Atypical Antipsychotics in Acute Agitation & Delirium: Are they just along for the RIDE?

Learning Objectives

- To provide pharmacists with an overview of non-drug measures and pharmacotherapy strategies in managing an acutely agitated patient.
- To review the efficacy evidence and the safety implications of using atypical antipsychotics to treat these patients.
- To review preferred treatment strategies based on the etiology of the agitation.

Delirium

Characteristics of Delirium

- Three psychomotor variants
  - Hyperactive
  - Hypoactive
  - Mixed
- Prevalence
  - 25 - 30% of hospitalized medical or cancer pts
  - 15-50% of post-op patients
  - 70-87% of ICU patients
  - 60% of nursing home residents

Differential Diagnosis of Delirium

- Infection
- Withdrawal
- A cute metabolic
- T rauma
- C NS pathology
- H ypoxia
- D eficiencies
- E ndocrine
- A cute vascular
- T oxins or drugs
- H eavy metals

Treatment of Delirium

- Identify & correct the underlying medical condition causing the disorder
- Provide supportive care
  - Hydration, nutrition, mobilizing pt, avoiding restraints, calm environment, assist orientation (clock, glasses, hearing aids), uninterrupted sleep
- Prevent complications
- Treat behavioral symptoms

Gleason OC, Am Fam Physician 2003;67:1027-34

Inouye SK, NEJM 2006;354:1157-65

Wise MG, Trzepacz PT. Textbook of consultation-liaison psychiatry, APP 1996

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Acute Agitation

- A state of motor restlessness accompanied by mental tension
- Heightened responsiveness to stimuli
- Irritability
- Inappropriate / purposeless verbal or motor activity
- Decreased sleep
- Fluctuation of symptoms over time

Causes of Agitation

- Psychiatric illnesses
- Drug intoxication or withdrawal states
  - cocaine, amphetamines, alcohol, benzodiazepines, opioids
- Medical conditions
- Medication toxicity

Pathophysiology of Agitation

- Multiple mechanisms involved
  - Depends on the different clinical disorder
- Dysregulation in neurotransmitter systems
  - Increased Dopamine, Norepinephrine
  - Decreased GABA
  - Decreased Serotonin (~increased)

Scales to Measure Severity of Agitation

Measuring Severity of Agitation

- PANSS-EC
  - Positive and Negative Symptom Scale – Excited Component (5 items from total 30)
  - 7-point scale (1 absent – 7 extreme)
    - Poor impulse control
    - Tension
    - Hostility
    - Uncooperativeness
    - Excitement
  - Possible score: 5 – 35
    - ≤ 5 = absent, 6-10 = minimal, 11-15 = mild, 16-20= moderate, 21-25 = mod-severe, 26-30=severe, 31-35 = extreme

Measuring Severity of Agitation

- PANSS-Ag (Agitation Component) score: 5-35
  - Poor impulse control
  - Hallucinatory behavior
  - Hostility
  - Uncooperativeness
  - Excitement

- ABS – Agitated Behavior Scale
  - 14 items, 4-point scale (1 absent, 4 extreme degree)
    - Possible score: 14-56

- BPRS – Brief Psychiatric Rating Scale
  - 24 items, 14 self-report and 10 observational
  - 7-point scale (1 absent – 7 severe)
  - Broad range of symptoms assessed
    - Possible score: 24-168
More Scales…

- OASS – Overt Agitation Severity Scale
  - 12 items, 5-point scale (0 absent, 4 always present)
  - Assesses behaviors = Intensity x Frequency = Severity Score
  - Possible score: 0 – 120

- OAS – Overt Aggression Scale
  - 16 items
  - 4 categories: verbal aggression, physical aggression to self, objects & others
  - Aggression score (max score 21)
  - Total aggression score (accounts for level of restricted intervention required) (max score 26)

- Clinical Global Impression – Improvement Scale
  - 7-point scale
  - various scores: very much improved, much improved, minimally improved, no change, minimally worse, much worse, very much worse

Limitations to Severity Scales

- Assess only one side of the spectrum
  - No Agitation
  - Severe Agitation

- Also need to consider the desirable or undesirable sedation – decreased level of consciousness
  - Unable to arouse
  - Calm

