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Report

B12
The Vital Vitamin

Oral B12 equivalent to B12 injections

by Terri Mitchell

For decades, people have been injecting themselves with vitamin B12 because they thought oral supplements were not adequately absorbed. New research indicates that oral B12 supplements may be as good or better than injections.

Those who have low levels of vitamin B12 in the blood have long resorted to injections of this essential B vitamin, an uncomfortable delivery method at best. New evidence suggests that oral B12 works as well as injections, according to a study published in the journal *Blood* -but high doses must be taken. This verifies reports from Sweden dating from the 1970s that pernicious anemia, a disease of B12 deficiency, can be controlled with oral B12. Resolving the debate over oral-versus-injections is very timely, given that vitamin B12 is a homocysteine-lowering factor. Homocysteine has emerged as a strong and independent risk factor for heart disease and stroke, and is also connected to chronic diseases such as arthritis, Alzheimer's and diabetes.

According to the recent data, 2,000 micrograms/day of oral B12 cures the symptoms of B12 deficiency, including elevated homocysteine, neurological problems, and elevated methylmalonic acid (a marker of B12 deficiency). The oral version works as well as injections, with the added feature of maintaining high levels in the blood over time. The study showed that after a month, the blood levels of the vitamin in people receiving injections dropped and stayed at a plateau, whereas blood levels of those receiving oral B12 continued to rise.

B12 lowers homocysteine

Although oral B12 did not reduce homocysteine in every case, when it did, the results were dramatic. Some of the people in the study had homocysteine levels as high as 175 micromoles per liter (the optimal safe range for homocysteine is under 6). In the case of one patient, 2,000 micrograms of oral B12 for four months reduced their homocysteine from 113.4 micromoles per liter to 8.2. Injected B12 also significantly reduced homocysteine - the main difference being that the injected version worked faster.

Interestingly, some of the patients did not respond to supplemental vitamin B12. It was discovered that they were also

deficient in folate, and until folate was replaced, their homocysteine remained elevated. Vitamin B12 and folate work synergistically in the chemical reactions that recycle homocysteine back to methionine in the methylation cycle. It is also interesting to note that participants in the study with both B12 and folate deficiencies were depressed, had anorexia, and addiction to alcohol. It is well-established that folate or B12 deficiency causes psychiatric problems ranging from loss of memory to insanity. This is probably due to the vitamin's role in methylation - a biochemical process crucial for the maintenance of brain chemistry and nerves. B12 plays a role in the synthesis of serotonin, dopamine and norepinephrine.

Intrinsic factor is secreted by the stomach to help the body absorb B12. Older people produce less intrinsic factor, and are thus more vulnerable to B12 deficiency. In the study mentioned at the beginning of this article, high-dose oral B12 was absorbed as well as injectable. No supplemental intrinsic factor was given. Intrinsic factor is usually associated with a chronic B12 deficiency known as pernicious anemia. Patients with pernicious anemia lack intrinsic factor usually because of insufficient stomach acid. Others may have antibodies to the factor - an inappropriate autoimmune response to one's own proteins. Injected B12 has traditionally been used for pernicious anemia because it bypasses the absorption problem. However, doctors are beginning to realize that pernicious anemia patients are not the only patients they see with B12 deficiencies. Anyone with elevated homocysteine, psychiatric disorders, eating disorders, sleep disorders, or who is elderly is potentially B12-deficient. These conditions are more likely caused by diet-induced B12-deficiency than a lack of intrinsic factor. All should respond to oral B12.

Different forms of vitamin B12

Cyanocobalamin is the usual form of B12 sold in this country. Hydroxocobalamin and adenosylcobalamin are two other forms. For the past 20 years English doctor Anthony G. Freeman has been attempting to get the cyano form of B12 removed from the market and replaced with the hydroxocobalamin. He points out that the cyano form is not effective for certain eye degenerations caused by smoking and alcohol.

But another form, methylcobalamin, may be the best of all. Research shows that this active form of B12 has the unique ability to provoke the regeneration of nerves without adverse side effects. This is because B12 facilitates methylation, the process that creates and maintains nerves and brain chemicals. Research shows that a lack of methylcobalamin causes degeneration of the brain and spinal cord - a condition known as subacute combined degeneration. In this disease, nerves lose their insulation and begin to deteriorate. This process, known as demyelination, occurs in other neurological diseases such as multiple sclerosis and chronic inflammatory demyelinating polyneuropathy.

