

Vitamin B₁₂ and Folate in the Treatment of Some Psychiatric Illnesses*

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Abstract *This article reviews a clinician's experience with vitamin B₁₂-folate administration in the treatment of some psychiatric illnesses. The psychiatric conditions most likely to respond to these vitamins, the physical and biological indicators of an increased need for these vitamins, and the therapeutic doses are highlighted.*

Introduction

In this paper I hope to make a few points that I believe have not been made, or not clearly been made about vitamin B₁₂ and folate. I will briefly review the literature on vitamin B₁₂-folate in mental illness, criticizing much of it on the ground of the inadequate awareness of the "tandem" nature of vitamin B₁₂ and folate. I will then have some general things to say about my own data and clinical experience with vitamin B₁₂ and folate in mental illness that I hope will be clinically and practically useful.

Published works implicating vitamin B₁₂ and/or folate deficiencies in mental disorders have appeared from time to time even since an interest in the disorders associated with pernicious anaemia and subacute combined degeneration of the spinal cord developed. Somewhat less than the majority of these have been "negative" studies which have often been based

on that most diabolically dangerous tendency of medical doctors to deify the laboratory report and discount their own perceptions. The studies purport to show no relationship because the patients have normal serum vitamin B₁₂ levels, or folate levels. I will attempt to show here, that these two nutrients in common with other nutrients (but emphatically in the case of these two) cannot be considered in isolation. Similarly, negative studies of treatment have invariably been one agent or the other alone, and I believe them to be invalid. Treatment with vitamin B₁₂ and folate for the patients that require it, or where it appears to be indicated, is almost invariably successful.

Eighteen Years of Clinical Experience

I've been interested in this subject for about 18 years now. Twelve years ago, in the context of a study pertaining to malabsorption of a large number of essential nutrients in a

*Editor's note: This paper was adapted (with permission) from a presentation delivered by Dr. Kotkas at the Canadian Schizophrenia Foundation meeting (forerunner of the Orthomolecular Medicine Today Conference) held on June 4, 1978. It was given to me by Ms. Audrey Alexander, a long-time supporter of orthomolecular medicine and board member of the International Schizophrenia Foundation. This paper by Dr. Kotkas, while decades old, provides helpful clinical insights that will no doubt assist practising orthomolecular clinicians in the proper application of vitamin B₁₂-folate therapy. We believe you will find it a valuable clinical reference in the service of your mentally unwell patients.

broad range of psychiatric disorders, I began asking for routine serum folate levels on all my patients, with interesting results. A large proportion, varying at times between 25-50% had abnormally low values, and these patients tended to be “sicker,” or more incapacitated, from the psychiatric point of view. Combined oral medication with folate and parenteral cyanocobalamin produced dramatic improvement in all cases treated; mainly in depressive symptomatology, but still useful across a very broad spectrum of psychiatric disorders.

The most significant thing is that the majority of patients with vitamin B₁₂ and folate responsive mental conditions had normal serum vitamin B₁₂ levels. But the folate levels were below normal. When the folate was given, the serum vitamin B₁₂ levels dropped. These observations are quite significant and may explain the negative studies in the areas of diagnosis and treatment. The tandem “partnership” between vitamin B₁₂ and folate has to be kept in mind constantly when dealing with these nutrients.

That vitamin B₁₂ and folate are observed and utilized together is a well and widely accepted opinion held by experts, and even physicians. This *in vivo* relationship should be studied more completely before any clinical research can have much value. There appears to be a tandem relationship in that a deficiency of one of these agents will result in “stockpiling” of the other, and normal serum levels because the other agent isn’t being utilized. At lower levels, deficiency of one agent interferes with the absorption of the other, and results in low levels of both and may be even more complicated than that.

When it came to doing “disciplined” studies, why did they forget the intimate and inseparable tandem of vitamin B₁₂ and folate? Well, the “discipline” is wrong. We can put the blame of Bishop Occam – a medieval monk – philosopher who said, translating from the Latin: “Entities are not to be multiplied unnecessarily.” Perhaps, it’s unfair to blame this clerical person as he was really a sensible philosopher in his time, and he was fighting to get the number of angels that could dance on the head of a pin down to at least one.