Full Spectrum Scales

- BARS (Behavior Activity Rating Scale) - 7 point scale
  - 1 - unarousable
  - 2 - asleep but responds
  - 3 - drowsy/sedated
  - 4 - quiet/awake
  - 5 - mild calmness
  - 6 - signs of overt activity but will calm
  - 7 - violent and requiring restraint

- ACES (Agitation-Calmness Evaluation Scale) - 9 point scale
  - 1 - marked agitation
  - 2 - moderate agitation
  - 3 - mild
  - 4 - normal
  - 5 - mild calmness
  - 6 - moderate
  - 7 - marked
  - 8 - deep sleep
  - 9 - unarousable

Provide less detail about the agitation, behaviors
Gives a sense on whether the patient may be assessed by physicians

Patient Case

Meet Patient JN (also known as JT)

- 45 yr old male
- Brought in to ER by police after altercation at a hotel...
- He is agitated, restless and uncooperative to questions or exam
- He is increasingly hypervigilant with the noises around him in the busy ER
- Denies drug/alcohol use
- No past med history available at this point

Goals of Therapy

- Safe and rapid control of symptoms
- Calming without excessive sedation
- Reduce danger to self and others
- Resumption of therapeutic alliance
- Minimize or avoid side effects

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**Non-drug Interventions**

- Environment
  - Interpersonal communication
  - Physical surroundings
- Non-violent crisis intervention (NVCI)
  - Verbal techniques for de-escalation
  - Physical principles for personal safety techniques
- Show of force
- Restraints
  - Seclusion rooms
  - Physical
    - Pharmacological interventions
  - Chemical

**Risks with Physical Restraints**

- Psychological trauma
- Immobilization – thrombosis, PE
- Rhabdomyolysis
- Catecholamine rush – arrhythmias
- Asphyxia … death
  - Position, neck compression, reduced forced vital capacity

**Back to JN**

- More info becomes available
  - Urine tox screen – negative
  - Other labs within normal limits
  - PANSS-EC = 17 (moderate)
  - No known drug allergies or ADR
- A medical resident wanders by and after observing JN – suggests the ‘usual remedy’ of “5-2-2” (IM Haloperidol, Lorazepam, Benztropine)

**Desirable Characteristics of Medication Choices**

- Anti-agitation efficacy
- Rapid onset of action
- Sustained effect
- Low adverse-effect profile
- Permits communication
- Choice of formulation
  - Tablet, rapid-dissolving tablets, liquid, short-acting IM
- Low risk of drug interactions

**Pharmacological Treatments of Acute Agitation**

- Benzodiazepines (BZD)
- Conventional Antipsychotics (CAP)
- Atypical Antipsychotics (AAP)
- Combination BZD and AP
- Formulation – IM vs. PO
- “Rapid Tranquilization” = calming without sedation
**Benzodiazepines**

- **Pharmacology**
  - Enhance GABA effects on chloride channel of GABA-BZD receptor – decreasing cellular excitability
- **Lorazepam - drug of choice:**
  - Most studied BZD in agitation
  - Predictable IM absorption
  - Intermediate half-life (10-20 hrs)
  - Dose: 1-2 mg SL/PO/IM q30 min
  - Onset: SL 15-30 min, IM 10-20 min
  - Peak effect: SL 60 min, IM 30-60 min
  - Duration: 3-6 hrs

**Evidence for BZD**

- BZDs at least as effective as Haloperidol (HAL)
- BZD superior than HAL
  - Measures of aggression
  - CGI (Clinical Global Impression)
  - Resolving catatonia
  - More acutely sedating than HAL
- Side effects
  - Excessive sedation, respiratory depression
  - Paradoxical disinhibition

**Conventional Antipsychotics**

**Commonly used agents:**

- Haloperidol (HAL) – liquid, tablet, short IM, depot IM
- Loxapine (LOX) – liquid, tablet, short IM
- Zuclopenthixol acetate (Clopixol Accuphase®) – special circumstances only

**Pharmacology**

- Dopamine (D2) blockade – “tightly bind”
- High potency vs. Low potency
- Histamine (H1) blockade
- Muscarinic blockade
- Alpha-1 blockade

