Extrapyramidal Symptoms (EPS): Approach in Primary Care

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Summary: While antipsychotic medications can be extremely helpful for certain symptoms such as psychosis, they can unfortunately cause various side effects including extrapyramidal symptoms (EPS). Management strategies include giving diphenhydramine for acute dystonia; stopping or reducing the dose of antipsychotic; switching to a second generation; using a lower risk second generation antipsychotic such as quetiapine.

Case, Part 1

D. is a 20-yo male in your practice. He was recently admitted to hospital for a brief psychotic episode and while in hospital was started on risperidone. He was discharged and is seeing you in follow-up. While his psychosis symptoms have improved and he is functioning much better, he is brought in for a same-day visit by his parents. He complains of neck stiffness and troubles moving his eyes...

Pathophysiology of EPS

Beneficial antipsychotic effects and extrapyramidal effects are due to binding to D2 receptors in the central nervous system.

Antipsychotic effects occur at 60-80% of D2 occupancy.

Acute EPS effects occur at 75-80% of D2 occupancy.

In other words, there is a very margin between therapeutic effects and extrapyramidal effects.

Though less frequent agents that block central dopaminergic receptors may also cause EPS (D'Souza, 2019) such as:

- Anti-emetics (metoclopramide, droperidol, and prochlorperazine)
- Lithium
- Serotonin reuptake inhibitors (SSRIs)
- Stimulants
- Tricyclic antidepressants (TCAs)

Risk Factors for EPS

Highest risk medications

- First-generation antipsychotic drugs (“typical antipsychotics”) such as
    - Haloperidol
    - Chlorpromazine
    - Prochlorperazine

Lower risk medications (SGAs)

- Second-generation antipsychotics (“atypical antipsychotics), with an atypical mechanism of action, are felt to be at a lower risk of EPS.
- Higher risk SGAs
    - Risperidone > compared to clozapine, olanzapine, quetiapine, ziprasidone.
    - Ziprasidone > compared to olanzapine and quetiapine.
    - Zotepine > compared to clozapine.

Neutral risk

- No significant difference between amisulpride and its comparators (olanzapine, risperidone, or ziprasidone).

Lowest risk

- Quetiapine (when compared with (olanzapine, risperidone, and ziprasidone).
- Clozapine

Physical Exam

Ask the patient to remove any gum or objects from their mouth.

Head / neck / cranial nerves:

- Impaired extraocular movements?
- Sustained gaze deviation (oculogyric crisis)?
- Abnormal movements of the face, mouth, lips, jaw or tongue?

Excessive salivation (sialorrhea)

Motor examination:

- Increased or a rigid tone?
- Cogwheeling?
- Abnormal movements present?
- Abnormal movement at rest? (dyskinesias)
- Restless with a constant need to move or pace? (akathisia)
- Abnormal postures? (dystonia)
- Tremor?

Coordination

- Movements slowed?
- Trouble with rapid alternating movements?
- Slow to stand from a seated position?

Gait

- Shuffling gait?
- Postural instability?

Mental Status Examination (MSE)

General	Alert and oriented with EPS Changes in level of consciousness suggest other causes, e.g. neuroleptic malignant syndrome Normal attention, memory, executive function
Affect	Decreased facial expression or a ‘mask-like facies?
Speech	Slow to move or speak? (bradykinesia) Dysarthria or dysphonia?

Vitals

Vital signs should be normal with EPS.
Are vital signs abnormal? Consider neuroleptic malignant syndrome (NMS) or other conditions instead.

Rating Scales

Standardized rating scales include:

- Extrapyramidal Symptom Rating Scale (Gharabawi, 2005).

Investigations

There are no laboratory nor imaging tests.

Management of EPS

Early EPS

Onset of early EPS

- Occurs within few weeks of starting new medication, or increasing dosage.

Prognosis of early EPS

- Symptoms reversible when antipsychotic is stopped
- Serious negative impact on medication adherence

Type of EPS	Symptoms	Management / Treatment

Acute dystonia	Sustained abnormal postures and muscle spasms, especially of the head or neck Examples • Retrocollis: Neck spasms caused by neck extension • Extension of trunk • Eye deviation • Forced jaw opening • Tongue protrusion • Torticollis: Spasm of neck muscles, causing abnormal neck position. • Trismus: Spasm of jaw muscles, usually forcing jaw closed • Laryngospasm: Spasm of vocal cords making it difficult to speak or breathe • Oculogyric crisis: Forced upward deviation of the eyes. DDx muscle rigidity / tension • Muscle rigidity and tension are nonspecific symptoms that may be observed in neuroleptic malignant syndrome, serotonin syndrome, and other movement disorders.	Stop antipsychotic Anticholinergic medications such as • Benztropine • Biperiden • Diphenhydramine (Benadryl) May relieve symptoms within minutes; repeat doses may be required if no response is seen within 30 min. May need to be IV / IM -- symptoms resolve within minutes with parenteral therapy. Tell patients/ families that if the patient has an acute dystonic reaction, they can give an oral dose of over-the-counter diphenhydramine (Benadryl) until they are able to see a professional. Is it a laryngeal or pharyngeal dystonic reaction? • If so, assess if emergency airway intervention is necessary • Contact Emergency Medical Services (EMS) for transfer to Emergency Department (ED) Is an antipsychotic absolutely required? • If the causative agent was a first-generation antipsychotic (FGA), then switch to a second-generation antipsychotic (SGA) • If already on SGA, switch to SGA with the least risk, e.g. Quetiapine or Clozapine.
Pseudoparkinsonism aka drug-induced parkinsonism	Resemble parkinsonism Tremulousness in the hands and arms, rigidity in the arms and shoulders, bradykinesia, akinesia, hypersalivation, masked facies, and shuffling gait	Stop or reduce the dosage of antipsychotic Switch to an atypical antipsychotic Give Parkinson medications such as (Shin, 2012): • Amantadine • Antimuscarinic agents • Dopamine agonists • Levodopa

