

NMS is an uncommon, idiosyncratic complication of antipsychotic therapy that can be potentially life-threatening if not diagnosed and treated early

NMS is a clinical diagnosis which must include recent use of dopamine-receptor blocker (antipsychotic) or withdrawal from a pro-dopaminergic drug (e.g., for Parkinson's disease).

More common with first generation, high-potency and depot antipsychotic preparations, but all can cause NMS.

Clinical Presentation:

- Can occur any time during antipsychotic therapy but usually in first 1-2 weeks or recent dose change. NMS develops over days as opposed to serotonin toxicity which has a more rapid onset. Toxicity may last many weeks (depot)

Classic tetrad of clinical features (evolving over 24-72 h):

- Hyperthermia (temperature > 38.5°C)
- Extrapyramidal effects ('lead-pipe' rigidity, bradykinesia, tremor, abnormal movements and posture)
- Autonomic dysfunction (labile BP, tachycardia, diaphoresis)
- CNS effects (drowsiness, confusion, coma, mutism)

DSM-5 diagnostic criteria: must have all 3 of: exposure to dopamine blocker, muscle rigidity, hyperthermia AND at least 2 of: diaphoresis, tremor, altered level of consciousness, labile BP, tachycardia, elevated CK, leukocytosis, mutism

Management

- Immediate cessation of dopamine blocker and cooling for hyperthermia
- Supportive care with aggressive fluid replacement, especially if hypotensive
- Prevention of complications such as thromboembolism, rhabdomyolysis, AKI, aspiration pneumonia
- Exclusion of other differentials (including withdrawal states (e.g., baclofen), CNS infection)

Cooling for hyperthermia

- If temperature > 38.5°C rapidly cool with tepid sponging, continuous fanning and ice packs
- Antipyretics are **not** effective

Sedation

- Behaviour management is not usually necessary but titrated diazepam may help with agitation
- remove mechanical restraints when possible
- *Sedation with antipsychotics such as droperidol is absolutely contraindicated*

Antidotes (please discuss with Clinical Toxicologist)

- Most cases do not require antidotal Rx as improvement occurs with cessation of dopamine blocker
- In severe cases or if prolonged symptoms, however, can use:
 - Bromocriptine:** 2.5 mg orally or via NG 8-hourly; can increase to 5 mg 4-hourly based on response
 - Endpoint of antidotal Rx is lowering of temperature and reduction in muscle rigidity
 - Therapy is usually for 7-10 days as slow taper is required to prevent recrudescence
- Dantrolene and ECT have been used in refractory cases – please discuss with Toxicologist