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Case Report

A Case of Parkinson's Disease Symptom Reduction with Intravenous NAD+

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Abstract

Neurological deterioration in Parkinson's disease (PD) and resulting motor dysfunction arises from Lewy body formation and dopaminergic neuronal death in the substantia nigra. Two factors contributing to PD-related apoptosis and subsequent motor dysfunction involve improper cellular metabolism of reactive oxygen species (ROS) and impaired mitochondrial functionality. The co-factor Nicotinamide Adenine Dinucleotide (NAD^+), reduction of which has been implicated in the development of neurodegenerative disease, is a critical player in maintaining cellular redox metabolism and mitochondrial function. We present a case study of a PD patient who has become near asymptomatic through the use of intravenous (I.V.) NAD^+. This report documents the patient's initial symptom changes while receiving I.V. NAD^+ over the course of eight treatment days, with two non-treatment days in between. The treatment entailed 1500 mg. I.V. NAD^+ on day one, 1000 mg. I.V. NAD^+ on day two, and 750 mg. I.V. NAD^+ on day three. Symptoms were documented by medical staff for the next two days of non-treatment. Following this, 750 mg. I.V. NAD^+ was administered on treatment days four and five, 500 mg. I.V. NAD^+ on treatment days six and seven, and 750 mg. I.V. NAD^+ on treatment day eight. Over the course of treatment, the patient's hand tremors decreased to a mild level, permitting coordinated use of a pen and utensils. Hand tremors were absent on days one and six. Visual hallucinations were absent on days two through seven. To maintain tremors at a tolerable level, aftercare involved I.V. NAD^+ every four to six weeks, with a daily regimen of 300 mg/ml NAD^+ nasal spray. Moreover, the patient discontinued PD-related medication, thereby preventing visual hallucination side effects. Although more research on NAD^+ in clinical use is needed, the evidence obtained from these symptom improvements indicates NAD^+ as having the potential for clinical use in at least a subset of PD sufferers.

Keywords: *Parkinson's disease, neurodegeneration, NAD+*

Introduction

Recognized as the world's second most common adult-onset neurodegenerative disease, Parkinson's disease (PD) is a progressively debilitating disorder characterized by disturbances in motor functionality, including resting tremors, bradykinesia and muscular rigidity [1]. Side effects of commonly prescribed anti-PD treatment may also result in medication-induced visual hallucinations and paranoid delusions [2].

It is understood that neurological deterioration in PD results from the formation of Lewy bodies and the selective death of dopaminergic neurons within the substantia nigra. Increasing evidence asserts the interplay of improper cellular metabolism of reactive oxygen species (ROS), coincided with impaired mitochondrial function, as two interwoven factors contributing to PD-related apoptosis and subsequent motor dysfunction [3,4]. The co-factor nicotinamide adenine dinucleotide (NAD^+) is a critical player in healthy cellular redox metabolism and mitochondrial energy production [5,6]. In fact, a decrease in available NAD^+ has been implicated in the development of neurodegenerative disease [7]. Thus, it may be worth considering the potential effects flowing from a dysregulation of this central molecule in understanding the metabolic dysfunctions driving the development of PD and subsequent treatment.

Case Report

We report a case of a patient diagnosed with PD and documents his symptom changes over eight days of intravenously administered supplemental NAD^+ therapy. An 80-year-old man with a fourteen-year history of PD, with no other documented health or psychiatric illnesses, sought treatment at an outpatient clinic specializing in intravenous NAD^+ therapy. He was observed over a period of eight treatment days, with a break of two non-treatment days in between to accommodate a prior engagement.

Before his arrival, his symptoms included severe bilateral hand tremors, inability to hold utensils or sign his name, peripheral hallucinations, decreased social interaction, and overall compromised quality of life. The patient utilized 1.5 mg per day of Mirapex to treat his symptoms at the time of intake. The following observations were documented by medical staff as well as by the patient himself.

Prior to infusion on day one, the patient reported experiencing severe bilateral hand tremors and visual hallucinations. Approximately two hours into his first NAD^+ infusion, his tremors became unnoticeable, remaining so throughout the rest of that day's treatment, and only returning mildly in the evening. Additionally, the patient was finally able to hold utensils comfortably. On treatment day two, some hand tremors were present throughout the day, yet were significantly improved compared to time of arrival. There was a newly marked absence of visual hallucinations. On treatment day three, he experienced minor hand tremors throughout the day.

The following two days were days of non-treatment. On the first day of non-treatment, the patient reported a mild shaking of his right thumb upon waking, and slight tremors in both hands as the day progressed. By the next day of non-treatment, the patient reported that his hand tremors increased somewhat with movement, yet not while at rest, as the day progressed.

