Parkinson’s disease managing reversible neurodegeneration

Abstract: Traditionally, the Parkinson’s disease (PD) symptom course has been classified as an irreversible progressive neurodegenerative disease. This paper documents 29 PD and treatment-induced systemic depletion etiologies which cause and/or exacerbate the seven novel primary relative nutritional deficiencies associated with PD. These reversible relative nutritional deficiencies (RNDs) may facilitate and accelerate irreversible progressive neurodegeneration, while other reversible RNDs may induce previously undocumented reversible pseudo-neurodegeneration that is hiding in plain sight since the symptoms are identical to the symptoms being experienced by the PD patient. Documented herein is a novel nutritional approach for reversible processes management which may slow or halt irreversible progressive neurodegenerative disease and correct reversible RNDs whose symptoms are identical to the patient’s PD symptoms.

Keywords: Parkinson’s disease, L-dopa, carbidopa, B6, neurodegeneration

Introduction

This study does not document a new Parkinson’s disease (PD) treatment, but discusses effective and novel side effect management associated with the most effective PD treatment known: L-dopa (L-3,4-dihydroxyphenylalanine). The following approach definitively addresses PD, L-dopa, and carbidopa-associated side effects and adverse reactions which interfere with achieving optimal L-dopa results.

PD is classified as a “progressive neurodegeneration” (PN) disease.1,2 With PD, irreversible brain damage involving the post-synaptic substantia nigra dopamine neurons3 induces fine motor control dysfunction4 (herein referred to as “electrical damage”).

A relative nutritional deficiency (RND) occurs when an optimal diet does not meet nutritional requirements.5–11 This paper demonstrates how the reversible PD symptoms induced by newly identified RNDs have been allowed to accumulate because of the disease process or traditional treatment. These symptoms have traditionally been exclusively attributed to irreversible PN. This novel approach breaks PN down into three subcategories: irreversible PN, reversible facilitated PN (FPN), and reversible pseudo-neurodegeneration (RPN).

PD electrical damage dysfunction is classically limited to the post-synaptic dopamine neurons.12,13 Electrical flow, regulating fine motor control, flows from the pre-synaptic neurons, across the synapse, then through the post-synaptic neurons. It is the novel primary hypothesis that if PD symptoms from post-synaptic neuron damage develop, then compromise at any point in the electrical event chain, to include outside the post-synaptic dopamine neuron focus, may exacerbate and mimic PD symptoms and/or disease progression.
With regard to the 29 depletion etiologies and seven primary RNDs illustrated in Figure 1, the medical care standard only addresses the dopamine precursor RND by incorporating L-dopa in a manner that accelerates other depletions while inducing RNDs and converts it to a drug with side effects, Figure 2.10,11

To prevent facilitated irreversible PN, carbidopa needs to be stopped while B6 and glutathione precursors need to be properly administered.

L-dopa may also deplete L-tryptophan, all thiols, and serotonin.33–40 Significant depletion induces an RND.5

Reversible pseudo-neurodegeneration

In the endogenous state there is an inverse relationship between central dopamine concentrations and PD symptom severity.37 Dopamine synthesis requires L-dopa and AADC.40 When B6 activates AADC it becomes the enzyme’s active site.41,42 The novel hypothesis is, if the post-synaptic electrical damage or compromise is no longer progressing, then dopamine precursor RND and/or B6 RND exacerbations will be responsible for the worsening PD symptoms due to inadequate dopamine concentrations. This novel RPN induced by L-dopa RND and B6 RND symptoms has been hiding in plain sight for years with symptoms identical to PD symptoms induced by irreversible PN.

The hypothesis is, if RPN is induced by carbidopa and carbidopa is discontinued without adequate B6 administration, then RND components may be misdiagnosed as irreversible PN.

B6 crosses the blood–brain barrier.74 At equilibrium, peripheral and central B6 represent one pool. Carbidopa-induced central B6 depletion has been known since 1978. With carbidopa administration the resulting B6 depletion may lead to collapse of central and peripheral B6-dependent enzymes including AADC which metabolizes L-dopa to dopamine. When L-dopa appears to stop working while carbidopa is administered, B6 driven AADC collapse needs to be considered as the etiology, not L-dopa tachyphylaxis. This is a reversible event which may wrongly be interpreted as irreversible PN.41

Other impacts

Carbidopa’s irreversible binding to B6 induces a double assault on B6-dependent enzyme integrity. It irreversibly binds to and then depletes the free B6 required to activate the enzyme. It irreversibly binds to the active site then irreversibly deactivates all B6-dependent enzymes.30,11

Carbidopa’s molecular weight is 244.3.51 Pyridoxal-5′-phosphate molecular weight is 247.140.74 One carbidopa molecule binds with one pyridoxal-5′-phosphate molecule. Administering carbidopa 100 mg has the potential to irreversibly deactivate B6 101.16 mg in the free and B6-dependent enzyme bound forms. A patient taking carbidopa 100 mg per day while ingesting the 2 mg B6 per day United States Recommended Dietary Allowance (US-RDA) for 5 years will have a potential 181,925 mg B6 deficit.

L-dopa was introduced in 1959. From its introduction until 1976 there was a year-to-year decrease in the PD mortality rate. B6 depletion is documented to increase death rates from heart failure, coronary artery disease, colorectal cancer, stroke, peripheral vascular disease, and atherosclerosis. Literature from 2014 linked the increasing PD death rate to carbidopa-induced B6-depletion. Carbidopa, whose mechanism of action is B6 depletion, was introduced in 1975. PD mortality increased over 328% between 1976 and 2011.11

Prior to 1976, an era with no carbidopa administration, irreversible dyskinesias were not reported. In 2014, the authors documented that irreversible dyskinesias are caused by carbidopa, not L-dopa. The mechanism of action is a carbidopa-induced B6 RND which compromises the two B6-dependent enzymes, histidine decarboxylase and AADC, which metabolize histidine to histamine. B6 depletion may induce profound carbidopa-induced antihistamine dyskinesias which have been wrongly described as L-dopa-induced dyskinesias in the past. Managing these dyskinesias requires stopping carbidopa and administering adequate B6. If adequate B6 is not administered the dyskinesias may be perceived as permanent and irreversible.11