“Occam’s Razor” as we now called this epigram is taken to mean that the simplest explanation found is most likely to be the correct one; maybe this is so, but it isn’t always so. The field of nutrition is an area where it isn’t so, and vitamin B₁₂ and folate are particular examples.

Using Vitamin B₁₂ and Folate in Mental Illnesses

When do you use vitamin B₁₂ and folate? Certainly not just when serum levels on clinical pathological testing are low. When serum levels are low there’s usually a problem, but the tests are not that reliable when normal.

An important point that I hope to make in this paper is that vitamin B₁₂ and folate deficiencies can and should be corrected long before there’s a macrocytic (or even iron deficiency) anaemia, but there are no central or clinical psychiatric features that I have found that will identify vitamin B₁₂-folate responsive conditions. Instead of a narrow focus on the “psychiatric” picture, the whole person should be evaluated, and in particular, all physical signs and symptoms must be taken into account. A Danish study claims to have a 10-point scale that when followed gives a strong indication of need for vitamin B₁₂-folate use. I haven’t been able to obtain the paper yet, but I’m certain their 10-points are not exclusive psychiatric signs and symptoms. In vitamin B₁₂-folate deficiency you can get every psychiatric diagnostic category in the book and a good many that aren’t; there is nothing regular, uniform, or pathognomonic about the resulting mental disorders. This deficiency creates an underlying predisposition and other factors determine the specific psychiatric clinical features, i.e., the “content” and even to a great extent the “form” of the illness.

Associated Physical and Biological Indicators of Vitamin B₁₂-folate Responsive Psychiatric Illnesses

Besides the obvious conditions of malnutrition and malabsorption, a selection of the biological contingencies where vitamin B₁₂-folate can be expected to play a part in mental illness is as follows:

1. Mental illness in the aged. In this situation, complex inadequacies of the requirements for brain function are almost the rule in the general population. Generally, older people absorb and retain vitamin B₁₂ and folate more avidly than other age groups. What may appear to be “classical” schizophrenia for example when it occurs for the first time in the older age group is usually nutritional, and vitamin B₁₂ and folate are often the key to treatment.

2. So called “Neurotic Depressions.” These are often fatigue states with an overlay of depression, some of which is psychogenic due to the anger at the self for not functioning as expected or wished. In this case, as in all mental illnesses, biological treatment isn’t enough and appropriately focussed psychotherapy is often also needed.

3. Conditions relating to the female reproductive cycle (e.g., pregnancy, menses, and the “pill”). A large proportion of postpartum psychoses respond to vitamin B₁₂-folate administration.

4. Other endocrine disorders, such as hypothyroidism and hypoadrenalism, with the latter disorder often causing hypoglycemic episodes.

5. Conditions where the body is absorbing significantly large amounts of chemicals foreign to the body’s needs (e.g., alcoholism, drug addiction, and the pharmacotherapy of epilepsy).

6. Iron deficiency. It is difficult to determine the complex status of the deficiency as vitamin B₁₂ and folate clearly are necessary for the adequate absorption and utilization of iron. You see the following symptoms: pallor, muscle tension, black shadows under the eyes, nail changes, headaches, and myoclonus (often brought on or dramatically intensified by the taking of tricyclic antidepressants and relative drugs).

Physical signs and symptoms and special biological contingencies are a better guide to vitamin B₁₂-folate responsive conditions. Some of the signs and symptoms that will be evident even on a narrower psychiatric assessment (in order of significance) are the following:

1. Lack of energy and fatigue. This is both

muscular and mental/intellectual. An added complexity here is that vitamin B₁₂-folate deficiency can lead to vitamin B₁ deficiency even when dietary thiamine is normal, perhaps the result of lessened absorption or utilization, or from some other factor. Thiamine is of course quite significant in fatigue states.

2. Lethargy – physical inactivity.

3. Lack of volition (“no ambition”).

4. Insomnia.

5. Irritability.

6. Pallor.

7. Forgetfulness.

8. Restless legs – muscular cramps, twitching, lighting pains.

The action of vitamin B₁₂ and folate on the central nervous system function is poorly understood, but some clinical impressions may be helpful, as well as giving direction to possible future research.

