

LEVODOPA: GOOD OR BAD?

Nina Brown

Since its discovery 34 years ago, levodopa, and then levodopa with carbidopa (Sinemet) has been the drug of choice, the “gold standard” of the medications for improving the symptoms of Parkinson’s disease.

But few things are ever perfect. Although Sinemet may be considered to be “as good as gold,” it may be “fool’s gold.” There continue to be questions as to whether it might tarnish around the edges not long after beginning treatment. Does Sinemet actually create dyskinesias (involuntary movements) and motor fluctuations (“on” and “off” periods) after the initial 3-6 year “honeymoon” period? Dr. Abraham Lieberman, national medical director for the National Parkinson Foundation, wrote “as Parkinson’s advances, the ability of the brain to process Sinemet into dopamine in a smooth and orderly fashion changes and responses become more erratic and less predictable. The problem is not the delivery of drugs to the brain. The problem is the processing in the brain itself.”

Researchers reviewed 2,478 publications dating back to the introduction of levodopa to help find the answer to that question. The following conclusions were reached from the 74 publications they ultimately found that had adequate data:

- Before there was levodopa, people who had Parkinson’s for a long period of time were more likely to have dyskinesias than those being treated now.
- At the present time, those treated with levodopa therapy for 4-6 years have approximately a 40% likelihood of experiencing motor fluctuations and a little less than 40% risk of having dyskinesias.

These findings represent incident data and the occurrence of truly troublesome or disabling complications may be substantially less than previously reported. And, while there is no clear consensus regarding the frequency (and hence the risk) of dyskinesias or motor fluctuations during chronic levodopa therapy in this study, another recent experiment with monkeys showed that taking levodopa *caused* dyskinesias whether there was nigrostriatal damage or not and that the effect was dose related.

There has also been the concern that levodopa might actually kill brain cells. A research team, led by Dr Bruce Yankner of Harvard Medical School, discovered when the brain protein alpha-synuclein combines with dopamine in nerve cells, it *can* trigger the production of toxic reactive oxygen molecules that kill the nerves.

Another recent study executed by leading research centers, the Parkinson Study Group and supported by NIH and the Department of Defense found no evidence that Sinemet harms or exacerbates Parkinson’s, yet the same patients were studied using a sophisticated new brain-imaging technique where it was unclear as to whether the findings showed a loss of dopamine neuron or whether it was a pharmacological property of levodopa.

So, some studies prove levodopa is toxic, others that it may *or* may not be beneficial to brain cells. As always, there are still unanswered questions.

FOLLOW- UP TO FEBRUARY 2003 ARTICLE

Last month I wrote an article discussing the good and bad of levodopa, a precursor to dopamine in the brain. With one study saying one thing and another coming up with the opposite theory, there was no definitive answer. Now, preliminary findings from a another study indicate that Parkinsonians may appear to have a higher than average risk of heart disease.

People who reported that they had taken levodopa tended to have higher levels of homocysteine in their blood than people who had never taken the drug. Homocysteine is an amino acid that has been associated with an increased risk of stroke and heart disease.

Previous research has shown that levodopa can boost body levels of homocysteine. People with the highest levels of homocysteine in their blood were more likely to have developed heart disease. Low levels of vitamin B12 and folic acid, or folate, are most often to blame for increases in homocysteine in the blood. Next month's article will go into more depth on this.

Previous studies have also suggested that high levels of homocysteine can boost the risk of dementia, and approximately one third of patients with Parkinson's disease eventually develop dementia. So the question arises whether levodopa could either worsen Parkinson's or increase the risk that people with the disease will develop dementia.

Although it may be a concern, the authors of the study state that the study results do not prove that levodopa causes the increases in homocysteine levels and heart disease risk. Sinemet (a combination of levodopa and carbidopa) may not be a cure, but it can greatly alleviate symptoms. No one is saying to stop taking it, but it may be a good idea to get your homocysteine levels checked when you have blood work done.