, Kawai S, Shimizu Y, et al. Clinical experience with methylcobalamin (CH3-B12) for male infertility. *Hinyokika Kiyo* 1984;30:581-586.
- Uchiyama M, Mayer G, Okawa M, Meier-Ewert K. Effects of vitamin B12 on human circadian body temperature rhythm. *Neurosci Lett* 1995;192:1-4.
- Tomoda A, Miike T, Matsukura M. Circadian rhythm abnormalities in adrenoleukodystrophy and methyl B12 treatment. *Brain Dev* 1995;17:428-431.
- Yamada N. Treatment of recurrent hypersonnia with methylcobalamin (vitamin B12): a case report. *Psychiatry Clin Neurosci* 1995;49:305-307.
- Ohta T, Ando K, Iwata T, et al. Treatment of persistent sleep-wake schedule disorders in adolescents with methylcobalamin (vitamin B12). Sleep 1991;14:414-418.
- Mayer G, Kroger M, Meier-Ewert K. Effects of vitamin B12 on performance and circadian rhythm in normal subjects. *Neuropsychopharmacology* 1996;15:456-464.
- Hashimoto S, Kohsaka M, Morita N, et al. Vitamin B12 enhances the phase-response of circadian melatonin rhythm to a single bright light exposure in humans. *Neurosci Lett* 1996;220:129-132.

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