The onset of action is rapid in most of the more “organic” physical symptoms, and in a few of the mental ones, such as irritability which may be reduced by feedback from the improved physical condition. Most responsive psychiatric conditions improve with intensive vitamin B₁₂ and folate replacement in 1-4 days.

We do know that vitamin B₁₂ and folate are absolutely necessary in the production of the cerebral neurotransmitters, noradrenaline and serotonin. Deficiencies of these can be responsible for some cases of schizophrenia. Some patients have recovered on vitamin B₁₂ and folate administration alone; we can only speculate on the mode of action. It’s clear from my clinical observation that vitamin B₁₂ and folate have an action more like the one we’d expect from an increased noradrenaline, and clearly not an action that would resemble adrenaline or amphetamines.

With adrenaline and amphetamines there is a driven, slightly manic “speedy” stimulation whereas with vitamin B₁₂ and folate there is relaxation and the heightened, increased volition, seems to come more from inside spontaneously – i.e., there is no stimulant “push.” In adrenaline and amphetamines there is a temporary euphoria or “high” feeling which doesn’t characterize vitamin B₁₂ plus folate where you

get a gentle increase in the sense of wellbeing. In a sense, the increase in adrenaline from the administration of amphetamines doesn't really touch the basic manic-depressive condition and their stimulant effect is usually to convert depression to mania, a spurious and even dangerous improvement, for the incidence of suicide goes up even when there is no sudden swing back from the mania to the depression. Methylphenidate and some of the diet pills are the only amphetamine-like agents available now, and for the reason noted above they are dangerous to give though the temptation exists in depression, schizophrenic depression, fatigue, etc. Vitamin B₁₂ and folate are much safer, though perhaps not as dramatically stimulating.

Another contrast with amphetamines and adrenaline to that of vitamin B₁₂ and folate is that in the first you get cold extremities (i.e., cold body, muscle tension, anorexia, malabsorption, gastrointestinal tract shut down) and autonomic imbalance. With vitamin B₁₂ and folate you get warm extremities, a general increase in subjective and objective body heat, almost certainly by stimulation of thyroid function. Vitamin B₁₂ and folate counteract nausea, improve appetite and absorption, and there is a stabilizing effect on autonomic imbalances such as menopausal hot flashes.

It's usually a waste of time and/or money to give vitamin B₁₂ by any other route than parenteral, although occasionally with children I've used large doses of a palatable vitamin B₁₂. The 1,000 mcg/mL strength is the best for office use in selected patients or dispensed from pharmacies that are reliable and carry it. The majority of patients will use the 1,000 mcg/mL strength.

Hydroxycobalamin is said to be more effective and longer lasting, but my impression is that any of its advantages are offset by the higher price and unavailability of stronger preparations. Vitamin B₁₂ is non-toxic in immense doses. Hydroxycobalamin has been used successfully in the detoxification of acute cyanide poisoning. The hydroxycobalamin avidly takes up the cyanide radicals to form cyanocobalamin and the large amounts of this substance are excreted. There is no up-

per toxic limit for vitamin B₁₂ dosage.

Daily doses as high as 10,000 mcg can be used. In some cases, such as multiple sclerosis, the patients seem to need, at times, several injections each day. Usually, however, the patient can clearly tell from how he is feeling, how often he needs the vitamin B₁₂ injections. Shots are given in the morning to avoid insomnia.

The folate is given every day in doses of 10-20 mg, and higher doses have never been required in the patients I've seen. They also take folate in the morning and at noon to avoid insomnia.

Conclusion

It has been difficult to avoid being over-inclusive when discussing vitamin B₁₂ in mental disturbances, as vitamin B₁₂-folate have such wide ranging effects in all areas of mind-body functioning. I've attempted to show that a failure to recognize that vitamin B₁₂ and folate work essentially together has possibly resulted in much of the reported failure to get therapeutic results. They must be used and studied together. A modest contribution from clinical experience has hopefully been made to isolating the cases where it's most likely to be of value. Most orthomolecular clinicians will try it, however, empirically, at some time or other if a patient doesn't improve on the usual megavitamin or super-nutrition regime.

Competing Interests

The author declares that he has no competing interests.



Lawrence Kotkas, front and centre, flanked by Erik Paterson, (l) and Abram Hoffer (r) at an Orthomolecular Medicine seminar in Calgary, 1995.