UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

# THE TABLET: PALLIATIVE CARE PHARMACY TIPS

July 30, 2021 Vol. 1, No. 18

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

## TODAY'S TOPIC:

### Review of Antipsychotic Characteristics to Aid in Antipsychotic Selection

**Background:**
Antipsychotics have been used for many years to treat mental health conditions. Generally, antipsychotics reduce dopamine neurotransmission. First-generation antipsychotics and second-generation antipsychotics differ with their degree of blockade of other neurotransmitters that can be helpful for palliation of a variety of symptoms.

**Importance:**
Antipsychotics are used in the palliative care population off-label to help mitigate a variety of symptoms such as delirium, agitation, nausea, anxiety, cachexia, and insomnia. Typically, we use the antipsychotic mechanism of action and pharmacokinetics to help guide our antipsychotic selection, while also considering patient-specific factors. Palliative care clinicians should be aware of individual antipsychotic characteristics to help select the most appropriate antipsychotic for each individual patient.

**The Literature:**
J Pain Symptom Manage. 2011 May;41(5):956-65.
**Antipsychotics, Therapeutic Review**

- Dopamine plays a central role in learning, motivation, attention, motor control; dysregulation of dopamine plays a role in several symptoms, but so does dysregulation of other neurotransmitters
- Weighing the favorable effects of antagonism at these receptor sites versus the negative effects (side effects) can help tailor your antipsychotic selection, for example if needing a more sedating antipsychotic – you may utilize one with more antihistamine activity such as choosing quetiapine over haloperidol

*Table 2*
**Receptor Affinities for Selected Antipsychotics[6–9]**

| | $D_2$ | $5HT_{2A}$ | $5HT_{2C}$ | $5HT_3$ | $H_1$ | $\alpha_1$ | $\alpha_2$ | $ACh_M$ |
|---|---|---|---|---|---|---|---|---|
| Aripiprazole | +++PA | +++ | +++ | - | +++ | +++ | ++ | - |
| Chlorpromazine | +++ | +++ | ++ | - | +++ | +++ | + | ++ |
| Clozapine | + | +++ | ++ | + | +++ | + | + | +++ |
| Haloperidol | +++ | + | - | - | - | ++ | - | - |
| Levomepromazine (not USA) | ++ | +++ | | | +++ | +++ | + | ++ |
| Perphenazine | +++ | +++ | + | | +++ | ++ | + | - |
| Prochlorperazine | +++ | ++ | + | - | ++ | ++ | - | + |
| Olanzapine | ++ | +++ | + | + | + | ++ | + | ++ |
| Quetiapine | + | + | + | - | ++ | + | ++ | - |
| Risperidone | +++ | +++ | ++ | - | ++ | + | +++ | - |

Affinity: +++ high, ++ moderate, + low, (+) borderline, - negligible or none; blank = no data. PA = partial agonist.

This table only depicts receptor affinities, not degree of affinity or dissociation rates

- The receptor affinity correlates with side effect profiles of these antipsychotics as well
- For instance, if wanting to avoid EPS, would choose an atypical antipsychotic

| Antipsychotic | Sedation | EPS | Antichol | Orthostasis | Weight Gain | QTc Prolong | Seizures |
|---|---|---|---|---|---|---|---|
| Chlorpromazine | ++++ | +++ | +++ | ++++ | ++ | ++ | +++ |
| Haloperidol | + | +++++ | + | + | ++ | +++ | ++ |
| Olanzapine | +++ | + | +++ | ++ | +++ | + | ++ |
| Risperidone | + | + | ++ | +++ | ++ | + | ++ |
| Quetiapine | ++++ | + | ++ | ++ | ++ | ++ | ++ |
| Aripiprazole | ++ | + | ++ | ++ | + | - | ++ |

- Pharmacokinetic properties of these medications also aid in antipsychotic selection.
- For instance, if you are trying to reduce pill burden for an actively delirious patient – you may choose to consider a medication that can be dosed once daily (olanzapine) versus one that may need to be dosed at a higher frequency to achieve a consistent response (quetiapine)

| Antipsychotic | Onset of Action | Time to Peak | Half Life | Metabolism | Dosing Adjustments |
|---|---|---|---|---|---|
| Chlorpromazine | IV: 15 mins<br>PO: 30-60mins | IV: 15-20 mins<br>PO: 2-4 hrs | 30 hrs | Hepatic; CYP2D6 | Dose adjust in liver impairment |
| Haloperidol | IV: 20 mins<br>PO: ~4-6hrs | IV: 10-20 mins<br>PO: 6 hrs | 13-34 hrs | Hepatic; multiple | Dose adjust in liver impairment |
| Olanzapine | IV: ~30 mins<br>PO: ~4-6hrs | IV: 15-45 mins<br>PO: 6 hrs | ~30 hrs | Glucuronidation; CYP1A2, CYP2D6 | No adjustment necessary |
| Risperidone | PO: ~1 hr | PO: 1-2 hrs | 24 hrs | Hepatic; CYP2D6 | Dose adjust in renal and liver impairment |
| Quetiapine | PO: ~1 hr | PO: 1.5 hrs | ~6 hrs | Hepatic; CYP3A4 | Dose adjust in liver impairment |
| Aripiprazole | IV: ~1 hr<br>PO: ~4 hrs | PO: 3-5 hrs | ~72 hrs | Hepatic; CYP2D6, CYP3A4 | No adjustment necessary |

- Available formulations may also contribute to your antipsychotic selection

| Antipsychotic | Tablet | Oral Disintegrating Tablet | Oral Solution | Intramuscular Solution |
|---|---|---|---|---|
| Chlorpromazine | X | | | X |
| Haloperidol | X | | X (2mg/mL) | X |
| Olanzapine | X | X | | X |
| Risperidone | X | X | X (1mg/mL) | X (ER Form) |
| Quetiapine | X | | | |
| Aripiprazole | X | X (10mg, 15mg only) | X (1mg/mL) | X (IR and ER form) |

**Bottom Line:**

- You can utilize receptor affinities, pharmacokinetics, and formulation to help assist with your antipsychotic selection

**CLINICAL PEARL: Utilize receptor affinity profiles, pharmacokinetics, and available formulations of antipsychotics to aid in your antipsychotic selection.**