December Pharmacy Newsletter

Adverse Effects of Second-Generation Antipsychotics (SGA)

The mechanism of action of most SGAs appears to be postsynaptic blockade of brain dopamine D2 receptors. Most SGAs differ from older antipsychotic medications such as first-generation antipsychotics (FGAs) in that serotonin 5HT2 receptor binding exceeds their affinity for dopamine D2 receptors. Most SGAs depend on cytochrome P450 enzymes for metabolism, and some have significant increases or decreases in serum levels when used with inducers or inhibitors of these enzymes. Select adverse effects include:

•Metabolic syndrome – Weight gain and metabolic effects are the most prominent side effects of SGAs. Clozapine and olanzapine are strongly associated with these effects, whereas aripiprazole, lurasidone, and ziprasidone are the preferred agents to minimize these issues. All antipsychotics carry recommendations for routine monitoring of metabolic parameters.

•Increased risk of mortality – Increased mortality has been found with all SGAs across all ages and diagnoses. Patients who are at highest risk are those who are older or have longer times of exposure to the drugs. No differences in risk have been demonstrated within this class of medications.

•Extrapyramidal symptoms and tardive dyskinesia – SGAs have lower risks of extrapyramidal symptoms (EPS) and tardive dyskinesia than most FGAs. Risperidone is associated with a higher risk of EPS compared with other SGAs; clozapine, iloperidone, and quetiapine carry the lowest risk.

•Anticholinergic effects – Anticholinergic effects of SGAs are most prominent with olanzapine, quetiapine, and clozapine. The most common side effects are dry mouth or constipation and, less often, blurred vision or urinary retention.

•Cardiovascular events – Prolongation of the QT interval tends to be mild with SGAs but somewhat greater with iloperidone and ziprasidone than with other agents. These two medications should be avoided in high-risk patients or those taking other QT-prolonging drugs.

•Orthostatic hypotension – Orthostatic hypotension is often accompanied by orthostatic tachycardia and is most common in the first few days of SGA administration or when the dose is increased. These are most commonly seen with clozapine, iloperidone, quetiapine, and paliperidone, less often with olanzapine, risperidone, and ziprasidone, and only rarely with aripiprazole, asenapine, brexpiprazole, and lurasidone.

•Falls – Treatment with SGAs can cause falls and fractures as the result of somnolence, postural hypotension, and/or motor and sensory instability. Monitor all individuals closely and complete a fall risk assessment at regular intervals.

•Sedation – Sedation may occur with any SGA but is usually associated with clozapine, olanzapine, and quetiapine. Asenapine, lurasidone, and ziprasidone have intermediate rates while aripiprazole more often causes insomnia than sedation.

•Prolactin elevation – Primarily associated with risperidone and paliperidone, this occurs infrequently with olanzapine and ziprasidone, and is rare with other SGAs. A serum prolactin level is indicated if the patient develops signs of sexual dysfunction or galactorrhea.

Antidepressant Medications and Some Caution Uses

When choosing an antidepressant medication consider side effects, personal and family history, drug interactions, and comorbidities. Here are some antidepressant drug class cautions:

DRUG CLASS	Avoid or Use Caution
SSRI i.e.: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline	• overweight or obese patients (paroxetine) • QT prolongation or torsade's risk (citalopram, escitalopram, fluoxetine, sertraline) • agitation or insomnia (fluoxetine) • elderly (paroxetine)
SNRI i.e.: desvenlafaxine, duloxetine, Fetzima, venlafaxine	• hypertension • agitation or insomnia • QT prolongation (venlafaxine)
MIRTAZAPINE	• overweight or obese patients • hyperlipidemia • QT prolongation
BUPROPION	• seizure disorders • hypertension • anxiety or insomnia

References:

1. https://www.uptodate.com/contents/atypical-antidepressants-pharmacology-administration-and-side-effects?search=antidepressant%20side%20effect&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2
2. https://pharmacist.therapeuticresearch.com/Content/Segments/PRL/2014/Jul/Choosing-and-Switching-Antidepressants-7193

PREFERRED DRUG LIST UPDATES CAN BE FOUND HERE:

Integrated (Title 19/21 SMI), ACC, DD, ALTCS and DCS CHP
https://www.mercycareaz.org/providers/pharmacy.html

Behavioral Health (Non-Title 19/21)
https://www.mercycareaz.org/providers/pharmacy.html

** Drugs that are not on the formulary will require a PA (prior authorization) request to be submitted**

Reminder for quicker determinations of a Prior Authorization use the ePA link for Our Providers: Please click here to initiate an electronic prior authorization (ePA) request

This newsletter is brought to you by the Mercy Care Pharmacy Team. For questions, please email Fanny A Musto (MustoF@mercycareaz.org), Denise Volkov (VolkovD@mercycareaz.org) or Trennette Gilbert (gilbert@mercycareaz.org)