Treating Dementia with Vitamin B_3 and NADH

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Abstract *Dementia affects approximately 5 million people in the United States, and about 475,000 elderly Canadians. Dementia is a debilitating and often progressive illness. The most common type of dementia is Alzheimer's disease, followed by vascular types. There is a need to investigate novel treatments because the current crop of medications have limited value. Niacin might be a worthwhile treatment to consider. Research has shown that the risks of incident AD increase when patients have insufficient intakes of niacin from diet or medical conditions that precipitate niacin deficiency. Clinical reports have documented therapeutic benefits when patients receive optimum daily doses of niacin. Preliminary trials evaluating the reduced form of nicotinamide adenine dinucleotide (NADH) found it a safe and effective treatment for AD. At present, research evaluating the therapeutic applications of niacin and/or NADH for dementia is at a standstill. However, niacinamide is being evaluated in a clinical trial to determine if it is safe and beneficial for patients with AD. Hopefully, the forthcoming results will encourage researchers and clinicians to study niacinamide further, and revisit the therapeutic potential of vitamin B_3 as a safe and an effective treatment for dementia.*

Introduction

Among elderly patients, Alzheimer's disease (AD) is the most common type of dementia, followed by vascular types. Worldwide, more than 30 million people suffer from AD. In the United States, AD affects approximately 5 million people.[1] About 475,000 elderly Canadians have dementia, with the majority of cases being attributed to AD.[2] Experts predict that the number of patients afflicted with dementia in Canada will increase to 778,000 by the year 2031.[2] The burden that this disease will place on health care systems is staggering when you consider that the elderly constitute the fastest growing population in all industrialized countries.[1]

Dementia is a debilitating and often progressive illness characterized by intellectual decline and the loss of higher cognitive functions, including language, motor skills, judgment, orientation ability, and, most notably, memory. Patients eventually lose themselves in the disease, unable to remember even vestiges of the lives they once lived.

The cognitive declines of AD are associated with problems in the cerebral cortex including the formation of senile plaques, neurofibrillary tangles, and granulovascular degeneration of neurons.[3] Various risk factors have been implicated in the susceptibility to AD. These include advancing age, family history, apolipoprotein E epsilon 4 genotype, obesity, insulin resistance, vascular factors, dyslipidemia, hypertension, inflammatory markers and Down syndrome.[1]

The medical treatment of AD uses acetylcholinesterase inhibitors or n-methyl-d-aspartic acid glutamate receptor antagonists,

with the former treatment having only weak evidence of benefit on cognitive function.[4] Clearly there is a need to investigate other treatments because the current crop of medications have limited value in mitigating the progression and symptoms of dementia, most notably, AD. In this article, I will summarize and comment on: (1) research linking a reduction in the incidence of AD with high dietary intakes of vitamin B_3; (2) the merits of using niacin or the reduced form of nicotinamide adenine dinucleotide (NADH) as treatments for dementia; and (3) current research investigating the safety and efficacy of niacinamide as a treatment for AD.

Preventing AD with Vitamin B_3

Research has shown a relationship between dietary niacin and the development of AD.[5] A total of 3,718 participants aged 65 years and older underwent at least two clinical assessments and provided dietary data for analyses over a median of 5.5 years. In this large, prospective study, dietary niacin deficiencies were associated with incident AD and cognitive decline. Niacin intake from foods was inversely associated with AD (p for trend = 0.002). A higher food intake of niacin was associated with a slower annual rate of cognitive decline. Specifically, an increased food intake of niacin slowed the annual cognitive decline by 0.019 standardized units per natural log increase in intake (mg), which was statistically significant (p=0.05). The participants in intake quintiles 2-4 had a statistically significant 70% reduction in risk compared to participants in the lowest quintile (median niacin intake 12.6 mg/day). The participants in the highest quintile (median niacin intake 22.4 mg/day) had an 80% statistically significant reduction in risk.

