Studies FOR - INFIRT GOAL 300 mg CAP.

CoQ10

Infertility is commonly attributed to the woman however facts show that for **one third of infertile couples the cause lies with the male partner.**

Not being able to have your own child naturally can be very frustrating and even devastating for many couples. There are **many causes** of infertility – genetic implications, physical or psychological problems, illnesses, nutritional deficiencies, medications, lifestyle factors, reproductive system function failures and hormonal imbalances.

Some studies on both male and female infertility have focused on the nutrient, Coenzyme Q10 (CoQ10), a substance that is found in the energy-producing centers of the body known as the mitochondria, and its possible link in improving fertility problems.

There are two main possibilities on the relationship of CoQ10 to fertility. One factor may be the **major dependence of female eggs on CoQ10 for energy**. The process of egg production, ovulation and embryo development in women consume a huge amount of energy and require high levels of CoQ10, which is involved in ATP production – also the major source of energy for muscle contraction and protein production.

As we age, our bodies produce less CoQ10 thereby affecting our fertility. This theory is supported by positive findings in Canadian research conducted in 2009 that showed test group subjects given CoQ10 supplementation **produced more and better quality eggs, recorded higher pregnancy rates and gave birth to larger offspring** than those who did not receive CoQ10.

Male fertility is also affected by decreased mitochondrial function since protein makes up most of sperm cells and depends largely on CoQ10 for synthesis.

Research shows that major causes of male infertility include low sperm count and poor sperm quality. Having strong antioxidant properties to counter these problems is another factor that makes CoQ10 beneficial for fertility. **Antioxidants work by protecting egg and sperm cells from oxidative damage** leading to cell death. This is one area that has more research completed so far, with results showing a direct relationship between **higher levels of CoQ10 and significant increase both in seminal fluid and in sperm cells, as well as an improvement in sperm motility.**

As an antioxidant, CoQ10 works against the action of reactive oxygen species (free radicals) which is proven to be deleterious to male fertility. **Reduced levels of oxidative stress created a healthier environment for increased sperm volume and improved quality.**

Overall the research is very clear – CoQ10 boosts both male and female fertility so speak to your naturopath about a high quality supplement with the correct therapeutic dose.

References:

http://www.livestrong.com/article/370907-coenzyme-q10-and-fertility/

http://eivf.net/blog/2012/03/31/coenzyme-q10-may-help-treat-female-infertility/

http://www.ncbi.nlm.nih.gov/pubmed/21989906

http://www.ncbi.nlm.nih.gov/pubmed/16873942

Studies FOR - INFIRT GOAL 300 mg CAP.

L-Arginine

- Long-term oral administration of L-arginine on erectile response
- Treatment of erectile dysfunction with Pycnogenol® and L-arginine

The Hardness Factor by Steven Lamm, MD

Newly published study results, as detailed in *The Hardness Factor*, by Steven Lamm, MD, show a combination of L-Arginine and Pine Bark Extract to be effective for the improvement of erectile function. The book, *The Hardness Factor*, arrived in bookstores May 31, 2005.

L-Arginine is an amino acid that plays an important role in nitric oxide mechanisms in the body, and Pycnogenol®, is a natural plant extract originating from the bark of French Maritime pine trees that expands and supports healthy blood vessels. Research in *The Hardness Factor* shows that this combination helps protect, restore and sustain blood flow to the genital area, naturally enhancing erections and the body's sexual response.

As detailed in Dr. Lamm's *The Hardness Factor*, thirty-seven men with milder forms of erectile dysfunction were given L-Arginine and Pine Bark Extract supplements for six weeks. At the end of the evaluation period, 81 percent stated that treatment with the dietary supplement improved their ability to engage in sexual activity and 73 percent reported that supplementation made it easier to initiate an erection.

More than 70 percent stated that supplementation made it easier to sustain an erection. Study results were also reflected in a defined and measured improvement showing higher penile rigidity through use of a digital inflection rigidometry (DIR) designed specifically and gently to measure the hardness of an erection. Overall, no side effects were reported and all men tolerated the supplements very well.

"This study confirms previous data showing a combination of Pycnogenol and L-Arginine to be effective in restoring healthy male sexual function. As outlined in my book, study results show that a combination of L-Arginine and Pine Bark Extract is particularly effective in aging men from 30 years of age and older who are experiencing the first signs of reduced sexual performance," said Dr. Lamm, who is also Clinical Assistant Professor of Medicine, New York University Medical School. "These supplements are a scientifically supported natural alternative that can help men achieve greater erectile quality, and restore sexual function permanently during supplementation."

