Don't let the problems associated with L-dopa and carbidopa stand in the way of your Parkinson's patient getting better.

Imagine a world where all the Parkinson's disease problems were manageable.

"It is asserted that virtually all of the problems encountered in the administration of L-dopa for Parkinson's disease are caused by the improper management of systems impacted by L-dopa and/or the concomitant use of carbidopa with L-dopa." (Hinz et. al. 2011c)

"The literature is clear that L-dopa holds the highest potential for relief of symptoms, but dosing values in many patients are limited by side effects. With administration of L-dopa, side effects and adverse reactions may be the dose-limiting event that prevents attaining optimal dosing values. The following discussion is aimed at defining the basis for an effective treatment that controls the problems associated with L-dopa administration." (Hinz et. al. 2011c)

Simply administering some 5-HTP, L-tyrosine and/or sulfur amino acids is not adequate; OCT assay interpretation needs to be utilized for optimal results.

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CASE REPORT

Amino acid management of Parkinson's disease: a case study

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Abstract: An extensive list of side effects and problems are associated with the administration of L-dopa (L-3, 4-dihydroxyphenylalanine) during treatment of Parkinson's disease. These problems can preclude achieving an optimal response with L-dopa treatment.

Purpose: To present a case study outlining a novel approach for the treatment of Parkinson's disease that allows for management of problems associated with L-dopa administration and discusses the scientific basis for this treatment.

Patients and methods: The case study was selected from a database containing 254 Parkinson's patients treated in developing and refining this novel approach to its current state. The spectrum of patients comprising this database range from newly diagnosed, with no previous treatment, to those who were diagnosed more than 20 years before and had virtually exhausted all medical treatment options. Parkinson's disease is associated with depletion of tyrosine hydroxylase, dopamine, serotonin, and norepinephrine. Exacerbating this is the fact that administration of L-dopa may deplete L-tyrosine, L-tryptophan, 5-hydroxytryptophan (5-HTP), serotonin, and sulfur amino acids. The properly balanced administration of L-dopa in conjunction with 5-HTP, L-tyrosine, L-cysteine, and cofactors under the guidance of organic cation transporter functional status determination (herein referred to as "OCT assay interpretation") of urinary serotonin and dopamine, is at the heart of this novel treatment protocol.

Results: When 5-HTP and L-dopa are administered in proper balance along with L-tyrosine, L-cysteine, and cofactors under the guidance of OCT assay interpretation, the long list of problems that can interfere with optimum administration of L-dopa becomes controllable and manageable or does not occur at all. Patient treatment then becomes more effective by allowing the implementation of the optimal dosing levels of L-dopa needed for the relief of symptoms without the dosing value barriers imposed by side effects and adverse reactions seen in the past.

Keywords: Parkinson's, Parkinsonism, Parkinson's disease, L-dopa, 5-HTP

Introduction

There is a need to effectively control and manage the problems associated with L-dopa treatment in every Parkinson's patient allowing full access to the L-dopa dosing level needed by each Parkinson's patient in order to achieve optimal relief of symptoms.[1,2]

This novel approach allows for the full access to the required L-dopa dosing values through minimization or elimination of the undesirable L-dopa side effects. This is the first attempt to formally document some of the results seen and the experience gained in refining this novel protocol as applied to Parkinson's disease.

Based on clinical experience gained with this novel protocol, it is asserted that virtually all of the problems encountered in the administration of L-dopa for Parkinson's

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Don't let the problems associated with L-dopa stand in the way of your Parkinson's patient getting better.

Category 1: Problems caused by depletion of serotonin by L-dopa

Category 2: Problems caused by imbalance of serotonin and dopamine

Category 3: Problems caused by dopamine fluctuations due to inadequate tyrosine levels

Category 4: Problems caused by depletion of sulfur amino acids by L-dopa

Category 5: Problems caused by paradoxical amino acid reactions

Category 6: Peripheral problems caused by peripheral depletion of serotonin and catecholamines by carbidopa

(Hinz et. al. 2011c)

Medical Food

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Pages 11 to 20 – The scientific basis for treatment

Medical Foods

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The Problem

"Parkinson's disease is associated with depletion of tyrosine hydroxylase, dopamine, serotonin and norepinephrine. Exacerbating this is the fact that administration of L-dopa may deplete L-tyrosine, L-tryptophan, 5-hydroxytryptophan (5-HTP), serotonin, and sulfur amino acids. The properly balanced administration of L-dopa in conjunction with 5-HTP, L-tyrosine, L-cysteine and cofactors under the guidance of organic cation transporter functional status determination (herein referred to as "OCT assay interpretation") of urinary serotonin and dopamine, is at the heart of this novel treatment protocol." (Hinz et. al. 2011cc)

Systems depleted by Parkinson's disease, treatment with only L-dopa, and treatment with carbidopa.