These researchers did not provide any robust explanations as to why diagnoses of AD increased among participants with low dietary intakes of niacin but they did note that the level of dietary niacin associated with pellagra (8.8 mg of niacin equivalents per 2000 kilocalories) was lower than the range of intake for the lowest quintile (13.2-27 mg per day). While none of the study participants were reported to have pellagra (i.e., diarrhoea, dermatitis, dementia, and shortly thereafter, death), some participants who demonstrated mental and cognitive declines may not have met the recommended dietary allowance for niacin (14 mg for adult females and 16 mg for adult males[6]). Some of the study participants may have had subclinical pellagra.

The mental signs of mild niacin deficiency (a.k.a., pellagra sine pellagra) often occur in the absence of any dermatologic, mucous membrane, or gastrointestinal symptoms.[7,8] The researchers did not acknowledge that niacin deficiency can lead to symptoms of AD, and thereby play a role in the pathogenesis of AD. Decades ago Aring and Spies reported that neurasthenic symptoms in 225 mild pellagrins were ameliorated by taking 300 to 600 mg of niacin every day for 1-12 days (3-6 pills , with each pill providing 100 mg of niacin).[8] The neurasthenic symptoms reversed by niacin appeared long before any other manifestations of the disease. These included fatigue, insomnia, anorexia, vertigo, burning sensations in various parts of the body, numbness, palpitation, nervousness, a feeling of unrest and anxiety, headache, forgetfulness, apprehension, and distractibility. These niacin-deficiency manifestations could easily be confused with prodromal symptoms of AD, and, if left untreated, they could become severe enough for a diagnosis of AD. The dementia of pellagra looks much like AD since its clinical presentation, while varied, includes aggression, apathy, confusion, depression, disorientation, hallucinations, insomnia, psychosis, and seizures.[9]

Low dietary intakes of niacin would not entirely account for the increased incidence of AD among the study participants. Many participants had varying intakes of alcohol and cigarette consumption, as well as the presence of diabetes and/or cardiovascular disease. These and other possible factors could have increased the participants' vulnerability to niacin deficiency during the study period (**Table 1**, opposite).[7]

Above all, this study demonstrates that insufficient intake of niacin from diet or

Table 1. Possible causes of niacin deficiency

Precipitating Factors	Explanations
Inadequate amount of niacin in diet	Inability to procure an adequate diet (e.g., socioeconomic reasons), or choosing a nutritionally unbalanced diet (e.g., due to ignorance, individual preference, or lack of advice about nutrition)
Interference with ingestion	Functional and organic conditions leading to anorexia or vomiting, gastrointestinal disease, psychiatric disorders (e.g., psychoneuroses, both organic and functional psychoses, and addiction to alcohol or other drugs), neurological and traumatic disorders that interfere with self-feeding, and oral diseases (e.g., sore mouth, or loss of teeth)
Interference with bio-synthesis	Inadequate intake of tryptophan, ingestion of structurally similar compounds that would inhibit the formation of niacin by substrate competition (e.g., maize), and destruction of intestinal bacteria (e.g., bowel "sterilizing" antibiotics)
Interference with absorption	Absence of normal digestive secretions (e.g., achlorhydria and obstructive jaundice), intestinal hypermotility (e.g., various types of diarrhoea), reduction in absorptive surface (e.g., disease or surgical removal of the gastrointestinal tract), and medications (e.g., mineral oil)
Interference with utilization	Problems with cellular metabolism (e.g., alcohol, general anaesthesia, and metabolic disorders such as hypothyroidism or diabetes), specific inactivation (e.g., sulphonamides exert an anti-vitamin effect by substrate competition with para-aminobenzioc acid, corn, and isoniazid)
Interference with storage	Any condition causing impairment of liver function would interfere with the amount of niacin retained in the body
Increased excretion or loss	Elevated metabolic rate (e.g., hyperthyroidism), periods of rapid growth, pregnancy and lactation, pyrexia from any cause, any condition requiring increased muscular activity, and specific treatments (e.g., high carbohydrate diets, insulin, thyroid medication, and overuse of stimulants (such as caffeine or amphetamines)
Increased nutritive requirements	Urinary loss (e.g., renal disease, and diabetes), or other routes (e.g., lactation, serous exudates due to burns, and severe blood loss)

conditions that can precipitate vitamin deficiency can increase the risks of incident AD. As more data emerges linking niacin insufficiency to AD, it might be prudent to create public health programmes to promote niacin consumption from foods or increase niacin fortification. Such measures could protect more of the population from mental and cognitive decline, and reduce the incidence of dementia.