**CAP - Pharmacokinetics**

<table>
<thead>
<tr>
<th>CAP - Pharmacokinetics</th>
<th>Haloperidol</th>
<th>Loxapine</th>
<th>Zuclopenthixol Acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>2-10 mg PO/IM q1hprn</td>
<td>12.5-25 mg PO/IM q1hprn (max 25 mg/hr)</td>
<td>50-150 mg IM pm may repeat dose in 12-24hr Max 400 mg (oral injection only)</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>PO 30 min IM 10-20 min</td>
<td>PO 20-30 min IM 15-30 min</td>
<td>2-4 hrs Sedation may be sooner</td>
</tr>
<tr>
<td><strong>Peak effect</strong></td>
<td>PO 3-6 hrs IM 30-45 min</td>
<td>PO 1.5-3 hrs IM ~similar</td>
<td>24-36 hrs</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>4-8 hrs</td>
<td>12 hrs</td>
<td>3 days</td>
</tr>
</tbody>
</table>

**Allen MH. J Clin Psych 2000;61(suppl 14):11-20**
Evidence for CAP

- Early studies in 1970’s showed CAP > Placebo
  - HAL (2.5-5 mg) similar efficacy to LOX (25-50 mg)
  - LOX more effective for sleep
  - LOX peak benefit by 2 hr vs HAL at 6 hr (po)

- Side effects
  - Hypotension, EPS (akathisia, tremor, rigidity, dystonic reactions), Sedation, Anticholinergic effects

Haloperidol, Lorazepam or Both?

- P
  - n = 98, RCT, DB
  - Mod – severe psychosis or behavioral dyscontrol
  - Excluded: obvious ETOH intox, delirium or CNS depression

- I
  - Haloperidol (HAL) 5 mg IM
  - Lorazepam (LRZ) 2 mg IM
  - Combination HAL 5 mg + LRZ 2 mg IM

- O
  - 1st 3 injections at least 1 hr apart, then q2hrpm
  - Hourly evaluations on BPRS, CGI and ABS for 12 hrs

Results - HAL, LRZ or Both? …

- All groups - significant improvement from baseline
  - Combination > LRZ on ABS at 1 hr, No diff by 2-3 hrs
  - Combination > LRZ or HAL on mBPRS at 2-3 hrs, No diff by 4 hrs
  - Less drug requirement (3 doses or less of study meds)
    - Combination 91%, LRZ 74%, HAL 71%

- EPS:
  - HAL 20% (11% dystonic rxn)
  - Combination 6%
  - LRZ 3%

Back to JN

- You opt to try reducing stimulation – quiet room with door open
  - PANSS-EC = 17 (mod)

- He is accepting of oral medications, consider
  - Lorazepam 2 mg PO
  - Loxapine 25 mg + Lorazepam 2 mg PO
  - LOX more sedating than HAL, less well-studied
  - Haloperidol 5 mg + Lorazepam 2 mg PO

- Re-assess in 30-60 minutes
- Check vitals if pt cooperative
- What about an Atypical Antipsychotic??

Atypical Antipsychotics (AAP)

- Available agents in Canada
  - Risperidone — liquid, tablet, rapid-disintegrating tablet, long-acting depot
  - Olanzapine — tablet, rapid-disintegrating tablet, short-acting IM injection
  - Quetiapine — tablet
  - Clozapine — tablet

- Pharmacology
  - Dopamine (D2) blockade – “hit and run” approach
  - Serotonin (5HT-2a) blockade
  - Histamine (H1) blockade
  - Muscarinic blockade
  - Alpha-1 blockade
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RSP po vs. HAL po (Veser 2006)

| P | n = 30; pilot study, RCT  
|   | Agitated or psychotic pts. (allowed substance abuse)  
|   | Mean age 40  
|   | Baseline PANSS total: RSP 88, HAL 90, PBO/LRZ 65  
| I | RSP 2 mg PO + LRZ 2 mg IM  
| I | HAL 5 mg PO + LRZ 2 mg IM  
| C | Placebo PO + LRZ 2 mg IM  
| O | BPRS and total PANSS at 30 & 90 min


RSP - Veser 2006 - Results

- Outcomes PANSS, BPRS at 30 & 90 min  
  - No SS differences between grps  
  - PANSS total reductions: RSP -31, HAL -24, PBO/LRZ -11  
  - BPRS total reductions: RSP -22, HAL -22, PBO/LRZ -12  
  - Trend for great improvement in RSP/LRZ and HAL/LRZ arms

