

Why Clozapine and Quetiapine Can Be Prescribed For Hallucinations Related To Treatment For Parkinson's Disease

by Norm Keltner

Recently I attended a continuing education program aimed at providing pharmacology hours for nurse practitioners. The very nature of the program dictated that the planners include content appealing to a variety of NPs. My interest varied according to the topic discussed. I particularly enjoyed the lecture on Parkinson's Disease drugs (primarily dopamine agonists). It was well done and provided a solid update for me.

One point however may have been expanded upon, namely the use of clozapine and quetiapine for the quite common PD-drug induced hallucinations. (It should be noted that hallucinations caused by dopamine agonist treatment are different from organic psychosis sometimes associated with PD.) The speaker noted that only these two antipsychotics were approved for treating this side effect but did not offer an explanation as to why. I thought I might tip-toe into that area briefly.

First, the reason the majority of antipsychotics cannot be used to treat these PD-drug induced hallucinations can be traced to their basic mechanism of action, i.e. the blockade of dopamine D2 receptors. The blocking of D2 receptors amplifies the overarching problem associated with PD- diminished dopamine synthesis due to the loss of dopamine generating cells in the midbrain. In a phrase, if you give most antipsychotic drugs to a PD patient experiencing hallucinations, you make the PD worse.

The reason clozapine and quetiapine can be administered when all the others cannot be used is theorized to be due to the rapidity with which these two drugs go on and off the D2 receptor. This phenomenon is called the dissociation constant. While a drug such as haloperidol binds to the D2 receptor longer and more tightly than dopamine itself, clozapine and quetiapine have a much “looser” (my word) binding capability. In fact, it has been reported that by the time haloperidol binds and dissociates from the D2 receptor one time, clozapine can be “on” and “off” 100 times.

So what does this mean? Clozapine and quetiapine bind D2 receptors in one part of the brain “long enough” to ameliorate hallucinatory effects of PD drugs but in the crucial area affected by PD (i.e. the nigrostriatal tract) they allow these dopamine agonists (i.e. the PD fighting meds) to continue their needed antiparkinsonian effect.

Finally, just a word about the aforementioned psychosis related to PD. There is a new drug in the pipeline that has been touted for just this very disorder, pimavanserin (Nuplazid). It has an interesting mechanism of action that we might take a look at next time.