	Status in Parkinson's disease	Status with L-dopa Rx	Status with Carbidopa Rx
Serotonin (Central)	Depleted	Further Depleted	
Dopamine (Central)	Depleted	Further Depleted	
Norepinephrine (Central)	Depleted	Further Depleted	
Epinephrine (Central)	Depleted	Further Depleted	
Serotonin (Peripheral)	Depleted	Further Depleted	Further Depleted
Dopamine (Peripheral)	Depleted	Further Depleted	Further Depleted
Norepinephrine (Peripheral)	Depleted	Further Depleted	Further Depleted
Epinephrine (Peripheral)	Depleted	Further Depleted	Further Depleted
L-tyrosine		Depleted	
Tyrosine Hydroxylase	Depleted		
L-tryptophan		Depleted	
5-Hydroxytryptophan		Depleted	
Sulfur amino acids		Depleted	

Source: Hinz et. al. 2011c.

"The hypothesis is that the majority of side effects and problems observed during treatment of Parkinson's disease with L-dopa are caused by mismanagement of the amino acid precursors and systems affected by L-dopa." (Hinz et. al. 2011cc)

The Fix

"When 5-HTP and L-dopa are administered in proper balance along with L-tyrosine, L-cysteine, and cofactors under the guidance of OCT assay interpretation, the long list of problems that can interfere with optimum administration of L-dopa becomes controllable and manageable or does not occur at all. Patient treatment then becomes more effective by allowing the implementation of the optimal dosing levels of L-dopa needed for the relief of symptoms without the dosing value barriers imposed by side effects and adverse reactions seen in the past." (Hinz et. al. 2011cc)

"Since the development of nausea from L-dopa is the result of serotonin levels that are either too high or too low and the high or low status of the serotonin relative to dopamine cannot be distinguished clinically, OCT assay interpretation is indicated to properly clarify and manage the problem." (Hinz et. al. 2011cc)

"The hypothesis of this writing is that the majority of side effects and problems observed during treatment of Parkinson's disease with L-dopa are caused by mismanagement of the amino acid precursors and systems affected by L-dopa." (Hinz et. al. 2011c)

Table 1: Parkinson's disease medical food protocol

	AM (pill / dose)	NOON (pill / dose)	4 PM (pill / dose)
Initial visit	4-D5	—	4-D5
After one week	4-D5 2-D5 Mucuna 40%	— 2-D5 Mucuna 40%	4-D5 2-D5 Mucuna 40%
Once a week after starting D5 Mucuna 40% two pills three times a day. Obtain a urine sample then submit it for Organic Cation Transporter assay interpretation.			

- All patients need to take CysReplete two pills three times a day, with the first dose at noon to prevent sulfur amino acid depletion by L-tyrosine and L-dopa.
- D5 Mucuna 40%" contains 40% L-dopa by weight.

"Everything used in this treatment approach (including L-dopa) is recognized by the FDA as GRAS (generally regarded as safe) and available over the counter without a prescription in the United States." (Hinz et. al. 2011c)

"Peer-reviewed literature suggests that L-dopa from the mucuna pruriens source has more rapid onset of action and a longer time of effectiveness leading to the conclusion that it may be a superior source of l-dopa in treating Parkinson's disease." (Hinz et. al. 2011c)

"The most prominent dose-limiting events in the use of L-dopa are the GI symptoms of nausea and vomiting along with psychiatric problems." (Hinz et. al. 2011c)

Selected Pearls of Treatment

1. Mastery of this approach requires experience. Full technical support is available at 877-626-2220.
2. No problems have been observed requiring permanent stoppage of the amino acids.
3. Patients at the first visit need to understand and be able to participate in weekly care that may take 2 to 4 months before stabilization occurs.
4. Patients need to be seen weekly. Failure to do so may greatly lengthen the amount of time needed to stabilize the patient.
5. Paradoxical reactions (see page 7) tend to occur in the Parkinson's patient late in treatment as the amino acid dosing values are on the verge of symptoms coming under control.
6. Read the peer-reviewed articles on the web site www.HinzMD.com.
7. The typical Parkinson's patient requires between 40 and 80 pills per day of D5 Mucuna 40% for stabilization, although 10% need more and 10% need less. This is too many pills to take. As the L-dopa dosing value increases, most patients are changed to "D5 Mucuna Powder" where 1 level tablespoonful equals 22 pills (one level teaspoonful equals 7.333 pills. The powder is mixed with any water-soluble liquid then swallowed.

DRUGS: Drugs used in the treatment of Parkinson's disease should be continued until the patient is stable, at which time they can be slowly tapered to a stop. If a drug side effect develops while starting or increasing the amino acid dosing value, treat this as a drug problem and not an amino acid problem. The side effects of drugs that work with neurotransmitters can be activated with the amino acids in about 5% of patients.

MEDICAL FOODS STATEMENT: 1) These medical foods are specially formulated and processed products for the patient by means of oral intake. 2) These medical foods are intended for the dietary management of a patient who has other special medically determined nutrient requirements needing increased levels of monoamine neurotransmitters, the dietary management of which cannot be achieved by the modification of normal diet alone. 3) These medical foods are intended to be used under active and ongoing medical supervision wherein the patient requires medical care on a recurring basis for, among other things, instructions on the use of the medical food. 4) They provide nutritional support specifically modified for the management of the unique (distinctive) nutrient needs that result from the specific disease or condition, as determined by medical evaluation.

