

Research Assessment #17

Date: February 5th, 2021

Subject: Increases and Decreases in Plasma Homocysteine following Levodopa Treatment

Source:

Valkovic P, Benetin J, Blazícek P, Valkovicová L, Gmitterová K, Kukumberg P. Reduced plasma homocysteine levels in levodopa/entacapone treated Parkinson patients. *Parkinsonism Relat Disord.* 2005 Jun;11(4):253-6. doi: 10.1016/j.parkreldis.2005.01.007. Epub 2005 Apr 20. PMID: 15878587.

O'Suilleabhain PE, Bottiglieri T, Dewey RB Jr, Sharma S, Diaz-Arrastia R. Modest increase in plasma homocysteine follows levodopa initiation in Parkinson's disease. *Mov Disord.* 2004 Dec;19(12):1403-8. doi: 10.1002/mds.20253. PMID: 15390053.

Assessment:

In this article, the side effects of a prominent Parkinson's Disease treatment are detailed. This treatment is Levodopa. Levodopa, in specific, is a treatment that requires a higher and higher dosage as usage continues. This is because the body increases its tolerance to the treatment, requiring more of the treatment to achieve the same effect. Due to this increase in dosage, it can be observed that there are negative side effects. The way Levodopa is broken down in the body is first it is methylated through means of a series of reactions using B vitamins, which convert methionine to homocysteine. Homocysteine is a non-proteinogenic amino acid. Elevated total plasma homocysteine in the blood has been found in Parkinson's Disease patients using Levodopa. Past studies have shown that high levels of homocysteine, also

known as Hyperhomocysteinemia, leads to many additional complications in patients such as an increased risk for dementia, potential heart disease, and an increased progression of Parkinson's Disease. The most prominent side-effect of high homocysteine levels is the development of early heart disease, a very deadly side-effect.

In order to test the effects of Levodopa usage and homocysteine levels in Parkinson's Disease patients, researchers collected paired plasma samples, at varying levels after several months of treatment, from patients just starting Levodopa, patients whose Levodopa dose was doubled, halved, or stopped, patients starting or stopping entacapone (a possible treatment for Hyperhomocysteinemia), and patients initiating or doubling dopamine agonist monotherapy. The baseline homocysteine concentration of 8.7 micromol/L increased to 10.1 micromol/L. Patients who doubled their daily Levodopa dose experienced homocysteine elevations from 9.5 to 11.1 micromol/L. The reduction of Levodopa, as well as the usage of entacapone, did not yield significant results.

Additional studies concluded that catechol-O-methyltransferase inhibitors can prevent the elevation of homocysteine concentrations from Levodopa by reducing the O-methylation in the body. Entacapone, a catechol-O-methyltransferase inhibitor, was hypothesized to be a possible solution to the negative side effects of increased Levodopa usage. In order to test its effectiveness, 19 Parkinson's Disease patients receiving only Levodopa and 21 Parkinson's Disease patients on a combination of Levodopa and Entacapone were used in the study. The effect on plasma levels of homocysteine, serum folate, and vitamin B12 was measured through the study. Through this study, it was suggested that Entacapone and catechol-O-methyltransferase inhibition may play a promising role in successfully controlling

hyperhomocysteinemia caused by Levodopa and in reducing the risk of the other side-effects of increased Levodopa usage.

Overall, through this article and study, it can be noted that while there are current treatments for Parkinson's Disease, most prominently Levodopa, there are still possibly serious side effects with it. Therefore, it is crucial that there be continued research on this topic in order to decrease these possibly life-threatening side effects. If eventually, a treatment for Parkinson's Disease with zero or minimal side effects is developed, it can save millions worldwide and prevent the additional pathologies associated with increased Levodopa usage. Through further research, I hope to find possible methods that are currently being researched to reach this goal.