Clinical studies conducted in the United States and Europe homogeneously demonstrated that male sexual function was permanently restored during supplementation with the combination of L-Arginine and Pine Bark Extract. Study participants said the supplement combination helped them recapture their sexual pleasure and passion. The supplement was preferred by many study participants as a natural alternative to improve erectile quality, minus the side effects and time-limitations of prescription medications.

"While prescription medication is a treatment for advanced sexual dysfunction, L-Arginine and Pine Bark Extract are all-natural and become part of your diet like any vitamin or health supplement. These supplements are a safe and effective long-term solution for men who wish to compensate for early signs of flawed sexual performances and regain spontaneous sexual arousal," said Dr. Lamm. "During regular supplementation, healthy production of nitric oxide is permanently restored, thus allowing men to enjoy a more fulfilling sex life."

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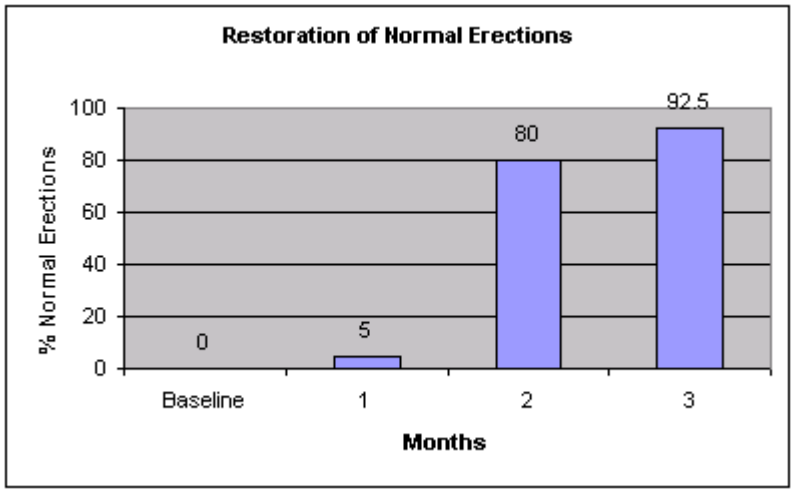
Study Results

The main characteristics of erectile response of patients who experienced restored erectile function are the time until erection developed in response to spontaneous sexual stimulation and the duration of the erection. These results were demonstrated in the 1993 study of 40 men published by Stanislavov and Nikolova of the Medical University of Sophia (Bulgaria). The men chosen for the study had an inability to achieve an adequate erection. Men with organic causes for erectile dysfunction were excluded from the study.



In the first month, the men, aged 25 to 45 years old, received 3 g/day of L-Arginine. In the 2nd month, these men received 3 g/day of L-Arginine plus 80 mg/day of Pycnogenol® Pine Bark Extract. In the third month, they continued to receive 3 g/day of L-Arginine and their dosage of Pycnogenol® was increased to 120 mg/day.

In the first month, 2 men (5%) experienced normal erections. In the second month, 32 men (80%) experienced normal erections. In the third month, 37 men (92.5%) experienced normal erections which lasted a mean time of 15 minutes.

	Baseline	1 Month	2 Months	3 Months
Responders (out of 40)	0 (0%)	2 (5%)	32 (80%)	37 (92.5%)
Time until response (Mean)	-	10 +/- 2 min	4 +/- 1 min	2 +/- 1 min
Duration (Mean time)	-	2 +/- 1 min	4 +/- 1 min	15 +/- 3 min

No side effects were noted, and no hyper-stimulation was observed.

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References

1. Stanislavov R, Nikolova V. Treatment of erectile dysfunction with pycnogenol and L-arginine. J Sex Marital Ther. 2003 May-Jun;29(3):207-13.

2. Lamm, Steven MD. *The Hardness Factor*. HarperCollins, 2005.

3. Lamm S, Schonlau F, Rohdewald P. Prelox® for Improvement of Erectile Function: A Review; Eur Bul Drug Res; 11(3)2003.

4. Moody JA, Vernet D, Laidlaw S, Rajfer J, Gonzalez-Cadavid NF. Effects of long-term oral administration of L-arginine on the rat erectile response. J Urol. 1997 Sep;158(3 Pt 1):942-7.