- Limitations  
  - lacked power  
  - short follow-up of 90 min (missed peak effects of AP)  
  - No SE reported

Olanzapine (OLZ) – RIDE Study (Baker 2003)

- Randomized, 4 day DB, 3 day OL trial (n = 148)  
  - Acutely agitated with Schizophrenia/affective, Bipolar mania  
  - Baseline PANSS-EC = 23 (moderate)  
  - Excluded substance-induced psychosis

RIDE: Rapid Initial Dose Escalation
OLZ 20 mg/d + prn OLZ 10 mg  
(Max OLZ 40 mg/d on Days 1-2; Max 20 mg/d on Days 3-4)

UCP: Usual Clinical Practice
OLZ 10 mg/d + prn LRZ 2 mg  
(Max LRZ 4 mg/d on days 1-2; Max 2 mg/d on days 3-4)

OLZ – RIDE Trial Results

- Medication Requirements at 24 hr  
  - RIDE: OLZ 29 mg, LZM 0.12 mg  
  - UCP: OLZ 10 mg, LZM 2.15 mg

- Number of doses at 24 hr:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
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</thead>
<tbody>
<tr>
<td>RIDE</td>
<td>1</td>
<td>25</td>
<td>32</td>
<td>34</td>
<td>34</td>
<td>32</td>
<td>25</td>
</tr>
<tr>
<td>UCP</td>
<td>1</td>
<td>25</td>
<td>32</td>
<td>34</td>
<td>34</td>
<td>32</td>
<td>25</td>
</tr>
</tbody>
</table>

OLZ – RIDE Results…

- 1° Endpoint: PANSS-EC change at 24 hrs  
  - RIDE: -7.01  
  - UCP: -5.51 (p=0.003)  
  - Absolute difference of 1.5 points / 35 total – ?? Clinical Significance  
  - Both groups (ss) improved from baseline

- 2° Endpoints

<table>
<thead>
<tr>
<th></th>
<th>24 hrs</th>
<th>48 hrs</th>
<th>72 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGH</td>
<td>RIDE = UCP</td>
<td>PANSS-EC: RIDE = UCP</td>
<td>CGH: RIDE &gt; UCP (by 5 pts/ 120 total)</td>
</tr>
<tr>
<td>OASS: RIDE &gt; UCP</td>
<td>CGI-I: RIDE &gt; UCP (by 0.6 pts/7 total)</td>
<td>OASS: RIDE &gt; UCP (by 5 pts/ 120 total)</td>
<td></td>
</tr>
</tbody>
</table>

OLZ – RIDE …

- Adverse events  
  - No significant differences between tx grps for abnormal movements or akathisia

- Excluded substance abuse, pts > 55yrs  
- No ECG monitoring done, no vital signs reported

<table>
<thead>
<tr>
<th></th>
<th>RIDE</th>
<th>UCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence</td>
<td>31%</td>
<td>26%</td>
</tr>
<tr>
<td>Headache</td>
<td>17%</td>
<td>8%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>15%</td>
<td>7%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13%</td>
<td>8%</td>
</tr>
<tr>
<td>Nervousness</td>
<td>7%</td>
<td>11%</td>
</tr>
</tbody>
</table>
| Wt gain at 1 wk | 1.45 kg | 1.21 kg

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OLZ po vs. HAL po (Kinon 2004)

**P**
- N = 100, 3 week, Randomized, DB
- Acutely agitated in pts with Schizophrenia, Schizoaffective d/o
- Mean age = 39, Baseline mPANSS = 38 (max 60)

**I**
- OLZ 10 mg PO + LRZ 1-2 mg po/im prn
- Could increase AP dose by 5 mg/day (range 10-20 mg)

**C**
- HAL 10 mg PO + LRZ 1-2 mg po/im prn

**O**
- mPANSS at 24 hr

OLZ - Kinon 2004 - Results

- Primary outcome mPANSS at 24 hr
- 24 hrs: Both grps improved from baseline
  - No difference between grps
  - ≤10 improvement on mPANSS
- 21 days: OLZ superior to HAL
  - mPANSS -14 vs. -11, p=0.044

- Mean dose at 21 days
  - OLZ 17.1 mg, HAL 15.7 mg

- Only 57 pts completed 3 wk study
  - Discontinued due to SE: OLZ 1.9%, HAL 16.7%

