Impact of Quetiapine Treatment on Duration of Hypoactive Delirium in Critically Ill Adults: A Retrospective Analysis

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Setup:

Objective
• to determine whether treatment of hypoactive delirium with quetiapine reduces the duration of delirium compared with no pharmacologic treatment.

Design
• Retrospective cohort study.

Setting
• Three medical-surgical ICUs within the two main campuses of an academic tertiary care hospital system.
Patients:

- routinely screened for delirium by trained bedside nurses using CAM-ICU and RASS during daily spontaneous awake
- Any patient who screened positive for hypoactive delirium at least once during their ICU stay was eligible to be included in the study.
- patients were stratified:
  - received at least one dose of quetiapine during their hypoactive delirium course
  - or having received no pharmacologic delirium treatment (including as-needed haloperidol).
Background + Definitions:

**Standard of care**
- analoog Comfort protocol

**Delirium assessment**
- a positive CAM-ICU and a RASS score of 0 to −3 to demonstrate a purely hypoactive delirium

**Duration of delirium**
- the number of days (to the nearest half day) from the first positive CAM-ICU screen to the start of the first 24-hour period of consecutive negative delirium screens.

**Statistical analysis**
- To detect a 0.5-day difference in the primary outcome of delirium duration with an overall two-sided $\alpha$ level of 0.05, an estimated 104 patients would need to be enrolled.
Patient selection:

493 Patients with Delirium

Hypoactive  n = 257

Hyperactive or Mixed  n = 236

Excluded*

Length of Stay < 72 Hours  n = 76
Treated with Other Antipsychotic  n = 22
Chronic Antipsychotic Use  n = 18
BZDs for Ethanol Withdrawal  n = 8
Insufficient Medical Records  n = 7
History of Dementia  n = 4
History of Parkinson  n = 4
History of Structural Brain Damage  n = 2
History of Torsade de Pointes  n = 2
Pregnancy  n = 1

Included  N = 113

Quetiapine  n = 52

No Quetiapine  n = 61

Abbreviations: BZD = benzodiazepine
* Other exclusion criteria included history of neuroleptic malignant syndrome, previous enrollment in the study, and incarceration; no patients were excluded for these reasons.
## Results:

<table>
<thead>
<tr>
<th></th>
<th>Quetiapine [median days]</th>
<th>No quetiapine [median days]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of hypoactive delirium</strong></td>
<td>1.5 [range 0.5–6.0]</td>
<td>2.0 [range 0.5–8.5]</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Days receiving mechanical ventilation</strong></td>
<td>7 [range 0.5–43]</td>
<td>7.5 [range 1–29]</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Time on ventilator after first positive delirium screen</strong></td>
<td>3 [range 0.5–35]</td>
<td>5 [range 0.5–20]</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>ICU LOS</strong></td>
<td>10 [range 3–41]</td>
<td>12 [range 3–37]</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Hospital LOS</strong></td>
<td>15 [range 4–64]</td>
<td>16 [range 4–38]</td>
<td>0.57</td>
</tr>
</tbody>
</table>
Probability of delirium persisting in the subsequent 24 hours
Subgroup analysis:

initiation of quetiapine within the first 24 hours of delirium

- median time in delirium 1 [range 0.5–5.5] day vs 3.5 [range 1–11] days, p<0.001
- median time to extubation 1.5 [range 0.5–5] days vs 5 [range 1–35] days, p=0.003
Risk of bias:

- Retrospective review
- Strict inclusion and exclusion criteria
- ICU LOS > 72 hours ➔ focus on incident delirium
- Exclusion if use of any antipsychotic other than quetiapine
- Use of dexmedetomidine: app. 25% of patients in both groups
- no formal treatment algorithm for delirium in place during the study period ➔ This most drastically affected the time to quetiapine discontinuation
- Excluding patients who received non-quetiapine antipsychotics may potentially have favored “quetiapine responders” by eliminating those who required, for example, haloperidol rescue therapy.