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Grape seed extract!

Added 15.04.2011

Many cases of infertility are due to irregularities in the male's sperm. Low sperm count, decreased motility or sperm that is abnormally shaped can make it difficult to fertilise an egg. There are various reasons for these irregularities, but given our increasingly polluted environment and lifestyle, sperm is often damaged by free radicals and oxidative stress.

Antioxidants are known to neutralise free radicals and grape seed extract has one of the highest amounts of free radical-fighting compounds.

Sperm quality improved by 38% with grape seed extract

In a scientific study grape seed extract improved the quality and function of sperm in sub-fertile men by 38% and 19% respectively. Grape seed extract is such a wonderful free radical scavenger that according to researchers it protects sperm fom oxidative damage and results in a larger probability of conceiving.

So, if you are trying to get pregnant why not try natural side effect-free supplements for infertility like grape seed extract.

References:

Roseff, S. & all. "Improvement in sperm quality and function with French maritime pine tree bark extract." The Journal of Reproductive Medicine. 2002.

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International Urology and Nephrology **34:** 369–372, 2002.

Lycopene therapy in idiopathic male infertility – a preliminary report

Narmada P. Gupta & Rajeev Kumar
Department of Urology, All India Institute of Medical Sciences, Ansari Nagar, 110029, New Delhi, India

Abstract. Excessive generation of reactive oxygen species (ROS) containing free oxygen radicals has been identified as one of the causes of male infertility. Lycopene is a component of human redox defence mechanism against free radicals. It is found in high concentrations in the testes and seminal plasma and decreased levels have been demonstrated in men suffering from infertility. We evaluated the effect of oral lycopene therapy in men with idiopathic infertility. Beginning March 2000, thirty men with idiopathic non-obstructive oligo/astheno/teratozoospermia were enrolled for the trial. All patients were administered 2000 mcg of Lycopene, twice a day for three months. Semen analysis was performed at three months and sperm concentration, motility and morphology were evaluated. All patients completed the trial without any complications. Twenty patients (66%) showed an improvement in sperm concentration, sixteen (53%) had improved motility and fourteen (46%) showed improvement in sperm morphology. In cases showing an improvement, the median change in concentration was 22 million/ml, motility 25% and morphology 10%. The improvement in concentration and motility were statistically significant. Baseline sperm concentration less than 5 million/ml was associated with no significant improvement. Higher baseline concentrations were associated with significant improvement and resulted in six pregnancies in 26 patients (23%). Oral Lycopene therapy seems to have a role in the management of idiopathic male infertility. Maximum improvement seems to occur in the sperm concentration (66% cases). Patients without severe oligospermia (sperm density >5 million/ml) may be given a trial of therapy with lycopene. However, larger randomised controlled trials are essential before definitive therapeutic guidelines can be made.

Key words: Andrology, Antioxidants, Carotenoids, Oxidative stress, Reactive oxygen species (ROS)

Introduction

Mammalian spermatozoal membranes are rich in highly unsaturated fatty acids. These are sensitive to oxygen induced damage by lipid peroxidation. A free radical is defined as a molecule containing one or more unpaired electrons. Reactive oxygen species (ROS) include super oxide anion (O_2) and hydroxyl radical (

-
OH) which contain highly reactive oxygen radicals. High levels of ROS seen in some infertile patients may be the cause of idiopathic infertility and higher ROS levels have been detected in the seminal plasma of infertile men while no ROS was detected in the control group [1, 2]. Lycopene is a naturally synthesized carotenoid found in fruits and vegetables. It is also a component of the human redox mechanism that scavenges free radicals including ROS. This study aims at determining whether oral supplementation with Lycopene improves fertility in patients with idiopathic infertility.