OLZ - Kinon 2004 – Adverse Effects

<table>
<thead>
<tr>
<th></th>
<th>OLZ</th>
<th>HAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia</td>
<td>0%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Hypertonia</td>
<td>0%</td>
<td>8.3%</td>
</tr>
<tr>
<td>↑ salivation</td>
<td>0%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Headache</td>
<td>11.5%</td>
<td>25%</td>
</tr>
<tr>
<td>Nervoussess</td>
<td>7.7%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>11.5%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>17.3%</td>
<td>25%</td>
</tr>
<tr>
<td>Wt gain</td>
<td>2.8 kg</td>
<td>-0.64 kg</td>
</tr>
</tbody>
</table>

Quetiapine (QTP) – (Currier 2006)

**P**
- Open-label pilot study, n = 20
- Pts exhibiting psychosis or mod-severe agitation.
- Mean age = 39, Baseline PANSS-EC = 17-18 (moderate)
- Excluded: obvious drug/alcohol intox, concurrent tx with CYP 3A4 inducers/inhibitors

**I**
- 100, 150, or 200 mg QTP - MD perception of clinical need
- 2nd dose of QTP or LRZ permitted at 90 min (dose not specified)

**O**
- 1: PANSS-EC at 120 min. (Success = 40% reduction from baseline).
- 2nd outcome: BARS
- Safety: SBP & pulse at baseline, 30, 60, 90, 120 and 180 min
  (Orthostasis defined as 20 pt change)

QTP - Currier 2006 - Results

- Median dose 2 mg/kg
  - 7 x 100 mg, 6 x 150 mg, 7 x 200 mg
- PANSS-EC reduction
  - ≤1/2 pts had a 40% reduction in scores (success)
  - BARS - reduction from 5 to 3
- Safety
  - ≤40% pts had orthostatic hypotension by 2 hrs
- Limitations
  - Very small pilot study
  - Agitated pts often present in volume depleted state and are at high risk for medication-induced hemodynamic instability

JN ...

- More information from family
  - JN has a history of Schizoaffective disorder
  - non-compliant with treatment due to lack of insight
    - Treated with Risperidone 3 mg/day in the past
- JN is exhibited psychotic symptoms – appears to be responding to auditory hallucinations
  - His behavior is escalating – PANSS-EC = 23
    (moderate-severe)

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Consider AAP
- RSP studied in broader agitated population (psychosis NOS)
- OLZ studied only in Schizophrenia, Bipolar agitated pts
- Limited data with QTP
  - Both have rapid disintegrating tablets (not studied)
If agitation worsens, consider IM injections
- HAL 5 mg + LRZ 2 mg, or LOX 25 mg + LRZ 2 mg
  - Re-assess in 30 minutes
- What about Olanzapine IM?

OLZ IM in Schizophrenia

| P | 2 trials, n = 555 total, RCT, DB, 24 hrs |
| I | Mean age 36-38 yrs, Baseline PANSS-EC = 19 (moderate) |
| I | OLZ 2.5 – 10 mg IM (dose finding) |
| I | OLZ 10 mg IM |
| C | Max 3 injections, 2 hr apart |
| O | PANSS-EC at 2 hrs |
| R | OLZ IM similar to HAL IM, both superior to PBO |
| | OLZ 2.5 mg arm not as effective as other doses. |


OLZ IM in Bipolar Mania

| P | n = 201, RCT, DB, 24 hrs |
| I | Mean age 40, Baseline PANSS-EC = 13 (moderate) |
| I | OLZ 10 mg IM |
| I | Max 3 doses in 3 hrs. |
| I | LRZ 2 mg IM |
| C | 3rd dose: OLZ 5 mg, LRZ 1 mg, PBO group were given OLZ 10 mg |
| O | PANSS-EC at 2 hrs |
| R | OLZ IM superior to LRZ IM and PBO |
| | LRZ similar to PBO at 2 hrs |


OLZ IM in Dementia

| P | n = 272, RCT, DB, 24 hrs (* not indicated for dementia in Canada) |
| I | Mean age 78, Baseline PANSS-EC = 19.7 (moderate) |
| I | OLZ IM 2.5, 5 mg |
| I | Max 3 doses in 3 hrs. |
| I | LRZ IM 1 mg |
| C | 3rd inj: ½ dose, PBO grp received OLZ 5 mg IM |
| O | PANSS-EC at 2 hrs |
| R | OLZ IM 2.5, 5 mg and LRZ IM superior to PBO |
| | No difference between OLZ IM or LRZ IM |

Meehan K et al. Neuropsychopharmacol 2002;26:494-504.

