NEUROLEPTIC MALIGNANT SYNDROME

ICU NEURO NUGGETS
Dr Hayden Stephenson, 2020

= rare but potentially fatal idiosyncratic drug reaction to anti-psychotic (neuroleptic) drugs

Incidence: **0.01-0.02%** of patients receiving neuroleptics

NMS results from dopamine antagonism/blockade in the striatum and hypothalamus. Massive glutamine release in response to dopamine blockade is thought to generate neurotoxicity, catatonia and myotoxicity. Commonly occurs 3-9 days after starting treatment, but can occur when the drug has been taken for a long time

RESPONSIBLE DRUGS:

Typical antipsychotics such as butyrophenones (eg haloperidol) and phenothiazines (eg chlorpromazine & prochlorperazine)

Less frequently associated with atypical antipsychotics such as aripipazole, clozapine, olanzapine, quetiapine & risperidone

Abrupt withdrawal of antiparkinson medication: L-dopa or dopamine agonist therapy

CLINICAL FEATURES:

- Exposure to dopamine antagonist, or agonist withdrawal, within past 72 hours
- Hyperthermia (>38 °C)
- **Extrapyramidal signs:** rigidity, bradykinesia, hyporeflexia
- **Altered mental state**: confusion, drowsiness
- Creatine kinase elevation (at least x4 normal)
- **Autonomic instability/sympathetic lability:** hypertension or fluctuating BP, sweating, urinary incontinence
- Hypermetabolism
- *Absence of toxic, metabolic, infectious, or neurological cause*

SEVERITY:

Severity generally correlates with severity of individual features, particularly temperature

Mortality 12-20% from multi-organ failure, hyperpyrexia, rhabdomyolysis, and DIC (disseminated intravascular coagulation). Electrolyte disturbances of K^+ and Na^+ may contribute to mortality

Important differential diagnoses to consider:

Serotonin syndrome

Malignant catatonia

CNS infection

Vasculitis

Drug toxicity

Malignant hyperthermia

MANAGEMENT:

- Maintain airway/breathing/circulation
  *severe rigidity may compromise ventilation
- **STOP** offending neuroleptics
- Supportive care mainstay in mild-mod NMS: temp control, fluid status, sedative agents
- Adequate hydration to maintain urine output
- Benzodiazepines: diazepam 10-20mg or lorazepam 1-2mg every 4-6 hours. Consider infusion in more severe cases
- Dopamine agonists (discuss with NPIS): Bromocriptine 2.5mg 8 hourly PO/NG up to 45mg/day (caution psychosis/vomiting/low BP)
- Amantadine 100mg 8-12 hourly PO/NG
- **Hyperpyrexia** >39°C = **URGENT COOLING**
  External cooling systems, ice-baths, ice packs, tepid water, fans, cooled IV fluids. Paralysis in I&V patients to reduce heat production
- **DANTROLENE** reserved for severe NMS
  Post synaptic muscle relaxant reducing excitation-contraction coupling by inhibiting calcium release from muscle cell SR

  Initial dose 1mg/kg ABW IV
  Repeat every 15minutes (max 10mg/kg/24hrs)
  Average dose needed 2.5mg/kg
- Rhabdomyolysis: risk of renal failure CK >5000 IV volume replacement, maintain U/O greater than 1ml/kg/hour. Monitor electrolytes. CVVHDF can remove myoglobin, treat AKI and refractory hyperkalaemia.

www.toxbase.org
OH's Intensive Care Manual 7th Ed 2014 pages 835-836

National Poisons Service UK: 0344 8920111