Materials and methods

Beginning March 2000, thirty men who presented to our clinic with idiopathic infertility with oligo/astheno/teratozoospermia were included in the study. Clearance of the Hospital Ethical Commitee was obtained prior to beginning the study. The patients' age ranged from 23–45 years (mean 26.5 years). Mean duration of infertility was 2.3 years (range 1.2–20 years). All men underwent a detailed physical examination, two semen analyses, semen culture, antisperm antibody levels and baseline hormone profile including serum FSH, LH, Prolactin and testosterone to exclude correctable cause for infertility. We defined abnormal semen parameters based on the values suggested by Sigman et al. [3]. This included sperm concentration below 50 million per ml, less than 50% motile sperms and less than 50% sperms with normal morphology. Patients with no discernible cause for their abnormal semen parameters were included in the study. The

Table 1. Semen parameters in cases with improvement (Wilcoxon Rank Sum test of significance)

Parameter	n	Baseline Median 25–75 percentile	3 Months Median 25–75 percentile	Improvement Median 25–75 percentile	*P*-value
Concentration (million/ml)	20	13.5 9.75–18.75	37.5 17.5–63	22 6.75–45.25	<0.05
Motility (% normal)	16	15 5–30	50 30–60	25 20–40	<0.05
Morphology (% normal)	14	30 20–37.5	40 30–48.75	10 10–10	NS

mean value of sperm density, motility and morphology from the two pre-operative semen values were used as the baseline for each patient. Twenty seven patients had oligospermia, 26 had impaired motility and 22 had abnormal morphology. 14 patients had all three parameters abnormal, 14 had two abnormal values while two had solitary factor abnormality.

All patients were administered 2000 mcg of Lycopene twice a day for three months. Semen analysis was performed at three months following initiation of therapy and the same parameters were evaluated. Any pregnancy during the follow up period was also documented. The values were compared with the baseline and the results are expressed as median values with intra quartile range. The Wilcoxon rank sum test, a non parametric test, was performed to verify statistical significance [4].

Results

All thirty men completed the trial with no adverse effects. Twenty patients (66.6%) showed improvement in the sperm concentration with median improvement of 22 million/ml. 53% cases showed improved sperm motility by a median value of 25% while 46% cases showed improved normal morphology by 10%. (Table 1). Twelve cases (40%) had improvement in all three parameters. Maximum sperm concentration improvement was noted in patients with baseline concentration greater than 5 million/ml (Figure 1).

The improvement in sperm concentration and motility was statistically significant. There were 6 pregnancies (20%). All pregnancies occurred in the group with baseline sperm concentration greater than 5 million/ml.

Discussion

Ten to fifteen percent of couples suffer from infertility [5] and in upto 50% cases, the male factor is involved [6]. After varicoceles, the most common diagnosis in the majority of these cases, 25% [3], is idiopathic.

One of the problems involved in the diagnosis of male infertility is the near complete overlap in the semen values of fertile and infertile men, barring those with absolute azoospermia. Men with sperm concentrations below 12.5 million/ml have upto a 25%pregnancy rate [7] whereas those with counts between 12.5 and 25 million have upto a 44% spontaneous pregnancy rate. These would otherwise be considered as abnormal semen parameters.

Idiopathic infertility continues to be a vexing problem for andrologists and no significant success has been noted with any form of therapy. In view of the fact that men with subnormal semen analysis can also be fertile while, on the other hand, men with normal semen parameters continue to be infertile [8], there is a possible etiological role for factors other than the routinely investigated semen parameters. Defective sperm function has been postulated to be one such factor [9] with free radical induced oxidative damage being one of the underlying causes.

Oxidative stress with excessive generation of ROS may play a role in the etiology of male infertility [1, 2]. A prospective study demonstrated that men with higher ROS generation had seven times lower chances of effecting a pregnancy than men with low ROS [10]. The total antioxidant capacity of the seminal plasma in infertile men is lower than that in fertile men [11]. In oligospermic men, the spermatozoa produce higher levels of ROS compared to fertile men [12]. High levels of ROS are found in upto 40% oligospermic men who show poor oocyte penetra-

Figure 1. Improvement with relation to baseline concentration.

tion [13]. Armstrong et al showed spermatozoal ATP levels decrease after treatment with ROS in an experimental model and this was associated with poor forward motility [14]. ROS is hypothesised to cause its effects on sperm function through peroxidation of polyunsaturated fatty acids in the sperm plasma membrane [12, 15]. Based on the above evidence, it is logical to assume a potential role of antioxidant

therapy in the management of ROS induced infertility. In-vitro experiments with vitamin E – one of the major membrane protectants against ROS – have shown significant protection of spermatozoa from peroxidative damage and loss of motility. Higher concentrations have also shown improvements in sperm function [12]. Oral vitamin E supplementation has proven to be efficacious in a double blind, placebo controlled randomised trial [16]. Another anti-oxidant, ascorbic acid, has also been found to have a positive correlation with normal sperm morphology [17].

