

## Valproic acid

Valproic acid and its derivatives are now commonly used to treat various psychiatric disorders in the elderly. Data indicates that the elderly patients are more susceptible to developing neuro-psychiatric complications when treated with these medications. In this report, we describe the case of a 66-year-old woman with early-onset, Alzheimer's type dementia, who developed myoclonus (involuntary contraction of muscles) when treated with a valproic acid preparation for behavioral disturbances associated with the dementia.

Developed originally as an anticonvulsant medication, the use of valproic acid (VPA) in patients with psychiatric disorders has increased in recent years. Given the current concerns regarding the use of the antipsychotic medications in older patients with dementia, there is interest in using mood stabilizing anticonvulsants for demented patients with agitation and behavioral problems. Although myoclonus in the absence of ammonemia and normal valproic acid level has been reported in a 42-year-old depressed patient treated with VPA, from our review of literature, this is the first reported case of myoclonus due to valproic acid in a patient with dementia when used to treat behavioral disturbances.

VPA is itself a simple fatty acid and can disrupt the urea cycle by causing impairment in the body's usual fatty acid metabolism. The disruption in the urea cycle causes high serum ammonia levels. Encephalopathy secondary to hyperammonemia caused by VPA has been reported by others as well as encephalopathy and myoclonus associated with VPA in the absence of a significantly elevated ammonia level.

Our patient's ammonia level was low normal, and her VPA level was not elevated. Her serum liver enzyme levels were normal. However, discontinuation of VPA was associated with a complete resolution of the myoclonus. Therefore, a serum level of VPA which would not normally be considered to be high appears to have been responsible

for her myoclonus. Because valproic acid is a mitochondrial toxin, it can cause myoclonus even when it does not cause high serum ammonia levels.

We considered delirium as a differential diagnosis for the patient's behavioral disturbances that give her age and her history of dementia. Although delirium remained a possibility, the lack of fluctuating levels of consciousness and no evidence for metabolic or infectious causes for her behavioral issues made this diagnosis less likely.

The patient came to us with a history of hypertension, but she was found to have several recordings of low blood pressures during her stay at our unit. After a careful review, we concluded that these blood pressure changes were due to autonomic failure associated with her severe dementia and the psychotropic medications that she was taking. Although she had her several blood pressure recordings that were low during her hospitalization, she also had several days where her blood pressure recordings were normal. Her blood pressures prior to discharge ranged 103–107/63–69 mm hg.

It remains unclear from literature as to when an elderly patient will be susceptible to the developing neuro-psychiatric side-effects from VPA. However, available data indicates that all elderly patients treated with VPA should be closely monitored regardless of the duration of therapy and especially during periods of acute illness. For those patients who develop myoclonus despite close monitoring, the VPA should be discontinued immediately.

Elderly patients are very sensitive to side effects of medications. In this patient, an anticonvulsant mood stabilizer, VPA, was given in an attempt to avoid the potential for the extra-pyramidal and cerebrovascular side effects of antipsychotic drugs profiles.

However, VPA was not effective in controlling her agitation and behavioral disturbances, and it caused its own untoward side effect of myoclonus. Although some psychotropic medications have been

found to be helpful in the treatment of BPSD, none of them have proven efficacy and benign side-effect profiles.

Elderly patients also have more medical co-morbidities and are possibly taking multiple medications. This puts them at higher risk for developing medical complications and medication side-effects along with drug-drug interactions profiles. These issues must be considered while giving a new medication to the older patient especially with dementia.