High doses of methylcobalamin have been used to treat degenerative neurological diseases in rodents and humans. People with amyotrophic lateral sclerosis (Lou Gehrig's disease) took 25 mg a day of methylcobalamin for a month. In this disease, the neurons that control muscle movements deteriorate. The double-blind, controlled study showed that methylcobalamin improved muscle response after a month of treatment. Methylcobalamin has been given to mice with the mouse version of muscular dystrophy. A remarkable reversal of degenerating nerves occurred. Methylcobalamin did not stop the disease, but it slowed it down.

It has been documented that the level of B12 decreases every year with age. Age-related deficiency is associated with hearing loss, memory impairment and psychiatric disorders, along with heart disease and stroke. Alzheimer's disease (AD) patients have less B12 in their spinal fluid than people without the disease. They also have less SAMe - the substance required to methylate cobalamin (B12) to methylcobalamin, the active form. The failure of B12 supplementation to improve AD patients in some studies may be due to their inability to activate B12 in the brain. Methylcobalamin is already methylated: it doesn't require SAMe.

Another feature of aging is the increase of free radicals. Free radicals are elevated in Parkinson's disease (PD) and AD. In PD, a substance known as MAO-B is also elevated. MAO-B creates free radicals, and the MAO-B inhibitor, selegiline, is often given to PD patients. MAO-B is linked to memory impairment. In 1992 Italian researchers reported that elevated MAO-B, dementia and B12 deficiency all go together.

B12 deficiency diseases

Diet, age and drugs are the prime culprits behind B12 deficiency. Meat is the primary source of vitamin B12. Strict vegetarians - people who eat no animal products whatsoever are at risk for B12 deficiency. (Vegetarians who eat eggs and fish will get B12 in their diet. In addition, some seaweeds contain the vitamin, and the gut may manufacture a certain amount.) However, a meat diet doesn't guarantee that a person won't be B12 deficient. Some elderly people, for example, can eat high quantities of meat but still be B12 deficient because they don't have enough hydrochloric acid in their stomach to maintain intrinsic factor. Meat-eaters taking certain drugs are also at risk for B12 deficiency. Cimetidine (Tagamet), omeprazole (Prilosec), and other drugs that inhibit gastric secretion can cause B12 deficiency. Anyone who chronically takes drugs for stomach ulcers, "heartburn" or gastroesophageal reflux may be creating B12 deficiency in themselves.

There appears to be something else causing B12 deficiency in older people that researchers don't yet understand. In a Dutch study, researchers found that about 25% of the participants had low B12. But gut problems only accounted for 28% of those cases. The cause in the remaining 72% is a mystery. Researchers do know that more people may be deficient than currently appreciated. When researchers at the Veterans Administration Hospital in Oklahoma used modified criteria for B12 deficiency (elevations in homocysteine and methylmalonic acid, plus serum B12 up to 300 pg/mL-the norm is usually 200), they uncovered twice as many people with B12 deficiency than would have been detected by serum values alone.

Elevated homocysteine is found in many chronic diseases including arthritis and diabetes. Researchers in Japan have discovered that noninsulin-dependent diabetes patients with blood vessel problems have elevated homocysteine. When treated with 1000 micrograms of vitamin B12 (methylcobalamin) daily for three weeks, homocysteine levels dropped significantly. Although the study didn't follow the patients long enough to see the effects of long-term treatment, the condition of the patients' blood vessels will likely improve as the levels of homocysteine are reduced, as homocysteine is extremely toxic to blood vessels.

B12 and sleep

Those who can't get to sleep at night may need vitamin B12. Studies show that B12 causes an earlier release of melatonin at night which resets the sleep-wake cycle. (Melatonin has been called "the sleep hormone" because of its effects on sleep). B12 acts directly on the pineal gland to provoke a faster release of melatonin. At the tail end, B12 causes melatonin to drop off faster. B12 helps you get to sleep earlier, and may help you wake up earlier if you leave a curtain open to the morning sun. B12 sensitizes you to morning light, which helps you wake up. Very serious sleep-wake disorders have been successfully treated with vitamin B12 in the methylcobalamin form, although it may not work for everyone. Unfortunately, the vitamin doesn't help people who want to cut down on their sleep time altogether.

During the 1950s, B12 was frequently given to heart patients. The vitamin fell out of vogue as drugs took over the therapeutic picture. New findings on the connection between homocysteine and vascular disease, plus the failure of drugs to have an impact on the number of heart attacks and strokes, have shifted the focus back to B12 and other homocysteine-lowering vitamins. The notion that B12 must be injected to be effective has been disproven in recent studies. Swedish experience shows that oral B12 is effective for the treatment of pernicious anemia.