Lycopene is one of 650 different carotenoids naturally found in fruits and vegetables. It has been found to have the highest physical quenching rate constant with singlet oxygen and its plasma level is higher than beta carotene [18]. Klebanov et al compared the antioxidant properties of Lycopene in three different model oxidative systems and confirmed its role as an important anti radical antioxidant in the protection of lipid peroxidation [19]. Lycopene deficiency may also be associated with immunoinfertility. Palan et al have demonstrated a significantly lower level of Lycopene in the seminal plasma of immunoinfertile men as compared to fertile men and they postulate a role for dietary antioxidants in the management of infertility [20].

This study was conducted with the hypothesis that oral supplementation of antioxidants would improve the oxidative stress status in patients with idiopathic infertility. Since lycopene has been shown to be an important anti-oxidant, and in the absence of any existing clinical trials using oral lycopene therapy, we performed this study to test the above hypothesis. The results suggest a significant improvement in both the sperm concentration and motility – the easily evaluable laboratory parameters. Improvement in sperm count could be the result of reduction of oxidative stress within the testis since Lycopene is known to exist within the testis and it associated with oligospermia [12]. Even among oligospermic men, it is associated with poor sperm function as demonstrated by poor oocyte penetration [13]. Since this parameter is not usually evaluated in semen analysis, it could be one of the causes for infertility in such men – the oligospermia may otherwise not be consequential. This is particularly true in cases without severe oligospermia since oxidative stress may not be the causative factor in cases where the sperm density decreases to below five million per ml. Poor motility has been demonstrated in earlier literature [14] and may be related

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to ROS induced damage to the flagellar membranes through lipid peroxidation.

Conclusions

Oxidative stress due to deficiency of antioxidants in the seminal plasma may be an important cause for idiopathic infertility. Oral supplementation with antioxidant therapy has shown improvement in semen parameters of such men. Lycopene is one of the most

abundant carotenoids in nature and it also forms an important part of the human free radical scavenging system. This study demonstrates a possible role of oral Lycopene therapy in the improvement of semen parameters of these men. A randomised, controlled clinical trial is essential to establish the indications for Lycopene therapy in idiopathic male infertility.

References

Aitken RJ, Clarkson JS. Cellular basis of defective sperm function and its association with the genesis of reactive oxygen species by human spermatozoa. J Reprod Fertil 1987; 81: 459–469.

Iwasaki A, Gagnon C. Formation of reactive oxygen species in spermatozoan of infertile patients. Fertil Steril 1992; 57: 409–416.

Sigman M, Howards SS. Male infertility. In: Walsh PC, Retik AB, Vaughan Jr ED, Wein AJ, eds. Campbell's Urology (7th edn.). Philadelphia: WB Saunders Company, 1998: 1287–1320.

Marmar JL, Kim Y. Subinguinal microsurgical variciocelectomy: a technical critique and statistical analysis of semen and pregnancy data.

Greenhall E, Vessey M. The prevalence of subfertility: a review of the current confusion and a report of two new studies. Fertil Steril 1990; 54: 978–983.

Mosher WD, Pratt WF. Fecundity and infertility in the United States: incidence and trends. Fertil Steril 1991; 56: 192–193.

Smith KD, Rodriguez-Rigau LJ, Steinberger E. Relation between indices of semen analysis and pregnancy rate in infertile couples. Fertil Steril 1977; 28: 1314–1319.

WHO. Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction (3rd edn.). Cambridge: Cambridge University Press, 1992.

Hull M, Glazener C, Kelly N et al. Population study of causes, treatment and outcome of infertility. Br Med J 1985; 291: 1693–1697.

Aitken RJ, Irvine DS, Wu FC. Prospective analysis of sperm oocyte fusion and reactive oxygen species generation as criteria for the diagnosis of infertility. Am J Obstet Gynecol 1991; 164: 542–551.

Lewis SE, Boyle PM, McKinney KA et al. Total antioxidant capacity of seminal plasma is different in fertile and infertile men. Fertil Steril 1994; 64: 411–419.

Sharma RK, Agarwal A. Role of reactive oxygen species in male infertility. Urology 1996; 48: 835–850.

Aitken RJ, Clarkson JS, Hargreave TB et al. Analysis of relationship between defective sperm function and the generation of reactive oxygen species in cases of oligozoospermia. J Androl 1989; 10: 214–220.

