

NEUROLEPTIC MALIGNANT SYNDROME (NMS)

A rare, idiosyncratic, potentially life-threatening response to neuroleptic medications

Pathogenesis: Dopamine receptor blockade or withdrawal of dopamine agonist → NOT ENOUGH DOPAMINE!

Risk of developing NMS is associated with Dopamine receptor blockade affinity (higher affinity=higher risk)

Incidence of 0.01%-0.1% in patients receiving neuroleptic medications

Approximately 2,000 cases are diagnosed annually in hospitals across the country

Mortality rate of about 10%

! Has been reported with all antipsychotics

SIGNS & SYMPTOMS

1. Hyperthermia (>104°F) -Diaphoresis
2. Muscle rigidity → Rhabdomyolysis...check reflexes, feels like metal
3. Altered mental status- Cataplexia or Mutism
4. Autonomic dysfunction → Hypertension, tachycardia, tachypnea

! Hyper-reflexive when compared to serotonin syndrome

POTENTIAL LABORATORY ABNORMALITIES

- ↑ Creatinine kinase → Myoglobinuria
- ↑ WBCs

RISK FACTORS

- Higher doses of medication
- Previous brain injury
- Rapid dose escalation
- Dehydration
- High potency medications
- Electrolyte abnormalities

TREATMENT

Discontinue dopaminergic antagonists

Supportive Care: IV fluids, resolution of electrolyte abnormalities, management of complications

Benzydiazepines: improve cataplexic symptoms

Dopamine agonists may be used to help reverse NMS symptoms: Bromocriptine and Amantadine

Electroconvulsive therapy for treatment-resistant patients with severe cases of NMS

Severe hyperthermia: treated with external cooling measures

RECHALLENGING AFTER NMS

- Re-challenge with a different antipsychotic class
- Wait a minimum of 2 weeks before re-challenge → **could have a relapse during that time!**
- Re-challenge with lower potency neuroleptic
- Titration should be performed slowly, starting with lower doses
- Avoid dehydration
- Monitor frequently for signs and symptoms of NMS

ANTI-PSYCHOTIC REVIEW

-Typical antipsychotics

- Only D2 blockade, work on positive symptoms
- More potent = more likely to cause EPS

-Atypical antipsychotics

- D2 blockade and 5HT (serotonin) blockade work on positive and negative symptoms
- Less likely to cause EPS
- **Must monitor for metabolic issues- not all atypicals have the same metabolic profile!**

-Blocking other receptors:

- Histamine: sedation, weight gain, distress
- Muscarinic: anticholinergic adverse effects
- Alpha: hypotension/orthostasis

Use KIMS (autonomic involuntary movement scale) to screen for EPS

-Use anticholinergics, beta-blockers and benzodiazepines to control EPS

-Advise patients to take medication as prescribed and on a regular schedule

-Some therapeutic effects can be noticeable in a few days (3-7 days)

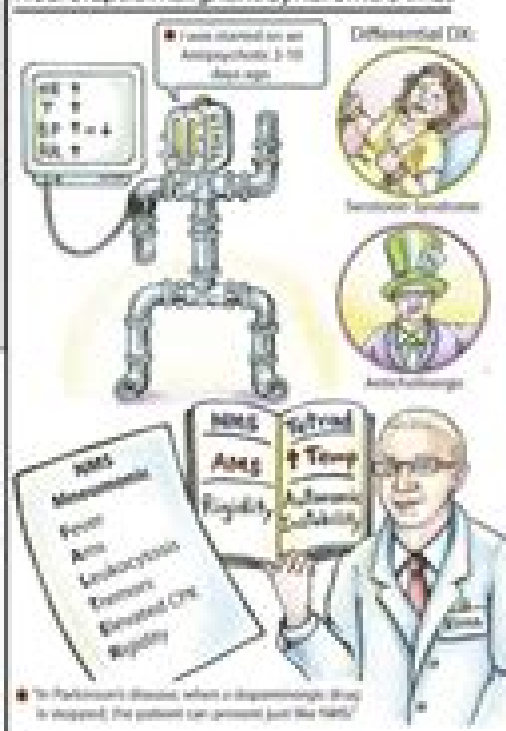
but significant improvement can take 2-4 weeks or longer

-Consider long acting depot medications for patients with difficulty maintaining medication regimen

-Patients should avoid excessive exposure to sunlight and heat (drugs make it so that patient's don't know they're hot)

-Avoid alcohol and illicit drug use

Neuroleptic Malignant Syndrome (NMS)



• In Parkinson's disease, when a dopaminergic drug is stopped, the patient can present just like NMS!

EXTRAPYRAMIDAL ADVERSE EFFECTS (EPS)

Serious neurological symptoms that are major adverse effects of antipsychotics

! Typical > atypical antipsychotics

*** Caused by blockade of dopamine 2 receptor in the midbrain region of the brainstem**

Risk Factors:

High potency typical antipsychotics

IM administration

Higher Doses

Young, African American, Male -subconsciously biased, d/t being "scared" of them

EPS	Clinical Characteristics	Onset	Treatment
Acute Dystonia reversible [sustained muscle contraction]	Muscle spasms, usually in eyes, face, neck and throat Torticollis- neck [head turned] Inpatient: give IM, they can't swallow...don't be that person	Hours to days	Anticholinergics: Benztropine or diphenhydramine IV, IM, PO Then lower dose or switch to antipsychotics
Acathisia "ants in the pants" reversible	Subjective feeling of restlessness and anxiety, plus objective signs of negative or restless motor activity	Days to weeks	hardest to treat! Beta Blockers, benztropine or diphenhydramine, amantadine Then lower dose or switch to antipsychotics
Secondary Parkinsonism reversible	Bradykinesia or akinesia, tremor, rigidity	Weeks to months	Benztropine or diphenhydramine, amantadine Then lower dose or switch to antipsychotics
Tardive Dyskinesia irreversible	Staccato tongue and face movements such as lip smacking and wormlike tongue movements, uncontrolled chewing movements	Years	New drugs on the market!



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