Phenomology of and Risk Factors for New-Onset Diabetes Mellitus and Diabetic Ketoacidosis Associated with Atypical Antipsychotics: An Analysis of 45 Published Cases

Jin H, Meyer JM,Jeste DV ANN Clin Psych 14;Mar 2002: 59-64

Answers That Matter.
Phenomology of and Risk Factors for New-Onset Diabetes Mellitus

• 45 cases of new-onset DM or DKA
  • Clozapine – 20
  • Olanzapine – 19
  • Risperidone - 3
  • Quetiapine – 3

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Phenomology of and Risk Factors for New-Onset Diabetes Mellitus

- 87% male
- 47% African American
- 42% presented with DKA
- Blood Glucose at time of diagnosis
  - 89% > 300mg/dL
  - 63% > 500mg/dL

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- 32 (71%) patients had weight measurement
  - 50 % (16) manifested no weight gain at time of presentation with DM
  - 84% were overweight (>5% over ideal weight) at baseline

- 77% received adjunctive medications

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Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus

Mean duration of antipsychotic prior to DM was 19 weeks.

Time to Presentation

<table>
<thead>
<tr>
<th>Duration of Antipsychotic Therapy</th>
<th>Percentage of Patients</th>
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<tr>
<td>&lt;30 days</td>
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<tr>
<td>4-6 months</td>
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<td>1-2 years</td>
<td>25</td>
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Age at Time of Diagnosis

<table>
<thead>
<tr>
<th>Age</th>
<th>Percentage of Patients</th>
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<td>&lt;30</td>
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</tbody>
</table>

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Phenomology of and Risk Factors for New-Onset Diabetes Mellitus

- Patients with DKA vs those with DM
  - Women
  - Younger
  - Less overweight at baseline
  - Presented with higher blood glucose

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Olanzapine-Associated Diabetes Mellitus

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852

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Answers That Matter.
Olanzapine-Associated Diabetes Mellitus

• 237 cases of olanzapine associated DM or hyperglycemia
  • 41 cases in 22 publications
  • 215 from the United States
  • 22 from outside the US

• 188 (79%) newly diagnosed
  – 153 met criteria for diagnosis of DM (mean age 40 years)
  – 35 contained insufficient information for diagnosis of DM
    – 19 treated with anti-diabetic therapy
• 44 (19%) exacerbation of preexisting DM (mean age 52 years)
• 5 (2%) could not be classified

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

• 150 patients had race information
  • 56% caucasian
  • 39% African American
  • 3% Hispanic
  • 3% Asian

Koller EA, Doraiswamy PM. Pharmacotherapy 2002; (7): 841-852
Olanzapine-Associated Diabetes Mellitus

• Time to Onset
  • All patients
    • 2-45 days
    • ≤ 6 months for 73%
  • Among newly diagnosed DM
    • ≤ 1 month for 13%
    • ≤ 3 months for 47%
    • ≤ 6 months for 70%
  • Among those with exacerbation of preexisting DM
    • ≤ 1 month for 55%
    • ≤ 3 months for 84%
    • ≤ 6 months for 97%

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

• Dose
  • All patients – 15.6mg
  • Newly diagnosed patients - 16.1mg
  • Exacerbation of preexisting DM – 13.2mg
  • Those with ketosis or acidosis – 16.6mg
  • Those without ketosis or acidosis –15.0mg

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

• Metabolic Acidosis
  • Among all patients 80 (34%)
  • Among newly diagnoses patients 74 (39%)
  • Among patients with exacerbation of preexisting DM 3 (7%)

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

• Deaths
  • 15 total
  • 8 male, 7 female
  • 14 occurred in newly diagnosed patients
  • Time to onset <3 months for 8 patients
  • Mean daily dose = 17.9 mg
  • 13 occurred during or soon after the hyperglycemic episode
  • 1 died of necrotizing pancreatitis 1 month after hyperglycemic episode

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

- Other Risk Factors
  - 76% were either overweight at baseline or gained a significant amount of weight
  - 43% of newly diagnosed patients had a family history of DM
  - 6 patients had hepatitis
  - 8 patients had been taking another atypical antipsychotic
  - 31% received valproate

Koller EA, Doraiswamy PM. Pharmacotherapy 2002;(7):841-852
Olanzapine-Associated Diabetes Mellitus

• Authors’ discussion and conclusions
  • Gravity of outcomes highlights need to further investigate the potential association
  • Relationship between olanzapine and DM established by:
    • Number of cases reported
    • Prompt reversibility when drug is withdrawn
    • Mean age at diagnosis is considerably less than that seen in general population
      • Frequency of newly diagnosed DM in people < 44 in the olanzapine-treated patients (66%) is twice that seen in the general population (33%)
    • Gender distribution is different than that of the general population (M:F 1.8 vs 0.8)
Olanzapine-Associated Diabetes Mellitus

• Authors’ discussion of limitations
  • Underreporting characteristic of this system
  • Distortions in reporting due to clinician awareness
  • Clinician awareness of weight gain may contribute to more frequent monitoring and detection of DM
  • Rate cannot be determined
  • Causality cannot be established
  • Contribution of other risk factors cannot be ruled out

• However, the authors conclude that their results suggest a causal relationship

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