The dosing range of serotonin precursors needed for the individual patient to achieve proper balance with L-dopa administration appears to be in a relatively narrow range with some of the side effects, such as nausea, being displayed if the serotonin is either too high or too low.

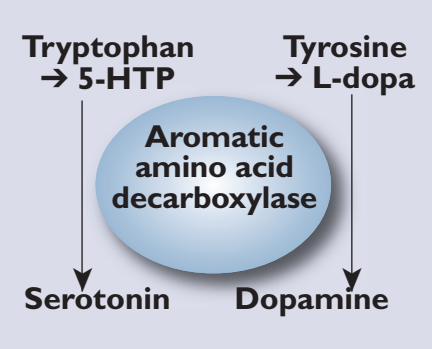
The Competitive Inhibition State

Observed only when serotonin and dopamine amino acid precursors are given in significant amounts.

In the competitive inhibition state, serotonin and catecholamine (dopamine, norepinephrine, and epinephrine) systems are completely intertwined; anything that affects one system affects the other system. For optimal group treatment results, both systems must be addressed in proper balance.

Some of the ways L-dopa depletes

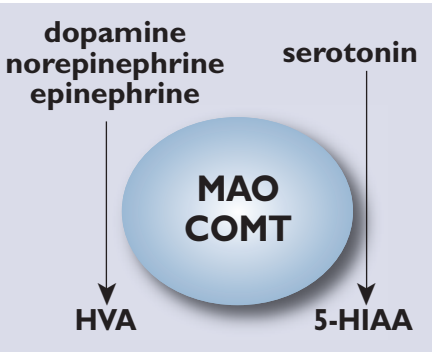
When serotonin depletion is great enough, L-dopa quits working.



The same enzyme, L-aromatic amino acid decarboxylase (AAAD), catalyzes the conversion of 5-HTP to serotonin and L-dopa to dopamine. The implications of this fact are profound.

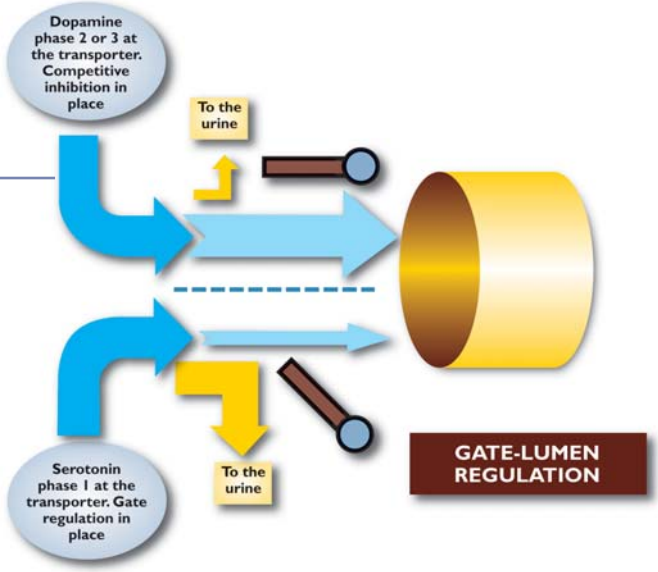
Administration of only L-dopa loads the enzyme blocking synthesis of serotonin by competitive inhibition. When serotonin levels drop low enough, tachyphylaxis (drug stops working) of L-dopa sets in. Nausea from L-dopa may develop along with other problems listed on pages 6 and 7 of this brochure.

The monoamine neurotransmitters do not cross the blood-brain barrie. The only way to increase central nervous system levels are with administration of amino acid precursors.



The monoamine oxidase (MAO) metabolizes both serotonin and catecholamines. The activity of this enzyme is not static. Increasing levels of dopamine increases the levels of activity of this enzyme system leading to increased metabolism and depletion of serotonin if additional serotonin amino acid precursors are not administered. When serotonin levels drop low enough, tachyphylaxis (drug stops working) of L-dopa sets in. Nausea from L-dopa may develop along with other problems listed on pages 6 and 7 of this brochure.

Administration of proper levels of serotonin and dopamine precursors guided by OCT assay interpretation minimizes side effects allowing for the dosing values of L-dopa needed for symptom control.



