Antipsychotics Triple the Risk of Type 2 Diabetes in Young People

Believing that there is considerable evidence to link antipsychotic use to the increased risk of type 2 diabetes (DM-2), a team of investigators conducted a retrospective cohort study of the Tennessee Medicaid program. The cohort included children and youth recently initiated on antipsychotics who had received a diagnosis for which there were other pharmacotherapies. The score-matched control group had also recently begun therapy but with other psychotropic medications, which included mood stabilizers, antidepressants, psychostimulants, alpha-agonists, and benzodiazepines. Data were obtained from the computerized files of the Tennessee Medicaid program and augmented with the state’s hospital discharge database and computerized birth certificates; medications were identified from Medicaid pharmacy files.

The study population included children and youth, 6 to 24 years of age, enrolled in Medicaid for at least one year between January 1, 1996, and December 31, 2007. The lower age limit was selected because it is the youngest age for which there are numbers of case reports of DM-2; the upper age corresponds to the World Health Organization’s definition of youth. The investigators sought a control group highly comparable to the antipsychotic users and, therefore, matched the controls within centiles of the tendency of the antipsychotic score distribution. The final group included 28,858 in the cohort and 14,429 in the propensity score-matched controls – one control for every two antipsychotic users. Patients excluded in the study were those diagnosed with conditions for which antipsychotics generally are the only recommended treatment. Diagnoses for exclusion were schizophrenia or related psychoses, organic psychoses, autism, mental retardation, Tourette syndrome, or other tic disorders. A prescription for clozapine or a long-acting injectable antipsychotic also was cause for exclusion. At baseline, antipsychotic users were classified according to daily dose expressed as chlorpromazine equivalents. By virtue of the matching, the baseline characteristics of the controls were entirely comparable to those of the antipsychotic users.

Findings included:
- During cohort follow-up, there were 106 cases of newly-diagnosed DM-2 (18.9 cases per 10,000 person-years). The mean age of the patients was 16.7 years, 37% were male, and 34% had Medicaid enrollment related to disability.
- Antipsychotic users had a three-fold increased risk for DM-2
  - The increased risk was apparent within the first year of follow-up
  - Risk did not vary significantly according to baseline dose but did increase with cumulative dose during the follow-up
  - The excess risk was present for children 6 to 17 years of age
- The increased risk persisted for up to one year following cessation of antipsychotic use

Limitations to the study were:
- Errant diagnoses for diabetes from clinical practitioners and prescriptions for antidiabetic drugs
- Incomplete identification of DM-2 in the cohort because many children and youth may not have undergone testing necessary for this diagnosis
- Guidelines published in 2004 were the first to recommend routine glucose monitoring; those taking the medications before that time may not have been as closely followed
- The authors state that they could not control for obesity, which is closely linked to DM-2
- The study cohort consisted of Tennessee Medicaid enrollees which limits the generalizability of study findings


Antipsychotics For The Treatment of Alcohol Dependence

Although antipsychotics lack FDA approval for the treatment of alcohol dependence, they are frequently used in practice for this indication. This may be due to the hypothesized abilities of these agents to decrease cravings and lessen symptoms, which may encourage relapse such as anxiety, depression, and impulsivity. In search of evidence to justify the effectiveness of this treatment, a team of researchers conducted a meta-analysis of randomized controlled trials that investigated antipsychotic monotherapy

This is a compilation of recent news and research that may be of interest to providers. It is for informational and educational purposes only. Although we make every effort to ensure that this material is accurate and up-to-date, it is provided for the convenience of the user and should not be considered definitive. Magellan does not participate in or endorse any of the particular studies contained herein. Whole Health Rx Quarterly Update is produced by Magellan Health Services.
Brintellix™ Approved for MDD

The FDA has approved the joint marketing of vortioxetine by two companies, Takeda and Lundbeck. Brintellix™ is approved for the treatment of adults with major depressive disorder (MDD); it will be available as 5, 10, 15 and 20 mg tablets. The mechanism of the antidepressant effect of Brintellix™ is not fully understood, but it appears to be from two mechanisms of action: receptor activity modulations and reuptake inhibition. It is an inhibitor of serotonin reuptake (S-HT) and is also an agonist at S-HT1A receptors, a partial agonist at S-HT1B receptors and an antagonist at S-HT3, S-HT1D and S-HT7 receptors. The clinical relevance of each of these activities is unknown at this time. It is considered to be the first and only compound with this unique mechanism of action. Launch is planned for 4th quarter 2013.

