Print this page

Drug Treatment of Schizophrenia Patients Sounds Alarms

15 January 2010. Two studies in the January Archives of General Psychiatry sound alarms about the treatment provided to psychiatric patients. In a study contracted by Pfizer, Inc., Elaine Morrato of the University of Colorado, Denver, and colleagues report that, despite warnings about the need to check blood glucose levels in patients who are taking antipsychotic drugs and who are at risk for diabetes, metabolic testing rates remain stubbornly low. However, the warnings apparently changed which drugs patients received. In the same issue, Ramin Mojtabai of Johns Hopkins University, Baltimore, Maryland, and Mark Olfson of Columbia University, New York, report that, from 1996 to 2006, visits to psychiatrists led to increasing prescriptions for psychotropic medication, including drug combinations of unknown safety and efficacy.

Patients with schizophrenia show increased rates of cardiovascular disease (see Mitchell and Malone, 2006 for a review of physical health in schizophrenia). This may stem from their tendency to develop metabolic syndrome, with its high insulin levels, hypertension, lipid abnormalities, and excess abdominal fat (Meyer and Stahl, 2009). Unhealthy behaviors, such as smoking, eating poorly, and inactivity, surely contribute, but the drugs that help people with schizophrenia function also tax their health. Patients taking second-generation antipsychotics (SGAs), in particular, are likely to gain excess weight and to develop ominous changes in glucose and lipid metabolism (see SRF related news story). In fact, a 2006 study (Basu and Meltzer, 2006) tied the emergence of these drugs to rising rates of diabetes in patients with schizophrenia (see SRF related news story).

Back in 2003, evidence of the adverse metabolic effects of SGAs spurred the United States Food and Drug Administration to order labeling changes for all drugs in the class. The revisions warn prescribers to check fasting blood glucose levels at the start of treatment in patients with diabetes or its risk factors and to watch for symptoms of hyperglycemia in all patients. The agency also told drug makers to send letters to healthcare professionals to inform them about the warning. Around the same time, the American Diabetes Association and other organizations issued a consensus statement that underscored the risks and the need to monitor all patients who are taking SGAs.

A partial response?

After the warnings, rates of lipid and glucose testing remained low in SGA users who had private insurance, according to prior studies (Morrato et al., 2009; Haupt et al., 2009). However, Medicaid recipients account for a large fraction of psychotropic drug use and costs (Zuvekas and Cohen, 2007), and Morrato and colleagues wondered whether the warnings had any effect on their care. In a study with an unusually big sample, the researchers examined medical, laboratory, and pharmacy claims from the years 2002 to 2005 for two groups of fee-for-service Medicaid patients.

One group consisted of 109,451 patients who started taking an SGA for a variety of disorders in addition to schizophrenia. The study excluded those on clozapine, due to the extra

monitoring needed to detect a white blood cell disorder caused by the drug. The control group of 203,527 patients had started treatment with albuterol, an asthma treatment, but were not taking antipsychotic drugs.

Before the FDA warning, 27 percent of patients with a new SGA prescription received baseline testing of their blood glucose levels. Only 10 percent underwent baseline lipid testing. However, during and after the nine-month warning period, blood glucose testing rates remained unchanged. Lipid testing rose by a statistically significant 1.7 percent during the warning period, but improved no further in the subsequent 16 months.

The warnings may have changed patient care in another way, however. During the warning period, new prescription claims for olanzapine, an SGA with relatively severe metabolic effects, decreased by about 20 percent per year. Meanwhile, those for aripiprazole, which causes less metabolic mayhem, rose; however, this may reflect a policy change that eased access to the drug in one of the states studied. Use of quetiapine, risperidone, and ziprasidone remained unchanged. Analyses limited to SGA users with schizophrenia revealed a similar, but less pronounced, prescribing shift (see SRF related news story).

The study did not explore the reasons for the lack of metabolic testing. However, the researchers point out that surveys of psychiatrists (e.g., Newcomer et al., 2004) suggest that they knew about the warnings. Morrato and colleagues speculate that prescribers may find it easier to switch drugs than to change their monitoring habits. They recall that the number of antidepressant prescriptions for children dropped after warnings about a possible drug-linked rise in suicidal thoughts and behavior, but the recommended stepped-up monitoring for suicidal tendencies or worsening depression did not occur. Even so, in the present study, the researchers could not say whether the behavior of prescribers, patients, or both explained the lack of metabolic monitoring.

More reasons to monitor

Treatment of serious mental illness often involves more than one medication at a time. Sometimes, this reflects a need to treat comorbid conditions or to improve upon a disappointing response to one drug. Patients with schizophrenia, in particular, often receive combinations of antipsychotic drugs, with the idea of targeting complementary receptors and symptoms. In reality, though, these combinations may work no better than a single antipsychotic (see SRF related news story).