Transport of the monoamines and their amino acid precursors into and out of cellular structures is facilitated by the Organic Cation Transporters (OCT). In transport there is competitive inhibition between serotonin, the catecholamines, and their amino acid precursors. Giving only L-dopa will exclude serotonin and its precursors from transport, leading to depletion of serotonin as amino acid uptake needed for synthesis is blocked. When serotonin levels drop low enough, tachyphylaxis (drug quits working) of L-dopa sets in. Nausea from L-dopa may develop along with other problems listed on pages 6 and 7 of this

OCT Assay Interpretation

(Continued on page 8)

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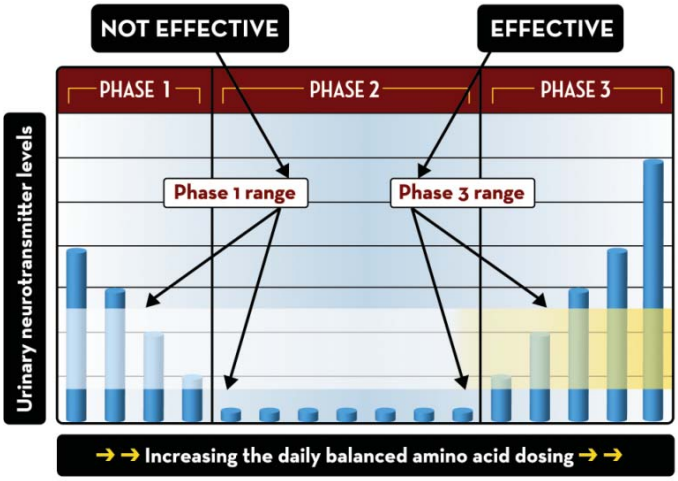
"The goal of this novel approach is to keep the urinary serotonin in the phase 3 therapeutic range, no higher than 800 µg serotonin per gram of creatinine, through proper manipulation of 5-HTP in combination with L-dopa dosing values under the guidance of OCT assay interpretation." (Hinz et. al. 2011c)

The source of urinary monoamine neurotransmitters

"The serotonin and dopamine filtered at the glomerulous are metabolized by the kidneys, and significant amounts do not make it to the final urine. Serotonin and dopamine found in the urine are monoamines synthesized in the proximal convoluted renal tubule cells and have never been found in the central nervous system or peripheral system. Serotonin and dopamine that are newly synthesized by the kidneys meet one of two fates. Urinary serotonin and dopamine levels are primarily dependent on the interaction of the basolateral monoamine transporters (OCT2s) and the apical monoamine transporters (OCTN2s) of the proximal convoluted renal tubule cells of the kidneys. The OCTN2s of the proximal convoluted renal tubule cells transport serotonin and dopamine that is not transported by the OCT2. While in the competitive inhibition state, serotonin and dopamine not transported by the OCT2s are found in the final urine as waste. Although there are numerous other forces that interact with the newly synthesized renal monoamines, they are small compared with the effects of these transporters. Proper interpretation of urinary serotonin and dopamine levels in the competitive inhibition state determines the functional status of the OCT2s of the proximal convoluted renal tubule cells of the kidneys, known as OCT assay interpretation. The OCT2s exist in three different phases dependent on the status of the entrance gate and lumen saturation. " (Hinz et. al. 2011c)



"With proper serotonin–dopamine balance nausea is no longer an L-dopa dose-limiting event for virtually all patients and the use of carbidopa is no longer needed. Since the development of nausea is the result of serotonin levels that are either too high or too low and the high or low status of the serotonin relative to dopamine cannot be distinguished clinically, OCT assay interpretation is indicated to properly clarify and manage the problem." (Hinz et. al. 2011c)

The 3 phase response of the organic cation transporters

"Serotonin and dopamine exist in two states. The endogenous state is found when no amino acid precursors are being administered. The competitive inhibition state is found when significant amounts of amino acid precursors of both serotonin and dopamine are administered simultaneously."

"The basis for OCT assay interpretation requires that the system be placed into the competitive inhibition state and then two or more urinary serotonin and dopamine assays performed while taking serotonin and dopamine amino acid precursors at significantly varied dosing values. The results are then compared in order to determine the change in urinary serotonin and dopamine levels in response to the change in amino acid precursor dosing values. Urinary serotonin and dopamine values found on assay were reported in micrograms of monoamine per gram of creatinine in order to compensate for fluctuations in urinary specific gravity. A urinary serotonin or dopamine value less than 80 or 475 µg of monoamine per 1 g of creatinine, respectively, is defined as a Phase 2 response. A urinary serotonin or dopamine value greater than 80 or 475 µg of monoamine per 1 g of creatinine, respectively, is interpreted as being in Phase 1 or Phase 3. Differentiation of Phase 1 from Phase 3 is as follows. If a direct relationship is found between amino acid dosing and urinary assay response, it is referred to as a Phase 3 response. An inverse relationship is referred to as a Phase 1 response. The Phase 3 therapeutic range for urinary serotonin is defined as 80–240 µg of serotonin per g of creatinine. The Phase 3 therapeutic range for urinary dopamine is defined as 475–1100 µg of dopamine per g of creatinine." (Hinz et. al. 2011c)

RESPONSE is like a light switch

Some patients get relief of symptoms in one week while others may not get relief of symptoms until 2 or 3 months into treatment. Along the way most patients do not get better gradually with each amino acid dosing value adjustment. For most the response to amino acids is like a light switch, "on or off", with no relief of symptoms occurring until the proper amino acid dosing value is found secondary to several urinary transporter assays being performed.

PROPER MANAGEMENT OF AMINO ACIDS

PATIENT ORIENTATION:

At the first visit all patients need to be instructed as follows: **"If there are any problems in the first week of treatment, stop the amino acids until you get back to clinic and I will tell you what to do."** Failure to properly orient patients at the first visit will result in patients dropping out of care if problems are experienced in the first week of treatment.