Treating Dementia with Niacin

Subsets of patients with early or even established dementia appear to require large daily doses of niacin to reverse and/or slow the progress of their disease. In 1941, Sydenstricker and Cleckley were two of the first clinicians to report impressive benefits from oral and intravenous niacin administration in 29 patients with stuporous or active psychoses of unknown origin.[10] Two-thirds of their patients were in the presenile or senile age range with severe psychiatric symptoms of a confusional nature, but none had physical signs of malnutrition or pellagra. Twenty-eight patients recovered after niacin treatment. Eight patients received oral niacin treatment, while the remaining 21 patients received intravenous niacin or a combination of oral and intravenous niacin. The oral niacin prescribed to patients ranged from 75-4500 mg daily until discharge. The intravenous doses of niacin ranged from 100-900 mg. For most patients, the intravenous administration continued until discharge, but for some patients, intravenous treatments were stopped and replaced by oral niacin until discharge. Within 4 days of niacin treatment, the majority of these patients experienced rapid and usually impressive improvements. While the duration of niacin treatment was unclear, estimates from the cited case reports suggest 7-30 days or longer since some patients continued with the niacin treatment following their hospital stay. The authors concluded that the majority of patients with toxic psychosis or exhaustion delirium, as well as those with unexplained clouding of consciousness, should be given a therapeutic trial of niacin. This was the only way to determine if a patient's psychiatric condition was due to a deficiency of niacin (i.e., an "avitaminosis") even though the aetiology was uncertain. In a discussion following their paper, other clinicians remarked that the therapeutic value of niacin could not necessarily be attributed to the correction of a vitamin deficiency. They reported that niacin might have helped some patients as a result of its physiological effects upon cerebral circulation, and/or as a result of its ability to facilitate carbohydrate metabolism within the brain.

In 1952, Gregory administered large doses of niacin orally (300 mg three times daily) and intravenously (100 mg/day) to 54 patients having organic psychoses of senility immediately following their admission to a private mental hospital.[11] During their hospital stays, patients were also given a nutritious diet and liberal amounts of other vitamins. All patients were evaluated before treatment and immediately following any degree of improvement. The evaluations included thorough psychiatric examinations (with particular reference to orientation, memory, and secondary symptoms), as well as intelligence tests. The duration of niacin treatment was approximately 3-12 weeks. Once patients became maximally improved, they were placed on a maintenance dose of niacin (100 mg orally/day). In the group of 14 patients 65 years of age and under, 8 patients improved dramatically following niacin treatment. They were able to leave the hospital, whereas the remaining 6 patients improved symptomatically or not at all. In the group of 40 patients over the age of 65, 31 completed the course of niacin treatment. Only 4 patients from the over-65 group improved enough to re-socialize. The author concluded that "nicotinic acid is most effective in those psychoses of senility that are of recent, and fairly rapid, onset," which was reported to be of a duration less than 6 months. The findings showed that the earlier niacin treatment was started, the better the prognosis, especially among patients 65 years of age and under. With respect to mechanism of action, the author discussed several possibilities including: (1) the correction of

a niacin deficiency; (2) a "saturation" effect in the absence of any deficiency; and/or (3) cerebral vasodilatation. The author also suggested that lesser amounts of niacin might delay or prevent the psychoses of senility if given to individuals in the presenile and senile age groups.

In 1962, Dr. Abram Hoffer and his colleagues discovered that 3,000 mg/day of niacin improved and sometimes reversed dementia.[12] Hoffer's patients required large daily doses of niacin to remain well (**Table 2,** below).

