Nicotine Toxicity in a Nursing Home Resident With Dementia Secondary to Nicotine Replacement Treatment

To the Editor: Nicotine replacement for patients with nicotine dependence is a common practice in most medical facilities, including nursing homes. It is difficult to distinguish the effect of nicotine on different organ systems and nicotine toxicity, especially in nursing home residents on nicotine replacement with multiple comorbidities, without checking the nicotine level. Nicotine can cause transient stimulation and later persistent depression of all autonomic ganglia and also release catecholamine in a number of isolated organs. Nicotine can stimulate the central nervous system and produce tremors, can increase heart rate and blood pressure, and can cause nausea, vomiting, and diarrhea.[1] Acute nicotine toxicity can cause nausea, salivation, abdominal pain, vomiting, excessive sweating, headache, disturbed hearing, and confusion with marked weakness. Toxicity can cause progressive decrease in blood pressure, respiratory failure, and even death.[1]

Case report. Ms A, a 73-year-old white woman with no significant past psychiatric history, was referred 2 years ago to the psychiatry outpatient clinic by the neurology department for evaluation of depression after the diagnosis and management of dementia. During her first visit to the psychiatry clinic, Ms A was started on an antidepressant. She was functional around that time and was living independently. During subsequent visits, she started having problems with agitation and paranoid ideation with progression of her dementia, thus risperidone was added to her medication regimen. She ended up in the psychiatric hospital due to agitation and paranoid ideation. She was discharged to a nursing home and was started on nicotine replacement therapy. A few months later, Ms A was noted to have a tremor; it was thought to be an extrapyramidal side effect of the antipsychotic. She was admitted to the general hospital for confusion and was started on olanzapine during her hospital stay. She was discharged to the nursing home after 4 days, with resolution of the presenting problems. Ms A continued to have tremors, so amantadine was started. When she returned to the psychiatry outpatient clinic for follow-up, she appeared to have an increase in her tremor. She also reported feeling frustrated. There were no changes to her medication. She was carrying her nicotine replacement with her. The nursing home was called, and it was reported that Ms A was allowed 2 mg of nicotine replacement every 2 hours. They stated that she asked for it regularly, and she was never turned away. Her nicotine level was assessed, and it was 4.6 µmol/L, with a normal level < 2 µmol/L. She was hospitalized for altered mental status and hallucinations shortly after this time. The frequency of nicotine replacement was decreased, and her symptoms resolved with no other abnormal laboratory findings. During subsequent follow-up visits, she reported continued improvement, and a repeated nicotine level was 1 µmol/L.

Nicotine is the main determinant of tobacco use and addiction. It is now available as a medication to assist smoking cessation and is being evaluated as a medication for a variety of other medical disorders.[2] Nicotine is a tertiary amine consisting of a pyridine and pyrrolidine ring. It is a weak agonist at cholinergic receptors. Nicotine cholinergic receptors are found in the brain and autonomic ganglia.[3] The neuromuscular nicotinic cholinergic receptor has been well characterized as a ligand-gated ion channel composed of 5 subunits. Chewing tobacco, snuff, and nicotine gum are buffered to an alkaline pH to facilitate the absorption of nicotine through the mucous membranes.[4] Concentration of nicotine in the blood rises gradually with use of smokeless tobacco and tends to reach a plateau after about 30 minutes, with levels persisting and declining slowly over 2 hours or more.[5] Evidence[6] implicates medicinal nicotine as potentially harmful to both neurodevelopment in children and catalyzing processes underlying neuropathology in Alzheimer's disease. Nicotine also induces 3 hepatic cytochrome P450 (CYP) isoenzymes, primarily CYP1A1, 1A2, and 2E1. Besides nicotine toxicity, there was concern of increased clearance of olanzapine due to the high nicotine level in this patient.

Physicians face a dilemma with regard to prescribing nicotine as replacement therapy in patients with dementia in nursing homes, especially in those struggling with agitation and behavioral changes secondary to their chronic dementia. It is also very important to monitor total doses of nicotine per day and to check nicotine levels in such patients as they are unable to remember vital information and understand the cause of their agitated behavior. Ms A had been taking a second-generation antipsychotic for mood stabilization. She may have needed a higher dose of the antipsychotic to control her mood symptoms` due to high metabolism at the CYP1A1 level. She was getting agitated more frequently, which could possibly be because of the availability of a lesser amount of antipsychotic medication secondary to higher metabolism or nicotine toxicity due to the frequent dose of nicotine. Her mood has been better and stable since the frequency of nicotine was dramatically reduced from every 2 hours to 2–3 times a day. She was admitted to the general medical department due to altered mental status secondary to nicotine toxicity. It would be helpful for the health providers to monitor nicotine intake and levels closely on a regular basis in nursing home patients. One study[7] showed that nicotine replacement therapy is associated with increased hospital mortality in critically ill patients. More studies are warranted on the safety of nicotine replacement therapy in nursing home patients with Alzheimer's disease, especially those with mood and behavioral problems. Given the cholinergic effect on the elderly, let alone dementia patients, nicotine replacement should be considered very carefully, and for nicotine dependence, treatment with noncholinergic medication options might be a better choice. In addition, if nicotine replacement is chosen, access to nicotine should be very carefully monitored in this population.

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