GI UPSET → ON START UP

THE PROBLEM: Approximately 1% to 2% of patients (higher in some medical practices where patients have been exposed at a higher rate to drugs that deplete neurotransmitters) experience GI upset or nausea on starting the amino acids. Typically, this starts with the first dose and builds with every dose until the third day, at which point the patient can no longer tolerate the symptoms.

THE CAUSE: The patients who are most depleted of neurotransmitters experience GI upset or nausea on starting the amino acids. *These are the very patients who need the amino acids the most*.

MANAGEMENT: Restart the NeuroReplete taking only one pill at bedtime. Bedtime is when the patient is ready to get in bed and go to sleep, not when the patient gets in bed and reads a book for an hour. If the patient can fall asleep within 20 minutes after taking the one pill of NeuroReplete there should be no problems with GI upset. After three or four nights with no GI problems increase the NeuroReplete to two pills at bedtime. When the patient is able to take two pills at bedtime with no problems, start one pill in the AM then increase to two pills after three or four days of no problems. In adults, when the patient is taking two pills of NeuroReplete, twice a day, submit a urine sample for transporter evaluation.

GI UPSET → CARBOHYDRATE INTOLERANCE

THE PROBLEM: Once the proper dosing values of the amino acids have been established, patients may experience transient nausea lasting 45 to 60 minutes periodically during the day. The etiology of this problem is distinctly different than "GI upset on start up" discussed above.

THE CAUSE: With optimization of neurotransmitter transporters, the way the body reacts to specific carbohydrates may change causing nausea.

MANAGEMENT: Usually only one food needs to be changed. Most of the time, it is a bread, cereal, or noodle that needs to be changed. Examples of effective management include 1) Changing from white to whole wheat bread. 2) Changing from one type of noodle to another. 3) Changing from one cereal to another, for example changing from Wheaties to Shredded Wheat. At times identification of the food can be difficult, one case of carbohydrate intolerance was tracked down to the breading on chicken eaten with most lunches.

HEARTBURN (PYROSIS)

THE PROBLEM: Intense substernal or epigastric burning or nausea after taking the pills.

THE CAUSE: When the veggie caps are simply gulped down with some water the surface does not liquefy properly causing the pills to stick in the esophagus and dissolve, at which time an intense substernal or epigastric discomfort is experienced.

MANAGEMENT: Hold the pills in the mouth with water for 10 to 15 seconds before swallowing so that the capsule surface starts to liquefy and slides down easily.

PRESCRIPTION DRUG SIDE EFFECTS

THE PROBLEM: The recommendation is to leave all drugs in place when starting the amino acids. Side effects not associated with the amino acids may occur in 3% to 5% of patients while starting or changing the amino acid dosing.

THE CAUSE: Drugs that work with neurotransmitters not only become more effective as neurotransmitter levels increase with amino acid administration; the side effects of these drugs may display as well.

MANAGEMENT: Proper management is to treat the event like a drug side effect. DO NOT stop the amino acids. Tapering or stopping the drug causing the side effect is proper management.

Amino acid only side effect profile

Dry mouth	2.1%
Insomnia	0.9%
Headache	0.7%
Nausea	0.6%
Dizziness	0.4%
Constipation	0.4%

All other side effects occur at a rate less than 1 in 500 visits

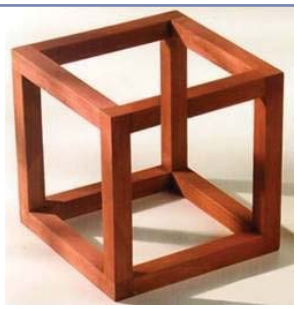
WHEN AMINO ACIDS STOP WORKING

THE PROBLEM: The patient's symptoms are under control, then it appears that the pills stopped working and symptoms of disease return.

THE CAUSE: Missing one or more doses of amino acids can cause symptoms of disease to return. It then may take three to five days for symptoms to get back under control once the pills are taken correctly. Missing one dose of pills every three or four days for several weeks may make it appear that the amino acids have stopped working for several weeks.

MANAGEMENT: In 99% of patients for whom the pills stop working it is a compliance issue relating to taking the pills properly. Have the patient journal (write down) all pills taken for seven to ten days. After journaling, if the patient's symptoms are not under control, submit a urine sample for transporter assay. Only 1% of patients experience a change in dosing needs during treatment and retesting can manage this problem.

PARADOXICAL REACTIONS



THE PROBLEM: A specific amino acid dosing value is started or changed and the patient complains of an exacerbation of symptoms related to one or more monoamine neurotransmitter related diseases (see page 8). For example, depression may get worse, sleep may get worse, the patient may get more agitated, anxiety may get worse, migraines may get worse, etc.

THE CAUSE: The exact cause of paradoxical reactions is unknown, but it is known that there is a dosing range within which they do occur.

