Neuroleptic malignant syndrome

Carolyn Michelle Tan MD MSc, Alexander Kumachev MD MSc

■ Cite as: *CMAJ* 2023 November 6;195:E1481. doi: 10.1503/cmaj.221763

1 Neuroleptic malignant syndrome (NMS) is a life-threatening adverse drug reaction to dopamine antagonists

The condition is characterized by rigidity, altered mental status, hyperthermia and autonomic dysfunction (i.e., diaphoresis, tachycardia, tachypnea and labile blood pressure).[1] It occurs in about 0.02%–0.03% of patients who receive antipsychotic medications, with mortality as high as 5.6% based on recent estimates.[2] It can also be caused by dopamine-antagonist antiemetics (e.g., metoclopramide).[2,3]

2 Symptoms typically begin between several days and 2 weeks after starting the drug or changing its dose

The creatine kinase level is often greater than 1000 IU/L.[1,3] Brain imaging, lumbar puncture, metabolic testing and drug immunoassays can be considered to exclude alternate causes (e.g., toxic, metabolic, infectious, structural).[1,2] A thorough medication history helps distinguish NMS from sympathomimetic or anticholinergic toxicity and serotonin syndrome.[2,4]

3 The condition can develop at any antipsychotic dose and most cases occur at therapeutic doses

Risk factors include use of high-potency first-generation antipsychotic agents (i.e., haloperidol, fluphenazine), high doses, rapid dose escalation, parenteral formulations and history of NMS. Patients on stable doses may develop NMS during acute illness.[2–5]

4 Management involves stopping the culprit drug and aggressive supportive care

Patients may require an intensive care setting to provide volume resuscitation, treat hyperthermia and manage end-organ dysfunction.[3,5] Benzodiazepines (i.e., intramuscular or intravenous lorazepam 1–2 mg every 4–6 h) are first-line treatments for muscle rigidity and sympathetic overactivity, including agitation and hyperthermia.[3,5] Cooling blankets and ice packs should also be used for hyperthermia. The efficacy of dantrolene, dopamine agonists such as bromocriptine, and electroconvulsive therapy is not well established. These may be considered for worsening symptoms despite initial treatment, with guidance on doses for pharmacotherapy provided by the local poison centre. Venous thromboprophylaxis should be considered in all patients.[4]

5 Symptoms typically resolve 7–10 days after stopping the drug

When recognized and treated early, most patients recover completely.[5] If ongoing use of antipsychotic medications is warranted, measures to decrease risk of recurrence (estimated at 10%–30%) include reinitiation at least 2 weeks after symptom resolution (4 wk for depot injections), use of low-potency antipsychotic agents, low doses and slow uptitration.[2–5]

References

1. Gurrera RJ, Caroff SN, Cohen A, et al. An international consensus study of neuroleptic malignant syndrome diagnostic criteria using the Delphi method. *J Clin Psychiatry* 2011;72:1222-8.
2. Pileggi DJ, Cook AM. Neuroleptic malignant syndrome. *Ann Pharmacother* 2016;50:973-81.
3. Chandran GJ, Mikler JR, Keegan DL. Neuroleptic malignant syndrome: case report and discussion. *CMAJ* 2003;169:439-42.
4. Strawn JR, Keck PE, Caroff SN. Neuroleptic malignant syndrome. *Am J Psychiatry* 2007;164:870-6.
5. Adnet P, Lestavel P, Krivosic-Horber R. Neuroleptic malignant syndrome. *Br J Anaesth* 2000;85:129-35.

Competing interests: None declared.

This article has been peer reviewed.

Affiliations: Department of Medicine (Tan, Kumachev), Department of Clinical Pharmacology & Toxicology (Tan, Kumachev) and Division of Geriatric Medicine (Tan), University of Toronto; Division of General Internal Medicine and Geriatrics (Kumachev), University Health Network, Toronto, Ont.

Correspondence to: Carolyn Tan, Carolyn.tan@sunnybrook.ca