In total, 12 of 15 elderly patients responded favourably to large doses of niacin. **Table 3** (p. 168) describes the type of clinical

Table 2. Treatment response from large (3000 mg/day) doses of niacin in 15 elderly patients fast becoming senile or with clear evidence of senile mental changes

Patient Initials	Age	Diagnosis	Clinical response	Duration (years)
OR	62	Psychosis with arteriosclerosis	Recovered	4
JC	80	Presenile psychosis	Recovered	1
HC	67	Presenile changes	Recovered	6
FM	72	Normal	Remains well	6
MT(f)	58	Normal	Remains well	3
MT(m)	63	Normal	Remains well	2
AC	79	Senile depression	Recovered	1.5
LW	74	Senile psychosis	Recovered	0.25
MC	70	Normal	Remains normal	0.75
BB	68	Senile depression	No response	0.25
GC	75	Psychosis with arteriosclerosis	Marked improvement	0.5
RR	67	Psychosis with arteriosclerosis	Marked improvement	1 month
DG	68	Psychosis with arteriosclerosis	No change	Not provided
NR	77	Psychosis with arteriosclerosis	No change	Not provided
HV	70	Depression	Remains well	1

Table 3. Brief clinical descriptions of the therapeutic effects of niacin in elderly patients

Case JC (Age 80): In February, 1959, this woman had a mild coronary occlusion. She developed generalized weakness, weakness grasping with one hand, anorexia, and ataxia. She was also nervous and had feelings of confusion and hopelessness. During April, 1959, she began to take three grams of nicotinic acid daily. Within a few weeks, her appetite improved and she felt stronger. By June, she was able to walk slowly but well. Mentally, she was much improved. She still had a few episodes of nervousness preceding social events. There was no more confusion and her memory was good. For the next year, she continued to improve and in April, 1960, she was quite well. In May, 1960, she had influenza and later that month she died from a coronary occlusion and secondary metastasis of a bowel carcinoma. She had been mentally alert up to three days before dying, when she sank quietly into her fatal coma.

Case GC (Age 75): For several months Mr. G.C. complained of violent dizzy spells, with headaches, vomiting and general deterioration. Physically he was normal. In November, 1959, he was given nicotinic acid, three grams daily. Two months later he was much improved. He had no more dizzy spells and regained his normal vigour. April 13, 1960, he ran out of tablets. There was a rapid relapse and again he complained of headaches and dizzy spells. Nicotinic acid tablets were sent to him and again he improved.

responses that were observed by Hoffer and his colleagues.[12] In many of these cases, patients who responded to niacin remained improved as long as they did not stop the vitamin. Once they discontinued it, they relapsed fairly quickly, but they improved again when they resumed the vitamin. Hoffer reasoned that these patients had metabolic conditions; vitamin dependencies which required more niacin than they obtained from their diets.

Another case reported by Hoffer in 1974 (and mentioned in his book, *Smart Nutrient*s) involved his mother who was 86 years old at the time of publication (**Table 4**, opposite).[13]

From the cited clinical reports, it is apparent that niacin administration offers clinical benefits irrespective of dietary intakes. There is likely some metabolic need for additional amounts of niacin among a subset of patients who show early signs of dementia or have established dementia. Two case-controlled studies reported lower blood levels of a nicotinic acid metabolite among patients with dementia compared to similarly aged controls.[14,15] Another study assessed plasma concentrations of tryptophan (a niacin precursor), other amino acids and thiamine, and found them reduced in patients with AD.[16] In these three studies, dietary intakes did not satisfactorily explain the findings.

Niacin might also aid dementia as a result of its well-established cholesterol-modifying properties (i.e., lowers low density lipoprotein-cholesterol, increases high-density lipoprotein-cholesterol, and lowers triglycerides).[17] Research has shown cholesterol reduction to possibly aid in the treatment of dementia.[18,19] While data regarding this relationship is emerging, some published reviews have shown contradictory results and even negative outcomes from cholesterol-modifying medication.[20,21] More studies are needed to determine whether cholesterol modification is a reasonable and effective intervention for dementia.