MANAGEMENT: When a paradoxical reaction is identified, it is an indication that the amino acid dosing value needs to be increased, at which point the paradoxical symptoms will resolve in one to two days. If the dose is lowered in hopes of increasing the dosing values slowly the patient's suffering will be unnecessarily prolonged as the patient is subjected to the dosing value range where symptoms occur for a prolonged period of time.

DIZZINESS

THE PROBLEM: Dizziness (vertigo) may be caused by many different things when taking amino acids. As with paradoxical reactions, in many cases it is an indication to increase the amino acid dosing.

THE CAUSE: While complaints of dizziness may have many etiologies, dizziness associated with inadequate amino acid dosing is responsive to food intake. If the patient complains of dizziness which resolves after eating a small amount of carbohydrate, such as a candy, cookie, pastry, etc. it is a carbohydrate-dependent vertigo which can develop during amino acid treatment.

MANAGEMENT: Management of "carbohydrate dependent vertigo" involves increasing the amino acid dosing values, when done properly symptoms will resolve in one to two days. Any patient taking amino acids with complaints of dizziness needs to be properly evaluated for "carbohydrate-dependent vertigo".

HYPERSOMNOLENCE

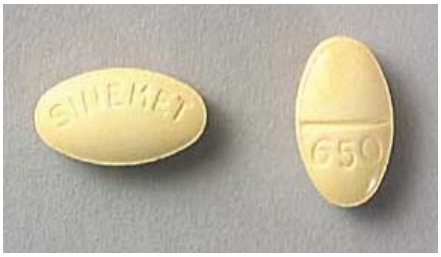
THE PROBLEM: The patient recently started on amino acids may present at the clinic complaining of excess sleepiness to the point of having problems staying awake at work or during other daily activities.

THE CAUSE: In general, these patients were suffering from poor sleep prior to treatment and have a "sleep debt" that needs to be repaid prior to feeling optimal again.

MANAGEMENT: The first thing to do when complaints of excessive tiredness are encountered is to take a medical history to determine whether the cause is an imbalance in the amino acids or if the patient is suffering from a sleep debt that needs to be repaid. In patients with very poor sleep prior to treatment (three to four hours per night), stop the amino acids and restart them on a Friday if the patient has the weekend off, telling the patient to sleep all weekend. If sleep was not a problem prior to treatment, cut the amino acid dosing in half, then obtain a urinary transporter analysis in order to determine the proper level of amino acids needed.

Two heads are better than one, and experience trumps all. There are no problems that should require long-term stoppage of the amino acids other than the patient quitting treatment.

The FDA-approved prescribing information for carbidopa/L-dopa preparations was reviewed and a list of side effects, adverse reactions, and problems associated with administration was generated. Each side effect was then placed in one or more of the general categories listed below by the authors of this paper. While the listing of each side effect may be open to further discussion, these are the categories that have evolved in this research project since 2001. The six categories of carbidopa/ L-dopa side effects are as follows: (Hinz et. al. 2011cc)

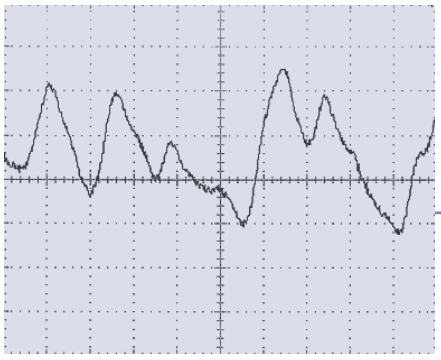


Category 1: Problems caused by depletion of serotonin by L-dopa:

Tachyphylaxis (the l-dopa stops working).

Category 2: Problems caused by imbalance of serotonin and dopamine:

Nausea, vomiting, anorexia, weight loss, decreased mental acuity, depression, psychotic episodes including delusions, euphoria, pathologic gambling, impulse control, confusion, dream abnormalities including nightmares, anxiety, disorientation, dementia, nervousness, insomnia, sleep disorders, hallucinations and paranoid ideation, somnolence, memory impairment, and increased libido.



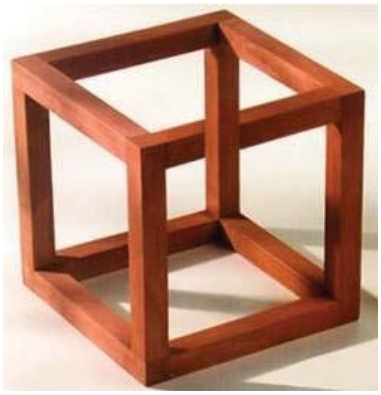
Category 3: Problems caused by dopamine fluctuations due to inadequate tyrosine levels:

On-off effect, motor fluctuations, dopamine fluctuations, implicated as an etiology of dyskinesia.

Category 4: Problems caused by depletion of sulfur amino acids by L-dopa:

Bradykinesia (epinephrine depletion implicated), akinesia, dyskinesia, dystonia, chorea, extrapyramidal side effects, fatigue, abnormal involuntary movements, and depletion of glutathione potentiating further dopamine neuron damage by neurotoxins.