Akathisia	Excessive restlessness with a need to move, e.g. pacing Symptom relief is achieved with movement. Patients report feelings of inner tension or restlessness. Movements such as shaking or rocking of the legs and trunk, pacing, marching in place, rubbing the face or moaning to relieve their discomfort. Young children not always able to explain akathisia; may describe vague sensations of internal restlessness, discomfort or anxiety Parents may report their child is more anxious, or irritable/agitated. DDx Akathisia • Anxiety • Agitation in a patient with psychosis	Stop or reduce the dosage of causative antipsychotic Beta-adrenergic blockers (such as propranolol (Inderal) at 20-80 mg / day). Benzodiazepines Amantadine Clonidine Mirtazapine Mianserin Cyproheptadine Propoxyphene

Late EPS

- Occurs after chronic, long-term or prolonged treatment (after several months).
- Serious negative impact on quality of life.

Type of Later EPS	**Symptoms**	**Treatment**
Tardive dyskinesia	Involuntary choreoathetoid movements affecting orofacial and tongue muscles (e.g. grimacing, tongue protruding, lips puckering) Less frequently torso and limb movements Cause difficulty with chewing, swallowing, talking DDx chorea and athetosis • Huntington's disease (distinguished based on family history and genetic testing), • Sydenham's chorea (identified with a history of streptococcal infection), • Wilson disease (adolescent-onset with a defect in copper metabolism), • Cerebrovascular lesions	Stop the offending agent Switching to one with a lower risk • Benzodiazepines • Amantadine • Dopamine-depleting medications (e.g. tetrabenazine)
Neuroleptic-induced parkinsonism	Tremor, skeletal muscle rigidity, bradykinesia DDx parkinsonism • Symptoms of dementia? If so, consider evaluating for Parkinson disease, Lewy body dementia, vascular dementia, and frontotemporal dementia • Idiopathic: Note that up to a third of new-onset schizophrenic patients who have never been medicated may present with parkinsonian signs.	Stop or reduce the dosage of causative medication. Switch to an atypical antipsychotic. Anti-parkinson medications: • Amantadine, • Antimuscarinic agents, • Dopamine agonists, • Levodopa

Prevention of EPS

Does the patient have EPS risk factors such as:

- Elderly females: Increased risk of drug-induced parkinsonism and tardive dyskinesia.
- Young males: Increased risk of dystonias.
- Previous history of EPS.

If so, consider pre-emptively doing the following:

- Use the lowest possible dose of low-risk antipsychotic medication (e.g. quetiapine).
- Treat for the shortest possible time.

Preventive Guidance for EPS

Let the patient and family know that if the patient has an acute dystonic reaction, they can give themselves a dose of over-the-counter diphenhydramine (Benadryl) until they see a health professional.

EPS in Children/Youth

Is the patient on a first-generation antipsychotic?

- If so, consider stopping the first-generation antipsychotic, given that there is a higher risk with first-generation antipsychotics.

Are there multiple antipsychotics?

- If so, consider reducing the number of antipsychotics.

Is the lowest possible dosage of the SGA being used?

- Consider lowering the dosage if possible.

Is quetiapine or clozapine being used?

- If not, consider switching to quetiapine or clozapine as they have a lower risk of EPS.

Has the patient been seen by neurology?

- If not, consider referral to a neurologist.

Are there still issues with EPS despite the above being tried, AND is antipsychotic treatment absolutely required? If so, then consider adding:

- Anticholinergic (Arana, 1988),
- Propranolol (Pringsheim, 2011)
- Clonazepam (Pringsheim, 2011)
- Mirtazapine for akathisia (Pringsheim, 2011)

Case, Part 2

D. is a 20-yo male in your practice. He was recently admitted to hospital for a brief psychotic episode and while in hospital was started on risperidone. He was discharged and is seeing you in follow-up. While his psychosis symptoms have improved and he is functioning much better, he is brought in for a same-day visit by his parents. He complains of neck stiffness and troubles moving his eyes...

What do you do?

You give him over-the-counter diphenhydramine (Benadryl), and symptoms improve within about 15-minutes. You ask him to stop his antipsychotic medications. You contact his treating psychiatrist to arrange rapid follow-up.

Reference

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Clinical Guidelines

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About this Article

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