Another possibility for niacin's effectiveness might involve its ability to increase cerebral blood flow due to its presumed ability to increase cerebral vasodilatation. When niacin is administered orally in amounts of 500 mg or topically via a 6-inch patch of 10^{-1} M aqueous methylnicotinate on the forearm, prosta-

Table 4. Hoffer's clinical description of his mother's response to a daily dose of 3000 mg of niacin

Case CH (Age 86): In 1954…my mother, then 67 years old, was very nervous and depressed and complained of severe pain in her joints, failing vision in one eye, generalized weakness and fatigue, and severe arthritis of her hands…Her memory was beginning to fail. It was clear that she was aging very quickly. I knew no treatment was effective but I was by then familiar with nicotinic acid used in megadoses. I decided to start her on 3 grams per day, more or less as a placebo…To my amazement, mother was nearly well six weeks later. Her arthritis had cleared, her fingers were straight, and Heberden's nodes began to soften and regress. Her vision in both eyes was normal, and her tension, anxiety, and depression were gone…Today (1974) at 86 she is physically weaker, does not hear as well, but is mentally well…She has been taking 3 grams each day of nicotinic acid for 18 years. I have not seen any evidence of toxicity, and there has been no progression of mental senility which was so apparent 18 years ago.

glandin D2 (PGD2) is markedly released in the skin and high amounts of its metabolite appear in the plasma.[22,23] It is not known if PGD2 causes vasodilatation of the intracranial blood vessels, but niacin's ability to abort acute migraine headaches suggests that this might be occurring.[24]

Old reports cited by Bicknell and Prescott,[25] indicated that niacin causes vasodilatation of the cerebral and spinal vessels. They also noted that intravenous niacin administration increases the rate of intracranial blood flow in human beings for 20-60 minutes without any significant change in blood pressure. Other published data pertaining to niacin's effects on cerebral vasodilatation has been equivocal. In one study, subjects having various diseases (e.g., pernicious anemia, congestive heart failure, hysteria, diabetes, and hypertensive vascular disease) were given intravenous niacin (300-800 mg in 200-300 mL of saline over 20-25 minutes). Numerous measurements were obtained, such as arterial pressures, blood oxygen contents, glucose, cerebral oxygen utilization, cerebral glucose utilization, and cerebrovascular resistance.[26] The results of this study failed to find any effect upon cerebral vasodilatation by the intravenous administration of niacin.

In an animal study using anesthetized cats, intravenous injection of niacin (0.5 mL/kg) caused a short-term increase in both cerebral blood flow and in arterial blood pressure in venous vessels of the head, but this was followed by a lowering of these parameters.[27] In a study assessing cerebral blood flow in baboons under anaesthesia using single photon emission computed tomography of the brain, a combination of niacin and pentifylline increased cerebral blood flow compared to the control baseline ($p<0.01$).[28] In another study of similar design, the cerebral blood flow was increased above that of the control when a combination of pentyifylline and niacin were administered to baboons.[29] The increase in cerebral perfusion (denoted as an increase in R-value) was +29 % from the pentyifylline-niacin combination (2.31 ± 0.19) compared to the control (1.79 ± 0.13).

Based on these reports, it appears that intravenously-administered niacin might increase cerebral blood flow. More intravenous niacin studies are warranted. Although no reports examine the effects of orally-administered niacin upon cerebral blood flow in human or animal subjects, niacin could be increasing cerebral blood flow since it has been shown to abort acute migraine headaches presumably by vasodilatation of the intracranial blood vessels.[24] This potential mechanism of action is important. Data demonstrate that as dementias of the Alzheimer and vascular types progress, cerebral blood flow and metabolism become

functionally low.[30] The severity of dementia symptoms have been correlated to deviations in cerebral blood flow and metabolism.[30] A more recent study found marked cerebral blood flow reductions in the frontal (p=0.001) and parietal (p=0.001) cortices in both vascular dementia and AD, when compared to aged-matched cognitively normal controls.[31] Since orally-administered niacin benefits some patients, its therapeutic properties might facilitate cerebral vasodilatation and increase cerebral blood flow.