The study by Mojtabai and Olfson examined recent trends in the prescribing of psychotropic drugs and especially multidrug regimens. Using data from the 1996 to 2006 National Ambulatory Medical Care Survey, they examined patient visits to a nationally representative sample of office-based psychiatrists. Specifically, they focused on 13,079 visits in which adult patients received a psychiatric diagnosis. The psychiatrist or a member of the psychiatrist's staff supplied data on the psychotropic drugs prescribed or given during the visit.

Results showed that from 1996 to 2006, the percentage of visits in which any psychotropic drug was prescribed increased from 73 percent to 86 percent. Visits involving prescriptions for two or more psychotropics rose from 43 percent to 60 percent, while those for three or more jumped from 17 percent to 33 percent. The most common drug combos consisted of antidepressants given with sedative-hypnotics, antipsychotics, or other antidepressants. During the study period, the fraction of visits resulting in prescriptions for two or more antidepressants, two or more antipsychotics, and antidepressants plus antipsychotics increased.

Multivariate analyses assessed prescribing trends over time, while controlling for such factors

as patient demographic characteristics, the kind and number of psychiatric diagnoses, payment source, practice type, and location. They showed that visits for schizophrenia, bipolar disorder, or major depression were especially likely to involve prescriptions for antidepressant-antipsychotic combos. Patients with schizophrenia or bipolar disorder were particularly likely to receive treatment that combined antidepressants with mood stabilizers, antipsychotics with mood stabilizers, antipsychotics with sedative-hypnotics, or mood stabilizers with sedative-hypnotics.

Mojtabai and Olfson acknowledge that certain drug combinations have some empirical basis, but many lack evidence of benefits beyond those bestowed by a single drug. Moreover, multidrug regimens may increase the risk of adverse drug interactions, such as metabolic side effects from treatment with two or more antipsychotics (Suzuki et al., 2008). As Mojtabai and Olfson write, "These data call for more careful monitoring of metabolic parameters in patients taking more than one antipsychotic medication."—Victoria L. Wilcox.

References:

Mojtabai R, Olfson M. National trends in psychotropic medication polypharmacy in office-based psychiatry. Arch Gen Psychiatry. 2010 January;67(1):26-36. Abstract

Morrato EH, Druss B, Hartung DM, Valuck RJ, Allen R, Campagna E, Newcomer JW. Metabolic testing rates in 3 state Medicaid programs after FDA warnings and ADA/APA recommendations for second-generation antipsychotic drugs. Arch Gen Psychiatry. 2010 January;67(1):17-24. Abstract

Comments on Related News

Related News: Some Antipsychotic Drugs Impair Glucose Metabolism

Comment by: James Manning IV
Submitted 25 November 2005 Posted 25 November 2005

This study is thoughtful and balanced, and driven by evidence.

View all comments by James Manning IV

Related News: Some Antipsychotic Drugs Impair Glucose Metabolism

Comment by: Patricia Estani
Submitted 27 November 2005 Posted 28 November 2005
☑ I recommend the Primary Papers

Related News: A Burden on the Heart—Schizophrenia and Coronary Heart Disease

Comment by: Kiumars Lalezarzadeh
Submitted 27 December 2005 Posted 28 December 2005
☑ I recommend the Primary Papers

The relation between fatty acid and dopamine needs basic consideration. Two-week-old pups of mother rats fed n-3 polyunsaturated fatty acid-deficient diets (3 weeks before and 2 weeks after birth) showed an increase of D2 (and D1) receptors in the mesolimbic-mesocortical pathways of mothers and many brain areas of the pups (Kuperstein et al., 2005). The depressing effects of increased cholesterol level may be seen in reverse.

The effects of different antipsychotics on the immune system and fungal pathogens need consideration also. Antipsychotics reduce calcineurin protein levels and elevate phosphatase activity of calcineurin in striatum and prefrontal cortex (Rushlow et al., 2005). Calcineurin increases fungal pathogens and its inhibition is related to immune suppression (Cruz et al., 2001). Antipsychotics need further study in relation to calcineurin, immune suppression, and fatty acids.

