Amantadine Use for Anxiety and Mood Lability in a Nine Year old Boy with Pitt-Hopkins Syndrome.

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Disclaimer:

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Key Words: Amantadine, Pitt-Hopkins Syndrome.

Abstract: A nine-year old boy with Pitt-Hopkins Syndrome presented with anxiety, mood lability, and difficulties with situational transitions. Such complaints are common in this population as it frequently manifests with features akin to autism spectrum disorders. He was given a trial of amantadine, which has been used to treat similar symptoms in children with autism (King, Wright, Handen, et al., 2001). This medication is thought to work by decreasing the toxic effects of the glutamatergic neurotransmitter system which is implicated in numerous psychiatric conditions that involve irritability, impulsivity, poor focus, anxiety, and depression. It does so through antagonism of the N-methyl-D-aspartate (NMDA) receptor (Blanpied, Clarke, & Johnson, 2005). It is generally well tolerated with few side effects. The child responded well to this medication and has been maintained on it successfully for over five years.

Case Presentation: A nine-year old boy with Pitt-Hopkins Syndrome presented with anxiety, mood lability, and difficulty with transitioning between activities. Pitt-Hopkins syndrome is a condition characterized by intellectual disability and developmental delay, breathing problems, recurrent seizures, and distinctive facial features. He was accompanied by his mother who reported her son aspirated mecomium at birth and initially had a low APGAR score. He did not meet developmental milestones on time and still only uses a few words. Most of his communication was through a computerized tablet that allows him to point to picture based icons. Like many children with Pitt-Hopkins, this patient experienced episodes of breathing difficulty and has had seizures which are now well controlled with lamotrigine, clobazam, and hemp oil.

He was being treated with fluoxetine 6 mg daily from his previous provider. This antidepressant was continued and the child was given a trial of amantadine 50mg in liquid form to be taken once daily for seven days followed by twice daily dosing. He was seen back in one month with his mother noting significant improvement in his ability to remain on task as well as a decrease in irritability. However, anxious behavior persisted and so did trouble with transitions. The evening dose did seem to activate him and keep him awake so the parents were only dosing him in the morning. As some benefit had been noted, we decided to stay at 50 mg daily and to increase Fluoxetine to 10 mg to address the ongoing anxiety. He was seen two more times for follow up at one month and at 3 months. He did well on the once daily Amantadine and the increased Fluoxetine. Seven months after starting Amantadine, he was seen again. The mother reported more signs of depression. His affect was flat and he was more withdrawn. In addition, his appetite was decreased. An additional dose of Amantadine 25 mg was added in the evening. When he was seen for follow up, his mother reported that appetite had improved and that her son was more engaged, seemed happier and was "more like himself." Additionally, his sleep did not

seem to be impacted by the higher dose as it had been in the past. The patient was seen six more times over a 16 month period and continued to do well without further problems with irritability and anxiety. Difficulties with transitions had greatly improved. At his next follow-up visit, the mother reported that there had been a significant increase in seizure activity and that he had been started on Valproic acid. The child seemed more depressed and his affect was extremely flat. Amantadine was increased to 50 mg twice per day. He was not able to be seen again for close to three months while his seizure activity was being stabilized. When he returned, his mood was significantly improved. He was also transitioned to Lamotrigine and off of Valproic acid. Additionally, the Fluoxetine was stopped as the patient had been without significant anxiety for several months and the parents wanted to see if he could be maintained off of it. He has been seen quarterly ever since that time. He is now fourteen and continues to do well on his current dose of Amantadine.

Discussion: This is the first report of using amantadine as a pharmacologic treatment for behavior problems associated with Pitt-Hopkins Syndrome. As there are no other approved treatments, experimental options are warranted. Amantadine did seem to improve irritability, anxiety, and problems with transitions in this child and would merit wider research in children similar to him. Limitations of this case include the fact that amantadine was never used as monotherapy and instead was combined at various times with lamotrigine, fluoxetine, and valproic acid. All of these agents could have contributed to his positive outcomes at different points in his treatment. It is also worth noting that there did appear to be a dose dependent effect. This patient showed improvement in symptoms when amantadine was increased from 50 mg in daily to 50 mg in the morning and 25 mg in the evening.

References:

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