B12 has many benefits, including the reduction of homocysteine, restoration of normal sleep patterns, and mood effects. B12 deficiency is a fairly common deficiency in elderly people who frequently have disrupted digestion. It can cause symptoms that look exactly like Alzheimer's disease, and it's crucial for the retention of folate in cells.

Testing for B12 deficiency

There are several tests geared towards diagnosing B12 deficiency. Homocysteine is an indirect test. A more direct method is

to measure methylmalonic acid which becomes elevated in B12 deficiency. There are other tests which measure gut secretions or antibodies to gut secretions. The Schilling test can help ferret out what is causing the deficiency, and a simple blood test can show blood levels.

Dosage

The dose of oral B12 supplements for sleep disorders is 3000 mcg a day, while 2000 mcg a day has proven useful in lowering homocysteine and correcting B12 deficiency. In published studies, it took four weeks for the sleep effect, and four months for the homocysteine-lowering effect-so be patient. People with degenerative diseases, including Alzheimer's, should take very high doses in the range of 3-4000 mg, supplemented with SAMe.

There is also the option of taking methylcobalamin, which is the neurologically active form of B12. The potential age-reversing benefits are well-worth the modest price. Methylcobalamin is a form of B12 that is sold as a drug in Japan. It is the methylcobalamin form of B12 that has been used in most European and Japanese studies showing efficacy against neurological disease. The liver converts about 1% of ingested cyanocobalamin into methylcobalamin, but it is far more efficient to dissolve a good tasting methylcobalamin lozenge in the mouth for immediately assimilation into the brain.

References

- Araki A, et al. 1993. Plasma homocysteine concentrations in Japanese patients with non-insulin-dependent diabetes mellitus: effect of parenteral methylcobalamin treatment. Atherosclerosis 103(2):149-57.
- Berlin R, et al. 1978. Vitamin B12 body stores during oral and parenteral treatment of pernicious anaemia. Acta Med Scand 204(1-2):81-4.
- Bernard MA, et al. 1998. The effect of vitamin B12 deficiency on older veterans and its relationship to health [see comments]. J Am Geriatr Soc 46(10):1199-206.
- Freeman AG. 1992. Cyanocobalamin-a case for withdrawal: discussion paper. J R Soc Med 85:686-7.
- Honma K, et al. 1992. Effects of vitamin B12 on plasma melatonin rhythm in humans: increased light sensitivity phase-advances the circadian clock? Experientia 48:716-20.
- Houston DK, et al. Age-related hearing loss, vitamin B-12, and folate in elderly women. Am J Clin Nutr 69:564-71.
- Kaji R, et al. 1998. Effect of ultra high-dose methylcobalamin on compound muscle action potentials in amyotrophic lateral sclerosis: a double-blind controlled study. Muscle Nerve 21:1775-8.
- Kamgar-Parsi B, et al. 1983. Successful treatment of human non-24-hour sleep-wake syndrome. Sleep 6:257-64.
- Kuzminski AM, et al. 1998. Effective treatment of cobalamin deficiency with oral cobalamin. Blood 92:1191-98.
- Mayer G, et al. 1996. Effects of vitamin B12 on performance and circadian rhythm in normal subjects. Neuropsychopharm 15:456-464.
- Parnetti L, et al. 1992. Platelet MAO-B activity and vitamin B12 in old age dementias. Mol Chem Neuropathol 16(1-2):23-32.
- Salom IL, et al. Effect of cimetidine on the absorption of vitamin B12. 1982. Scand J Gastroenterol 17(1):129-31.
- Shane B, et al. 1985. Vitamin B12--folate interrelationships. Ann Rev Nutr 5:115-41.
- van Asselt DZ, et al. 1998. Role of cobalamin intake and atrophic gastritis in mild cobalamin deficiency in older Dutch subjects [see comments]. Am J Clin Nutr 68(2):328-34.
- Watanabe T, et al. 1994. Ultra-high dose methylcobalamin promotes nerve regeneration in experimental acrylamide neuropathy. J Neurol Sci 122:140-3
- Yamazaki K, et al. 1994. Methylcobalamin (methyl-B12) promotes regeneration of motor nerve terminals degenerating in anterior gracile muscle of gracile axonal dystrophy (GAD) mutant mouse. Neurosci Lett 170:195-7.

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