
Neuroleptic Malignant Syndrome (NMS)

Last updated October 2023

Characteristics: A rare but potentially life-threatening drug reaction presenting with muscle rigidity (“lead pipe”), hyperthermia, and altered mental status. May present similarly to serotonin syndrome although may be less acute in onset (within days vs hours).

Meds That Cause It: Antipsychotics. Occasionally other antidopaminergic medications (eg, metoclopramide).

Mechanism: D2 blockade.

General Management:

- Discontinue antidopaminergic agents.
- Monitor vital signs and creatinine kinase levels to assess severity and to guide supportive care, including stabilizing vital signs and intravenous fluids if necessary.

First-Line Medications:

Benzodiazepines. Any of them will work (eg, lorazepam [Ativan] 0.5–1 mg BID or diazepam [Valium] 10 mg BID).

Second-Line Medications:

- Bromocriptine (Parlodel) 2.5–5 mg Q6–8 hours.
- For severe rigidity, dantrolene (Dantrium) 3–5 mg/kg IV divided TID or 100–400 mg/day oral divided QID. Monitor liver function.
- Bromocriptine or dantrolene should be continued for 10 days beyond symptom resolution.

Clinical Pearls:

- Most cases, especially if caught early, will resolve quickly after antipsychotic discontinuation.
- Avoid bromocriptine if serotonin syndrome is not ruled out (eg, patient taking both antipsychotics and serotonergic agents). Bromocriptine has some proserotonergic activity and could worsen serotonin syndrome.
- Up to 50% of patients who have experienced NMS may have another episode. To minimize risk of recurrence in patients who require ongoing antipsychotic therapy, wait until symptoms have completely resolved (at least two weeks). Choose a different agent, ideally a second-generation antipsychotic as they are less likely to cause NMS. Never use a long-acting antipsychotic injection in patients with a history of NMS.

Fun Fact:

Mortality rates from NMS had previously been reported to be as high as 20%–38%. In more recent years, the mortality rate has fallen to below 10%. This has been attributed to earlier recognition and better management.