Fact Sheet: Antipsychotic-Induced Akathisia

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Revised: 10/22/24

Definitions[1,2]

Akathisia- Greek term meaning “not to sit.” Subjective anxiety or dysphoria and motor restlessness (usually lower extremities). Patients may have a strong subjective component in the absence of typical motor symptoms (pacing, inability to sit still, etc.).[3] Akathisia can result in worsening of psychopathology, suicidal ideation/attempts, and violence.[4,5,6]

Acute Akathisia- Akathisia symptoms developing within hours to days of initiation or an increased dose of antipsychotic or change in antipsychotic drug (≤ 6 weeks).

Tardive Akathisia- Delayed onset of akathisia, symptoms beginning ≥ 3 months after medication initiation or dose change, can persist following discontinuation of medications.

Chronic Akathisia- Continuation of akathisia symptoms > 3 months after last dose change. May have more objective symptoms and less subjective distress vs. acute akathisia. [7]
Withdrawal Akathisia- Occurs after the reduction of dose or cessation of antipsychotic medication

Pseudo-Akathisia- Objective movements observed but subjective awareness is absent.

Pathophysiology[3]

The pathophysiology is hypothesized to be due to complex interactions involving dopamine, noradrenaline, and serotonin, as well as gamma aminobutyric acid (GABA) receptors. Dopaminergic neurons in the ventral tegmental area project to the limbic system via the nucleus accumbens. The shell and core of the nucleus accumbens receive input from DA neurons from VTA. Dopamine inhibits inhibitory GABAergic neurons projecting to the limbic system and the cortex and affect goal-directed behaviors. Noradrenergic neurons from the locus coeruleus project to the amygdala and nucleus accumbens shell. When antipsychotics are present, the nucleus accumbens shell becomes hyperactive from unopposed noradrenergic innervation resulting in purposeless movements and intense dysphoria. Propranolol is hypothesized to exert its effect via reduction of noradrenergic overactivation. The VTA neurons receive inhibitory serotonergic inputs from the dorsal raphe nucleus which may be why 5HT2A and 5HT2C antagonists improve acute akathisia.

Prevalence

Acute akathisia- 14-35%(7)
Chronic akathisia- 24-33% of outpatients with schizophrenia[2]
There has been limited data related to the incidence of individuals with acute akathisia developing chronic akathisia.

Funding for SMI CalAdviser was made possible by the State of California Department of State Hospitals (DSH) (the Department), but does not necessarily represent the views of the Department or any of its employees except to the extent, if any, that it has formally been approved by the Department.

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Risks

Antipsychotic-naïve, increased risk with > 1 antipsychotic, rapid dose increases, > risk with high doses, higher-potency antipsychotics, older age, female sex, negative psychotic symptoms, iron deficiency, cognitive dysfunction, and bipolar disorder diagnosis.[2]

Treatment of Acute Akathisia[8,9,10]

1. Dose reduction or alternative antipsychotic

2. Addition of adjuvant medications

1. **Propranolol 40-120 mg divided**, response observed ≥ 6 days, monitor blood pressure and heart rate. AT higher doses use the long-acting formulation, e.g., 40 mg b.i.d.
2. **5-HT2a Antagonists**
    a. **Mirtazapine 15 mg qhs, response observed ≥ 5 days.** Avoid in patients with a bipolar diathesis due to risk of destabilization.
    b. Trazodone 50-100 mg qHS, response observed ≥ 5 days. Avoid in patients with a bipolar diathesis due to risk of destabilization.
    c. Cyproheptadine (8-16 mg), response observed ≥ 4 days.
4. Vitamin B6 300-600 mg BID, response observed ≥ 5 days, taper off as chronic use at high doses (≥ 50 mg/day has been associated with neuropathy).(11)
5. Clonazepam 0.5-2.5 mg/day
6. Akathisia + parkinsonism, consider an anticholinergic medication such as benztropine.

Long term treatment with an anti-akathisia drug is NOT recommended, dose reduction or removing causative medication is the primary intervention. *Anti-akathisia medication may need to continue for weeks to months, particularly if the antipsychotic medication has a long half-life, i.e., long-acting injectable antipsychotics.*

Treatment of Chronic/Tardive Akathisia[3,12]

1. Gradual dose reduction or alternative low potency antipsychotic or second-generation antipsychotic.
2. Switch the patient to clozapine.

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