Category 5: Problems caused by paradoxical amino acid reactions:



Confusion, dizziness, headache, palpitations, dyspnea, anxiety, agitation, increased tremor, faintness, exacerbation of any disease related to the monoamine (serotonin, dopamine, norepinephrine, and epinephrine) neurotransmitters, and exacerbation of any central disease process associated with the serotonin and catecholamine systems.

CARBIDOPA

Carbidopa is a general decarboxylase inhibitor. It inhibits L-aromatic amino acid decarboxylase (AAAD), the enzyme that catalyzes synthesis of both serotonin and dopamine from 5-HTP and L-dopa, respectively. Carbidopa does not cross the blood–brain barrier. It exerts its actions peripherally. In Parkinson's disease it is administered to decrease peripheral conversion of L-dopa to dopamine. This results in the need for a lesser dose of L-dopa peripherally while still giving the higher level in the CNS with fewer side effects, especially nausea. Carbidopa is used to address the side effects seen when improperly balanced L-dopa is administered; there is no direct therapeutic value of carbidopa in treatment of Parkinson's disease.

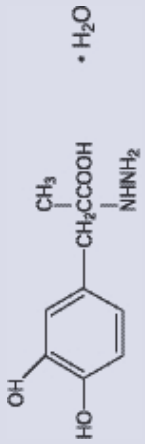
Carbidopa's inhibition of AAAD potentiates peripheral serotonin, dopamine, norepinephrine, and epinephrine depletion as synthesis by AAAD is compromised. Norepinephrine and acetylcholine regulate autonomic nervous system function. The administration of carbidopa with L-dopa is replete with peripheral autonomic dysfunction problems that often develop.

Administration of carbidopa/L-dopa preparations leads to a "double depletion" of peripheral serotonin. One cause of depletion is carbidopa inhibition of AAAD; the other cause is improperly balanced administration of L-dopa which decreases peripheral serotonin synthesis and transport through competitive inhibition along with increasing the metabolism of serotonin. (Hinz et. al. 2011c)

This novel approach for the treatment of Parkinson's disease is dependent upon the administration of L-dopa in adequate amounts to control symptoms through minimization of side effects and adverse reactions by establishing a proper balance between the dopamine and serotonin systems with the concomitant use of 5-hydroxytyrptophan (5-HTP), l-tyrosine, and a sulfur amino acid under the guidance of organic cation transporter (OCT) assay interpretation.

Category 6: Peripheral problems caused by peripheral depletion of serotonin and catecholamines by carbidopa:

Glossitis, leg pain, ataxia, falling, gait abnormalities, blepharospasm (which may be taken as an early sign of excess dosage), trismus, increased tremor, numbness, muscle twitching, peripheral neuropathy, myocardial infarction, flushing, oculogyric crises, diplopia, blurred vision, dilated pupils, urinary retention, urinary incontinence, dark urine, hoarseness, malaise, hot flashes, sense of stimulation, dyspepsia, constipation, palpitation, fatigue, upper respiratory infection, bruxism, hiccups, common cold, diarrhea, urinary tract infections, urinary frequency, flatulence, priapism, pharyngeal pain, abdmoninal pain, bizarre breathing patterns, burning sensation of tongue, back pain, shoulder pain, chest pain (non-cardiac), muscle cramps, paresthesia, increased sweating, falling, syncope, orthostatic hypotension, asthenia (weakness), dysphagia, Horner's syndrome, mydriasis, dry mouth, sialorrhea, neuroleptic malignant syndrome, phlebitis, agranulocytosis, hemolytic and non-hemolytic anemia, rash, gastrointestinal bleeding, duodenal ulcer, Henoch-Schonlein purpura, decreased hemoglobin and hematocrit, thrombocytopenia, leukopenia, angioedema, urticaria, pruritus, alopecia, dark sweat, abnormalities in alkaline phosphatase, abnormalities in SGOT (AST), SGPT (ALT), abnormal Coombs' test, abnormal uric acid, hypokalemia, abnormalities in blood urea nitrogen (BUN), increased creatinine, increased serum LDH, and glycosuria.



Carbidopa

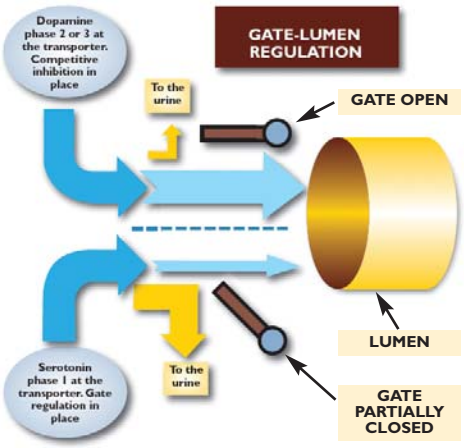
TRANSPORTER FUNCTIONAL STATUS DETERMINATION

(Continued from page 5)

Neurotransmitter levels for all systems are primarily dependent on the functional status of the organic cation transporters.