Niacin might also benefit patients with dementia as a result of its ability to stimulate cellular metabolism. The brain is almost entirely dependent on the metabolism of glucose by oxidative processes. In a decades-old study, patients with organic brain syndromes (mean age: 68 years) had their cerebral blood flows evaluated.[32] Clinical deterioration and functional decompensation was associated with a worsening in cerebral and oxidative metabolism, and a resultant shift to anaerobic glycolysis. Significantly heightened cerebral metabolic rates of lactate were considered a causal quantitative factor in the pathogenesis, manifestation, and severity of organic brain syndromes.

An insufficient supply of nicotinamide adenine dinucleotide (NAD) is known to inhibit the conversion of lactate to pyruvate, and contribute to a high lactate-to-pyruvate ratio.[33] Therapeutic doses of niacin might diminish the shift in anaerobic glycolysis (and lower lactate levels) as a result of niacin's ability to increase the synthesis of NAD.[34] The increased synthesis of NAD might drive the conversion of lactate to pyruvate, enhance oxidative processes within the brain, and mitigate cerebral metabolic disturbances associated with increased cerebral lactate levels.

Yet another potential mechanism might explain how niacin benefits some patients with dementia. Niacin might reduce axonal damage and increase axonal density. Research has shown that neuronal damage in the brains of patients with AD leads to activation of brain immune cells – microglia and astrocytes – and stimulates them to produce interleukin-1 (IL-1) and a soluble astrocyte inflammatory cytokine known as S100.[35] IL-1 promotes the synthesis of beta-amyloid precursor protein (β-APP) in neurons, and promotes β-APP outside the cell where it forms plaques.[35] A preliminary study using rats found that slow-release niacin, or a combination of slow-release niacin and simvastatin, were able to reduce axonal damage and increase axonal density by decreasing the expression of amyloid precursor protein.[36] While this study is very preliminary, these results suggest that supplemental niacin might offset the production of amyloid plaques, which are perhaps the most important histopathological markers in AD. Amyloid plaques also occur within the brain when ischemia is present,[36] which suggests that supplemental niacin might lessen axonal damage associated with vascular types of dementia as well. **Table 5,** (opposite) summarizes niacin's purported mechanisms of action in the treatment of AD and vascular types of dementia.

Treating Dementia with NADH

NADH is a coenzyme in all living cells, including the brain. As a component of the electron transport chain, it plays a central role in intracellular energy production. NADH is also believed to increase the synthesis of the neurotransmitters dopamine and norepinephrine in the brain.

In an open-label pilot trial involving 17 AD patients taking 10 mg of NADH 30-minutes before their first meal for 8 to 12 weeks, all patients had demonstrable cognitive improvements (as per favorable changes in their mini-mental state exams and global deterioration scales).[37] No side effects were associated with the NADH treatment. Some patients took NADH for more than one year. They also reported no side effects.

Following the pilot trial, 25 patients with mild to moderate dementia of the Alzheimer, vascular, and fronto-temporal types received 10 mg of NADH daily in addition to their cholinomimetic medication.[38] Nineteen of the 25 patients completed this 3-month open-label trial. The results showed no evidence of benefit (as per established psychometric tests), so the authors concluded that

NADH is unlikely to enhance cognitive ability and could not treat dementia.

The most recent trial, published in 2004, was favorable.[39] In this randomized, placebo-controlled, matched-pairs, double-blind, 6-month clinical study, patients with probable AD (n = 26) were randomized to receive either NADH (10 mg/day) or placebo. At the conclusion of the trial, AD patients who received the NADH treatment had no evidence of further cognitive deterioration. Their dementia rating scales showed improved scores compared to the AD patients in the placebo group ($p<0.05$). Specifically, the NADH treatment was associated with significantly better verbal fluency ($p=0.019$) and visual-construction ability ($p=0.038$), with a trend toward improved abstract verbal reasoning ($p=0.08$). No differences were found between the AD patients and placebo group in measures of attention, memory, or clinician ratings of dementia severity.

