Pharmacologic Management of Delirium

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Treatment Guideline
1. Treat reversible causes (infection, constipation, urinary retention, etc.)
2. Evaluate and eliminate contributing drugs
3. Use antipsychotics to treat agitation and confusion

Non-pharmacologic treatments of delirium
1. Control environmental stimuli (light and sound)
2. Psychosocial support
3. Distraction (relaxation and music)
4. Adequate sleep

Mechanism of antipsychotics for the treatment of delirium
The potency of all antipsychotic drugs correlates well with their affinity for Dopamine-2 (D2) receptors.

Benzodiazepines for use in delirious patients:
May cause or worsen delirium (esp. in elderly)
Use for the treatment of delirium only if:
1. Delirium is related to withdrawal from a CNS-depressant agent
2. Needed for sedation when all other appropriate agents have failed

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Haloperidol</th>
<th>Chlorpromazine</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2-Dopamine</td>
<td>+++</td>
<td>++ to +++</td>
<td>+</td>
<td>+</td>
<td>++ to +++</td>
</tr>
<tr>
<td>H1-Histamine</td>
<td>0</td>
<td>++ to +++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>alpha1-Adrenergic</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>M1-Muscarinic</td>
<td>0 – +</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>0 to +</td>
</tr>
<tr>
<td>5-HT2A-serotonin</td>
<td>+</td>
<td>++</td>
<td>+++</td>
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<td>+++</td>
</tr>
</tbody>
</table>

References:
<table>
<thead>
<tr>
<th>Generic Name (Brand Name)</th>
<th>Usual Starting Dose</th>
<th>Route</th>
<th>Available Dosage Forms</th>
<th>Onset of Action*</th>
<th>Time to Max Response</th>
<th>Sedation</th>
<th>Anti-cholinergic</th>
<th>EPS</th>
<th>QTc</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical Antipsychotics</strong></td>
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<tr>
<td>Haloperidol (Haldol®)</td>
<td>0.5-1mg BID scheduled, additional doses every 4 hours prn</td>
<td>PO/SL/PR IM/IV</td>
<td>Tablet: 0.5 mg, 1 mg, 2 mg, 5 mg, 10 mg, 20 mg Oral Concentrate: 2 mg/mL Injection: 5 mg/mL</td>
<td>Oral: 1 hour IV may be effective (cause sedation) as soon as 2-5 minutes but may take up to one hour</td>
<td>4-7 10,11 days</td>
<td>+</td>
<td>Doses greater than 2 mg are typically reserved for psychosis and are more sedating.</td>
<td>+</td>
<td>+++</td>
<td>Avoid in patients with Parkinson’s Disease and Lewey Body Dementia</td>
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<tr>
<td>Chlorpromazine (Thorazine®)</td>
<td>12.5-50 mg TID. Additional doses every 4 hours prn</td>
<td>PO/SL PR IV/IM</td>
<td>Tablet: 10 mg, 25 mg, 50 mg, 100 mg, 200 mg Injection: 25 mg/mL</td>
<td>Tab: 30-60 min IV: 15 min</td>
<td>5-14 days 13</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>Modest orthostatic changes due to effects on α1-adrenergic receptors. Contraindicated in myelosuppression Manufacturer reports agranulocytosis, eosinophilia, leucopenia, hemolytic anemia, aplastic anemia, TTP</td>
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<tr>
<td><strong>Atypical Antipsychotics</strong></td>
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<tr>
<td>Risperidone (Risperdal®)</td>
<td>0.5-1.0 mg PO BID Additional 0.5 mg doses q4h prn (typical dose range is 0.25 – 2 mg q 12-24 hours)</td>
<td>PO</td>
<td>Tablets: 0.25, 0.5, 1, 2, 3 mg, 4 mg Orally disintegrating tablets: 0.5, 1, 2 mg Oral solution: 1 mg/mL</td>
<td>1-3 hours 14</td>
<td>4-7 days 15</td>
<td>+</td>
<td>0-+</td>
<td>++</td>
<td>+</td>
<td>Low daily doses (4-6 mg) are associated with lower risk of EPS than typical antipsychotics Average effective dose for delirium in clinical trials is 3 mg/day</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa ®)</td>
<td>2.5–5 mg PO/IM Daily (typical dose range is 2.5 – 10 mg q 12-24 hours)</td>
<td>PO IM</td>
<td>Tablets: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg Orally disintegrating tablets: 5 mg, 10 mg, 15 mg, 20 mg Oral solution: 10mg/vial</td>
<td>&lt;24 hours 16 IM formulation may have onset of about 2 hours for treatment of agitation.</td>
<td>3-7 days 17</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>0</td>
<td>Modest orthostatic changes due to effects on α1-adrenergic receptors. Highest risk of weight gain of atypical antipsychotics with long term use Sedation and appetite stimulation due to effects on H1- histamine receptor Oral disintegrating tablets still need to be swallowed for effect and share the same pharmacokinetic properties as the oral formulation</td>
</tr>
<tr>
<td>Quetiapine (Seroquel ®)</td>
<td>25 mg PO BID</td>
<td>PO</td>
<td>Tablets: 25 mg, 50 mg, 100 mg, 200 mg, 300 mg</td>
<td>&lt;24 hours 18</td>
<td>4-7 days 19</td>
<td>++</td>
<td>0-+</td>
<td>0</td>
<td>+/-</td>
<td>Most sedating of all atypical antipsychotics The preferred agent in patients with Parkinsons Disease due to decreased incidence of EPS. Typical dose range is 12.5 – 200 mg q 12-24 hours</td>
</tr>
</tbody>
</table>

*In clinical trials, the "Onset of action" is usually measured by sedation, while the "Time to maximal response" is typically measured with an established delirium scale. Underlined products available on OSUMC formulary