Let’s Talk!

Choosing Wisely® is an initiative of the American Board of Internal Medicine (ABIM) Foundation. Along with the American Psychiatric Association (APA), ABIM has developed “Five Things Physicians and Patients Should Questions to be used to prompt conversations between patients and physicians about what care really is necessary. APA’s list includes the following recommendations:

• Don’t prescribe antipsychotic medications to patients for any indication without appropriate initial evaluation and appropriate ongoing monitoring.
• Don’t routinely prescribe two or more antipsychotic medications together.
• Don’t prescribe antipsychotic medications as a first-line intervention to treat behavioral and psychological symptoms of dementia.
• Don’t routinely prescribe antipsychotic medications as a first-line intervention for insomnia in adults.
• Don’t routinely prescribe antipsychotic medications as a first-line intervention for children and adolescents for any diagnosis other than psychotic disorders.

http://online.wsj.com/article/SB1000142412788733477604578654130865747470.html

Treatment of Alcohol Dependence (cont.)

for patients with primary alcohol dependence. Eligible trials were randomized, placebo-controlled, double-blind studies that lasted at least two weeks and had participants with no comorbid psychosis or bipolar disorders.

Thirteen trials published before December 2012 collectively examined six different antipsychotics (tiapride, olanzapine, quetiapine, aripiprazole, flupenthixol decanoate, amisulpride) and their effectiveness, efficacy, and tolerability against placebo. There were a total of 1,593 patients in the meta-analysis who were classified according to alcohol intake characteristics at baseline.

The researchers reported no significant difference between pooled or individual antipsychotics and placebo in their analysis. Of interest was the following:

• Patient average age was 43.7 years, with 77.2% of patients being white and 73.3% being male
• Antipsychotic use was inferior to placebo regarding percentage of days abstinent
• Antipsychotic and placebo use had similar effects on craving, heavy drinking, time to first alcohol consumption, and prevention of relapse
• Antipsychotic use resulted in greater all-cause discontinuation of medication
• Discontinuation due to tolerability issues was similar between antipsychotic and placebo groups; drowsiness, increased appetite, and dry mouth occurred more frequently in those taking antipsychotics
• Treatment adherence was similar between antipsychotic and placebo groups

These points should be noted:

• There were only six antipsychotics studied and just three of those are available in the U.S.
• Small sample sizes of individual trials (20–299 patients per trial) may not have had enough statistical power to capture certain effects or outcomes
• The majority of the study durations were 2–12 weeks
• Efficacy measures differed among studies, which could have affected comparison of outcomes
• Most studies did not assess psychiatric symptoms, such as anxiety and depression, which could have contributed to alcohol dependence
• Some studies used adjunctive treatments, which may have confounded the results
  o Seven of 13 studies provided psychotherapy co-treatment
  o One study provided naltrexone to both placebo and treatment groups


Psych Drug Use Probe

The majority of prescriptions for atypical antipsychotics is now used to treat bipolar disorder, affective disorders, and behavior and conduct problems, rather than schizophrenia and other psychotic disorders. Antipsychotics are often a secondary or off-label therapeutic choice in these instances.

Federal health officials have launched a probe into the use of antipsychotic drugs in children in the Medicaid system, amid concern that the medications are being prescribed too frequently. The inspector general’s office at the Department of Health and Human Services (DHHS) reports it recently began a review of antipsychotic drug use by Medicaid recipients age 17 and under. Along with this, various agencies within DHHS are requiring officials in all 50 states to tighten oversight of prescriptions for such drugs to Medicaid-eligible young people.

According to an analysis by Mathematica for Centers for Medicare and Medicaid Services, the number of people under age 20 receiving Medicaid-funded prescriptions for antipsychotic drugs tripled between 1999 and 2008, and children, ages 6 to 17 years old, on Medicaid in 2004 were prescribed antipsychotics at four times the rate of privately insured children. The probe by DHHS’s inspector general, Daniel R. Levinson, has been under way for several months and focuses on the five largest Medicaid states: California, Florida, Illinois, New York and Texas. It covers a six-month period from January to June 2011, when 84,654 children age 17 and under in those states received prescriptions for antipsychotics paid for by Medicaid. U.S. Probes Psych Drug Use on Kids. The Wall Street Journal. Accessed October 22, 2013.

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