Commencing day four of treatment, the patient reported slight tremors upon waking which remained mild throughout the day. On treatment day five, while he still experienced mild bilateral tremors throughout the day, it was observed that he could write legibly. On treatment day six, he reported slight shaking in both thumbs only upon waking, which later disappeared throughout treatment. On treatment day seven, he reported no feeling of shakiness in either hand upon waking, although shakiness returned slightly as the day progressed. Upon waking the next morning prior to the eighth day of infusion, the patient only reported some peripheral hallucinations. His hallucinations disappeared over the course of this final, eighth NAD^+ infusion. He was observed to have slight hand tremors, which remained throughout this treatment day. By the end of his treatment program, he had received a total of 6500 mg of I.V. NAD^+ (Table 1).

Table 1: Summary of Treatment Days and Corresponding PD Symptoms

Day	Amount of NAD+ Delivered (mg)	PD Symptoms and Symptom Changes
Baseline	0	• Severe bilateral hand tremors • Inability to hold utensils • Inability to sign name and write legibly • Visual hallucinations • Decreased social interactions
Day 1 Treatment Day 1	1,500	• Hand tremors absent, returning slightly into evening • Ability to hold utensils*
Day 2 Treatment Day 2	1,000	• Mild hand tremors present • Visual hallucinations disappear
Day 3 Treatment Day 3	750	• Mild hand tremors present
Day 4 Non-treatment	0	• Mild hand tremors present
Day 5 Non-treatment	0	• Mild hand tremors present
Day 6 Treatment Day 4	750	• Mild hand tremors present
Day 7 Treatment Day 5	750	• Mild hand tremors present • Ability to write legibly*
Day 8 Treatment Day 6	500	• Hand tremors absent
Day 9 Treatment Day 7	500	• Mild Hand tremors present
Day 10 Treatment Day 8	750	• Peripheral hallucinations present in morning, but later disappear • Hand tremors present with movement only
*This symptom change began on this day and follows into the patient's current state.		

For follow-up PD maintenance, the patient regularly receives 1,000 mg of intravenous NAD^+ boosters, approximately every 4-6 weeks. He also maintains his symptoms with a 300 mg/ml NAD^+ nasal spray (0.1 ml per spray), twice in each nostril daily. This regimen continues to maintain his tremors at a tolerable, mild rate, allowing him significantly greater participation in daily activities (e.g. he has begun riding a bike again). In addition, as the patient's neurological symptoms have been significantly improved, he has been able to discontinue his PD-related medication. Using NAD^+ therapy alone has also enabled him to live without visual hallucinations. In all, he reports his quality of life as far more manageable and enjoyable, allowing him the ability to participate in many activities previously rendered impossible.

The reduction in PD symptoms this patient experienced during initial treatment, including the eventual discontinuation of anti-PD medication, lends significant anecdotal support for the use of NAD^+ as a potentially useful treatment for at least a subset of Parkinson's disease patients. Although the biochemical processes involved in PD pathogenesis are complex and varying between cases, the association between increased oxidative damage and reduced

NAD^+ availability in the pathobiochemistry of neurodegenerative disease provide at least some rationale for the marked symptom reduction in this case [7,8]. Additionally, as prior research suggests, increasing the availability of NAD^+ to dopaminergic neurons in the nigrostriatal tracts may have the potential to promote healthy mitochondrial function and DNA repair. Moreover, in a murine model, NAD^+ supplementation has demonstrated neuronal restoration following the induction of neurodegeneration [9,10]. Furthermore, one recent study has directly linked NAD^+ precursor administration to preventing dopaminergic neuronal loss in PD patient derived induced pluripotent stem cells [11]. Overall, our current study supports the notion that NAD^+ supplementation may be increasing cellular resilience to ongoing dopaminergic neuronal loss in this particular PD sufferer.

Although the evidence obtained from observations reported for this single individual does not claim that NAD^+ targets disease pathogenesis, the significant clinical improvements indicate that NAD^+ therapy can alleviate symptoms in at least a subset of PD sufferers. These extraordinary observations warrant further clinical investigation of NAD^+ and its potential to modulate key cellular processes impaired in neurodegenerative diseases such as PD.

While further research will be needed, these observations implicate that NAD^+ supplementation can have therapeutic value for at least symptomatic treatment in this neurodegenerative disease.

Conflict of Interest

Erin Gadol and Richard F. Mestayer are members of a research company on NAD^+ called NAD Research, Inc.

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