GATE-LUMEN TRANSPORTER STATUS FOR EACH PHASE

	Gate	Lumen
Phase 1	Partially closed	Unsaturated
Phase 2	Open	Unsaturated
Phase 3	Open	Saturated



**Dual-gate lumen organic cation transporter model developed by Hinz et al 2010.*

As noted in numerous peer-reviewed scientific writings, determination of transporter functional status can only be done in the "competitive inhibition state" found when significant amounts of serotonin and dopamine amino acid precursors are being taken simultaneously. Assays in the endogenous state performed while taking no amino acids are meaningless.

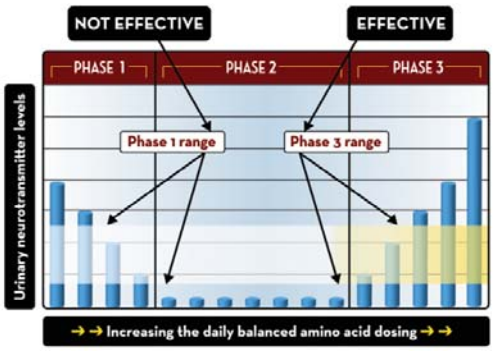
The goal of treatment is to get both the serotonin and dopamine into the phase 3 responses with urinary levels just over the phase 2 threshold (80 to 240 µ of serotonin per g of creatinine and 475 to 1,100 µ of dopamine per g of creatinine).

Interpretation of urinary data for phase determination rests on some simple concepts, but actual interpretation can become quite complex.

With each urine sample submitted to DBS Labs, a formal lab report is generated, followed the next day by a phase interpretation with suggested recommendations for moving serotonin and dopamine closer to the desired phase 3 ranges.

The phases of serotonin and dopamine occur independent of each other. One can be in any of the three phases while the other is likewise.

Relief of symptoms is like shooting at a target, where urinary serotonin and dopamine in the phase 3 therapeutic ranges is the bull's eye. Some patients are symptom free by merely hitting the edge of the target; others need to be fully into the phase 3 therapeutic ranges before relief of symptoms is seen.



The organic cation transporters of the kidneys, brain, liver, and bowels are "identical and homologous". Once the amino acids and neurotransmitters are at equilibrium, determining the functional status of one set of transporters will give insight into other sets of transporters.

Monoamine Neurotransmitter Diseases

(Partial listing)

- Parkinsonism
- Obesity
- Bulimia
- Anorexia
- Depression
- Anxiety
- Panic Attacks
- Migraine Headaches
- Tension Headaches
- Premenstrual Syndrome (PMS)
- Menopause Symptoms
- Obsessive Compulsive Disorder (OCD)
- Compulsivity
- Insomnia
- Impulsivity
- Obsessionality
- Inappropriate Aggression
- Inappropriate Anger
- Psychotic Illness
- Fibromyalgia
- Chronic Fatigue Syndrome
- Adrenal Fatigue/Burnout
- Hyperactivity
- ADHD/ADD
- Hormone Dysfunction
- Adrenal Dysfunction
- Dementia
- Alzheimer's Disease
- Traumatic Brain Injury
- Phobias
- Chronic Pain
- Nocturnal Myoclonus
- Irritable Bowel Syndrome
- Crohn's Disease
- Ulcerative Colitis
- Cognitive Deterioration
- Functional Deterioration
- Increased Mortality Rate
- Organ System Dysfunction
- Chronic Stress
- Cortisol Dysfunction
- Hormone Dysfunction
- Restless Leg Syndrome

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MEDICAL FOODS based on scientific writings found in the following peer-reviewed scientific research:

Hinz, M. 2009 Depression, In: Kohlstadt I. editor. Food and Nutrients in Disease Management CRC Press; 465-481.

Hinz, M. Stein, A, Uncini T. 2010a The dual-gate lumen model of renal monoamine transport Neuropsychiatric Disease and Treatment 6 387–392

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Hinz, M. Stein, A. Uncini T. 2010c A pilot study differentiating recurrent major depression from bipolar disorder cycling on the depressive pole, NeuroPsychiatric Disease and Treatment Neuropsychiatric Disease and Treatment:6 741–747

Hinz, M. Stein A. Uncini T. 2011a Treatment of attention deficit hyperactivity disorder with monoamine amino acid precursors and organic cation transporter assay interpretation Neuropsychiatric Disease and Treatment 2011:7 31–38

Hinz, M. Stein, A. Uncini T. 2011b Urinary neurotransmitter testing: considerations of spot baseline norepinephrine and epinephrine Open Access Journal of Urology 2011:3 19–24

Hinz, M. Stein, A. Uncini T. 2011c Amino acid management of Parkinson's disease: A case study International Journal of General Medicine 2011:4 1–10

Stein, A. Hinz, M. Uncini T. Amino acid responsive Crohn's disease, a case study. Clinical and Experimental Gastroenterology 2010:3 171–177

Trachte, G. Uncini, T. Hinz, M, 2009 Both stimulatory and inhibitory effects of dietary 5-hydroxytryptophan and tyrosine are found on urinary excretion of serotonin and dopamine in a large human population Neuropsychiatric Disease and Treatment:5 227–235