The rationale for using NADH as a treatment for dementia comes from several sources of evidence which suggest that this treatment can reverse some of the defects associated with AD (**Table 6**, below).[40] Clearly more studies are needed. The initial dosage of NADH should be 10 mg/day about 30-minutes prior to a meal. The label or package insert must state that the particular NADH product is stabilized; otherwise, it will be de-

Table 5. Niacin's purported mechanisms of action in the treatment of AD and vascular types of dementia

- Resolves metabolic dependency by repleting enzyme co-factors
- Modifies lipid levels (i.e., the cholesterol profile)
- Increases cerebral blood flow via vasodilatation
- Stimulates cellular metabolism by increasing the production of nicotinamide adenine dinucleotide
- Reduces axonal damage and increases axonal density by decreasing the expression of amyloid precursor protein

Table 6. NADH's purported mechanisms of action in the treatment of AD

AD Defects reported in the scientific literature	NADH's biochemical effect
Dopaminergic neurotransmitter system dysfunction	Increases dopamine production by regenerating tetrahydrobiopterin, an essential cofactor in tyrosine hydroxylase
Increased oxidative stress	Repletes antioxidant level
Reduced activity of enzymes (i.e., NADH ubiquinone oxidoreductase and NADH diaphorase) important for energy metabolism in the brain	Reverses oxidative phosphorylation defects

graded by the hydrochloric acid in the stomach and rendered ineffective.

Current Research

At present, research evaluating the therapeutic applications of niacin and/or NADH for dementia is at a standstill. However, niacinamide is being evaluated in a clinical trial to determine if it is safe and beneficial for patients with AD.[41] Patients will be randomized to treatment or placebo groups. Those given niacinamide will take 1,500 mg twice daily for 24 weeks. The results of this study should be available within the next year. The rationale for using niacinamide is that it can prevent nerve cell degeneration in animal models of various neurodegenerative diseases (e.g., amyotrophic lateral sclerosis, Huntington's disease, and Parkinson's disease).[42-44] In addition, niacinamide was shown to markedly improve learning and memory in transgenic mice that develop AD. Treatment with the vitamin also resulted in decreased accumulation and increased stabilization of tau, a protein that accumulates excessively in AD.[45]

The earliest report showing that niacinamide can assist in dementia was written by Foster, in 1949, after he gave niacinamide to 40 patients with toxic psychosis (considered an organic reaction accompanied by memory defect, disorientation, and other mental deficits).[46] Twenty-three of the 40 patients were over the age of 60. Foster concluded that niacinamide therapy should be commenced at the onset of psychosis. He noted that the response is usually rapid and dramatic even when the toxic psychosis presents without signs of vitamin deficiency.

Current research demonstrates that niacinamide is likely to benefit patients with AD and vascular types of dementia because it provides global protection against neuronal and vascular injury.[47] Although the mechanisms that account for the vitamin's unique therapeutic properties are complex and require further delineation, niacinamide therapy may benefit patients by reducing neuronal damage associated with anoxia and nitric oxide cytodegeneration.[47]

Conclusion

Numerous clinical reports have shown that patients with dementia can benefit from niacin supplementation. Niacin can also help to prevent the incidence of AD. This makes niacin therapy a clinically-plausible intervention which merits further study. One open-label and one small randomized controlled trial have shown NADH to benefit patients with AD, but no substantive clinical trials have been done to confirm these preliminary findings. Only niacinamide is currently being investigated as a treatment for AD. Hopefully, the forthcoming results will be positive and encourage researchers and clinicians to review the literature and perform additional research to verify the benefits of vitamin B_3 therapy for treating dementia, develop dosage recommendations and revise clinical guidelines.

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Competing Interests

The author is a consultant for Veeva Inc., a company that develops and sells natural health products with a strong focus on stress, anxiety, sleep and overall mental health wellness. Veeva Inc. has not seen this manuscript nor do they have any knowledge of it.

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