Demystifying Psychiatry

A resource for patients and families

by Charles Zorumski, M.D., and Eugene Rubin, M.D., Ph.D.

Can a Blood Pressure Medicine Help Treat Psychotic Symptoms?

Nitroprusside, a blood pressure medication, may alleviate acute psychosis.

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Schizophrenia is associated with a variety of "positive" symptoms such as hallucinations, delusions (fixed false beliefs), and language dysfunction (formal thought disorder in which the expressed flow of ideas is disorganized and unclear) and "negative" symptoms such as decreased motivation, cognitive dysfunction, and limited interactions with others. The more dramatic, positive symptoms are often alleviated by antipsychotic medications, and these medicines can enable a person to function somewhat independently in terms of living arrangements and jobs. However, schizophrenia is usually a chronic condition, and positive symptoms may reappear, even when a person takes the medications as prescribed. When symptoms re-emerge, a person often loses insight and stops complying with treatment. Symptoms escalate, and the person is often brought to an emergency room in an agitated, psychotic state.

When a psychotic patient comes to an emergency room, they are evaluated to see if a medical condition is contributing to the psychosis. Also, drugs of abuse can exacerbate psychotic symptoms, and psychotic persons are routinely evaluated for drug use. When a person's psychotic symptoms are severe, rapid treatment with intramuscular antipsychotic medication is frequently necessary. Patients may then be admitted to the hospital for medication adjustments and re-establishing psychosocial support systems. Unfortunately, some patients do not respond well to currently available antipsychotic medications, and the negative symptoms of the disorder are particularly difficult to treat.

In an exciting, provocative study published recently in JAMA-Psychiatry, Jaime Hallak and colleagues reported on the effects of sodium nitroprusside, an anti-hypertensive medication, on acute psychotic symptoms in patients with an exacerbation of schizophrenia. Why would anyone expect an anti-hypertensive medication to alleviate symptoms of schizophrenia? The answer to this question is related to our increasing knowledge of the biology underlying psychotic illnesses.

Many are aware that a neurotransmitter called dopamine is thought to be involved with schizophrenia, and currently available antipsychotic medications target this system. However, there are other neurotransmitter systems that may be even more closely linked to the neurochemical defects found in this disorder. Increasing evidence indicates that abnormalities involving the function of the neurotransmitter glutamate and a receptor related to glutamate (the NMDA receptor) are involved in schizophrenia.

Glutamate influences numerous biochemical systems including those involving two endogenous neuromodulators: nitric oxide and cyclic GMP.

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When glutamate interacts with NMDA receptors, production of nitric oxide is stimulated in the brain. Nitric oxide in turn stimulates the production of cyclic GMP among other mechanisms. These actions have short- and long-term effects on the strength of connections between nerve cells.

Schizophrenia is thought to involve diminished NMDA receptor function, leading to decreased production of both nitric oxide and cyclic GMP. It turns out that nitroprusside has a strong effect on both of these substances, and Hallak and colleagues reasoned that these effects of nitroprusside might help correct some of the deficits found in persons with schizophrenia. Importantly, sodium nitroprusside breaks down to nitric oxide as one of its mechanisms of action and may provide a way to replenish levels of nitric oxide and stimulate the production of cyclic GMP. Thus, the use of nitroprusside could represent a way to correct brain network defects in certain neuropsychiatric illnesses, although this remains a hypothesis and will require much more data before being accepted by the scientific community.

Due to the nature of the drug, nitroprusside must be administered intravenously. The dose picked for this study is low compared with the dose used to treat hypertension, but it should still be effective in increasing levels of nitric oxide. This study compared the effect of a 4-hour administration of intravenous nitroprusside with a 4-hour administration of a placebo solution. Both the participants and the researchers were unaware of who received the active agent versus the placebo. The study participants continued on whatever antipsychotic medications they had been taking, and no changes in these medications were permitted for 7 days following the intravenous administration. (Of course, provisions were made for emergencies.)

The results of this small, preliminary study were remarkable. Substantial improvement was observed within 4 hours and continued for 4 weeks following a single administration of nitroprusside. Both positive and negative symptoms of the disorder showed substantial improvement.

These results are rather dramatic and, as such, there is need for caution. They will need to be replicated in larger studies and by different groups of researchers. In addition, risks versus benefits must be evaluated. In this particular study, there were no differences in side effects between the group receiving the sodium nitroprusside and those receiving placebo.

If these results are replicated, however, this is an extremely important finding. Not only is nitroprusside available already to physicians, but this study also points toward a different method for attacking the symptoms of schizophrenia, opening the door for the development of new types of treatments, including treatments that have more rapid onset of action. This could have a significantly positive impact on the lives of patients and their families and friends.

This column was cowritten by Eugene Rubin MD, PhD and Charles Zorumski MD.