OLZ IM – Safety information

- ECG monitoring done at baseline, 2 hrs, 24 hrs
  - Clinically significant QTc prolongation
    - OLZ 4-10%, HAL 14%, PBO 19%
    - Missed the peak effects of OLZ IM
- Schizophrenia trials
  - OLZ – Hypotension 4%, Parkinsonism 3%, Akathisia 5%
  - HAL – Parkinsonism 17%, Akathisia 8%, Acute dystonia 5%
- Bipolar trial
  - OLZ – one case of syncope
  - No difference for EPS, no acute dystonic rns (vs. LRZ)

OLZ IM – Safety Information...

- Safety notification letter from manufacturer in Sept/04
  - SAEs reported with co-administration of OLZ IM with other drugs
    - IMojo – Haloperidol, Lorazepam, Midazolam, Chlorpromazine
    - Combination can induce hypotension, bradycardia, respiratory/CNS depression
- Recommended
  - NOT to co-administer with parenteral BZDs (** within 1 hr)
  - NOT for use in pts whom substance use is suspected
OLZ IM Study Limitations

- Not compared against standard clinical practice (HAL 5 mg + LOX 2 mg IM)
- Comparative HAL dose too high – impact on SE
- Not compared to LOX (more sedating, less dystonia than HAL)
- Studied in mild-moderate agitation with defined psychiatric diagnoses without serious medical co-morbidities
- No data on use in Substance abuse
- Cost implications ~ $20/10 mg dose
  - $2-5 for IM LOX or HAL
  - $1-6 for rapid-dissolving RSP or OLZ
  - pennies for PO LOX or HAL

Suspected Substance Induced Agitation

- BZDs are treatment of choice
  - Would NOT use monotherapy APs, avoid if possible
  - Deleterious effects on BP
  - Potential for QTc prolongation, arrhythmias
  - Additional anticholinergic effects (hallucinogens)
  - Potential for serotonin syndrome (amphetamines)
  - Potential for EPS, Neuroleptic malignant syndrome
- BZDs offer seizure protection

Remember Drug Interactions

- Olanzapine
  - Metabolized by CYP 1A2
  - UDI is strongly induced by cigarette smoking
  - UDI is inhibited by ciprofloxacin, fluoxetine, fluvoxamine
  - May need higher doses in heavy smokers
- Risperidone
  - Metabolized by CYP 2D6
  - 2D6 is inhibited by paroxetine, fluoxetine, fluvoxamine
  - RDI is induced by carbamazepine
- Haloperidol
  - Metabolized by CYP 3A4, 2D6
  - Inhibited by carbamazepine, rifampin
  - Induced by phenytoin
- Quetiapine
  - Metabolized by CYP 3A4, 2D6
  - As above

Summary of Drug Interventions

- Offer PO if patient cooperative
  - PO CAP studied in broader pt populations (+ BZD)
  - PO AAP studied mainly in psychiatric populations
  - Consider long-term treatment plan, rapid-dissolve tabs
  - Would NOT recommend RIDE strategy for OLZ
- IM evidence
  - Mainly with HAL, although LOX used in clinical practice
  - OLZ evidence limited to mild-mod agitation with defined psychiatric diagnoses
  - NOT combined with BZDs

Patient Case

Meet SL…

- 39 yr old male
- Brought to ER from an after-party of Banff Seminar
- He has been dancing all night but has become increasingly agitated & restless
- Friends report he had only 2 drinks – they wonder if something was slipped in his drink?
- No past med hx
- T 39 C, BP 195/110

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September 16, 2006
Summary…

- Substance-induced agitation suspected
  - BZD 1st choice
  - Monotherapy AP not recommended
    - These pts usually excluded from the trials
  - No data with IM OLZ
- Re-assess for efficacy and toxicity!!!
  - 30-60 min post PO dose
  - 15-30 min post IM dose

Thank-you !!
Any questions??