Armstrong JS, Rajasekaran M, Chamulitrat Wet al. Characterization of reactive oxygen species induced effects on human spermatozoa movement and energy metabolism. Free Radic Biol Med 1999; 26: 869–880.

Sikka SC. Oxidative stress and role of antioxidants in normal and abnormal sperm function. Front Biosci 1996: 78–86.

Kessopoulou E, Powers HJ, Sharma KK et al. A double blind randomised placebo crossover controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated male infertility. Fertil Steril 1995; 64: 825–831.

Thiele JL, Freisleben HJ, Fuchs J, Ochsendorf FR. Ascorbic acid and urate in human seminal plasma: determination and interrelationships with chemiluminiscence in washed semen. Hum Reprod 1993; 10: 110–115.
Di Mascio P, Kaiser S, Sies H. Lycopene as the most efficient biological carotenoid singlet oxygen quencher. Arch Biochem Biophys 1989; 274: 532–538.
Klebanov GI, Kapitanov AB, Teselkin YoU et al. the antioxidant properties of Lycopene. Membr Cell Biol 1998; 12: 287–300.
Palan P, Naz R. Changes in various antioxidant levels in human seminal plasma related to immunoinfertility. Arch Androl 1996; 36: 139–143.
***Address for correspondence*: Prof. N.P. Gupta, Department of Urology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, 110029, India**
Phone: 91-11-6594293, 91-11-6594884; Fax: 91-11-6862663
E-mail: narmadagupta@hotmail.com

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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 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.

Clinical Applications

Bell’s Palsy: Evidence suggests methylcobalamin dramatically increased the recovery time for

facial nerve function in Bell’s palsy.
[2]
Cancer: Cell culture and in vivo experimental results indicated methylcobalamin inhibited the
proliferation of malignant cells.
Research indicated that methylcobalamin enhanced survival time and reduced tumor growth following inoculation of mice with Ehrlich ascites tumor cells.
[3]
Methylcobalamin
has been shown to increase survival time of leukemic mice. Under the same experimental conditions,
cyanocobalamin was inactive.
[5]
[4]
Although more research is required to verify findings, experimental evidence suggested methylcobalamin might enhance the efficacy of methotrexate.
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.
Deterioration
of accommodation following visual work has also been shown to improve in individuals
receiving
methylcobalamin.
[9]
[6]
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.

[8]
[1]
Methylcobalamin

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 Impotence: In one study, methylcobalamin, at a dose of 6 mg/day for 16 weeks, improved
sperm count by 37.5 percent.**
**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]
[13]
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.

Dosage

[15-20]
The dosage for clinical effect is 1500-6000 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.

Safety, Toxicity, and Side Effects

Methylcobalamin has excellent tolerability and no known toxicity.

References

1. Okuda K, Yashima K, Kitazaki T, Takara I. Intestinal absorption and concurrent chemical changes of
methylcobalamin. J Lab Clin Med 1973;81:557-567.
2. 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.
4. Shimizu N, Hamazoe R, Kanayama H, et al. Experimental study of antitumor effect of methyl-B12. Oncology
1987;44:169-173.
5. Tsao CS, Myashita K. Influence of cobalamin on the survival of mice bearing ascites tumor. Pathology
1993;61:104-108.
6. 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]
7. 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.
9. Iwasaki T, Kurimoto S. Effect of methylcobalamin in accommodative dysfunction of eye by visual load. Sangyo
Ika Daigaku Zasshi 1987;9:127-132.

10. 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.
12. 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.
14. Isoyama R, Kawai S, Shimizu Y, et al. Clinical experience with methylcobalamin (CH3-B12) for male infertility.
Hinyokika Kiyo 1984;30:581-586.
15. 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.
16. Tomoda A, Miike T, Matsukura M. Circadian rhythm abnormalities in adrenoleukodystrophy and methyl B12
treatment. Brain Dev 1995;17:428-431.
17. Yamada N. Treatment of recurrent hypersomnia with methylcobalamin (vitamin B12): a case report. Psychiatry
Clin Neurosci 1995;49:305-307.

18. 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.
19. Mayer G, Kroger M, Meier-Ewert K. Effects of vitamin B12 on performance and circadian rhythm in normal
subjects. Neuropsychopharmacology 1996;15:456-464.
20. 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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THANK YOU !!