References:
Kuperstein F, Yakubov E, Dinerman P, Gil S, Eylam R, Salem N Jr, Yavin E. Overexpression of dopamine receptor genes and their products in the postnatal rat brain following maternal n-3 fatty acid dietary deficiency. J Neurochem. 2005 Dec;95(6):1550-62. Epub 2005 Nov 23. Abstract Rushlow WJ, Seah YH, Belliveau DJ, Rajakumar N. Changes in calcineurin expression induced in the rat brain by the administration of antipsychotics. J Neurochem. 2005 Aug;94(3):587-96. Abstract Cruz MC, Fox DS, Heitman J. Calcineurin is required for hyphal elongation during mating and haploid fruiting in Cryptococcus neoformans. EMBO J. 2001 Mar 1;20(5):1020-32. Abstract

View all comments by Kiumars Lalezarzadeh

Related News: A Burden on the Heart—Schizophrenia and Coronary Heart Disease

Comment by: Robert Peers
Submitted 30 December 2005 Posted 31 December 2005

In what may be a landmark study of lifestyle intervention in schizophrenia, Australian dietitian Sherryn Evans was highly successful in limiting weight gain in newly diagnosed schizophrenia patients treated with olanzapine (Evans et al., 2005). Nutritionally educated patients were only 2 kg heavier after 3 months and 6 months, and were happier; controls were 6 kg and 9.9 kg heavier at the same time points.

The key to nutritional success is close supervision, best provided in community centers accessible to schizophrenia patients. A gym would help. F. M. Baker once ran a program in a poor area of Baltimore, in which the patients were collected daily and brought in, to cook their own (healthy) meals and take part in psychosocial therapy; medication compliance improved, and readmission rates fell dramatically.

The adverse metabolic effects of most newer antipsychotic drugs have stimulated a renaissance of interest in nutritional factors and physical health in schizophrenia that will hopefully encourage the entry of dietitians and exercise physiologists into the treatment arena. They have much to offer.

A well-planned low-fat, grain- and legume-rich diet, as in the Australian study, will improve cell membrane structure in brain and body by allowing omega-3 and -6 essential fatty acid levels to rise (the key to controlling diabetes and heart risk). The same diet also provides the key nutrient inositol, a seed-derived glucose isomer that imitates the anxiolytic action of clozapine-type drugs, and so would treat the comorbid anxiety seen in a third of patients with schizophrenia (which promotes hypertension, diabetes, cardiac mortality, smoking, negative symptoms, and suicide).

The inositol hexaphosphate in edible seeds is itself a potent iron-binding antioxidant (Graf et al., 1987), prominent in the diet of healthy centenarians, and in the whole grains is known to reduce coronary disease progression in the Iowa Women's Health Study (Erkkila et al.,

2005): So here is a simple life-extender and artery protector for schizophrenia patients, too, anxious or not, who eat corn, grains, and beans.

Omega-3 fatty acids already look promising in schizophrenia (Puri and Richardson, 1998), so if oily fish intake is low, two or three fishoil capsules a day—costing little—might help both brain and cardiac risk.

View all comments by Robert Peers

Related News: A Burden on the Heart—Schizophrenia and Coronary Heart Disease

Comment by: Patricia Estani
Submitted 3 January 2006 Posted 4 January 2006
☑ I recommend the Primary Papers

More studies must be designed to research variables that affect heart disease in schizophrenia. I think that integrating medical services, for example, adding nutritional treatment or dietary services to psychiatric support is essential to prevent the metabolic syndrome commonly observed in schizophrenic patients.

View all comments by Patricia Estani

Related News: A Burden on the Heart—Schizophrenia and Coronary Heart Disease

Comment by: SuSanne Henriksen
Submitted 10 January 2006 Posted 10 January 2006
☑ I recommend the Primary Papers

Is there any evidence of an increased incidence of arrhythmias, especially tachycardia, in schizophrenia?

View all comments by SuSanne Henriksen

Related News: Trial Fails to Support Polypharmacy in Refractory Schizophrenia

Comment by: William Carpenter, SRF Advisor (Disclosure)
Submitted 15 February 2006 Posted 15 February 2006
☑ I recommend the Primary Papers

Evaluating the effect of adding risperidone to clozapine is an example of clinical practice getting out ahead of evidence and theory. It has become common practice, so we need to know the answer. The combination surely will add adverse effects, but what hypothesis supports the notion of increased efficacy? Clozapine has superior efficacy for psychosis in treatment-resistant patients and low occupancy (fast on/off) at the dopamine 2 receptor. Is this important for diminished motor adverse effects or for superior efficacy? If so, adding risperidone will terminate this advantage. I think this may be the case for adverse effects, but we tested the partial occupancy hypothesis and the D2/5HT ratio hypothesis for clozapine (Carpenter et al., 1998) and found that full D2 occupancy did not interfere with clozapine superiority. But in this analysis, we found no evidence that being on a drug with high affinity for the D2 receptor combined with clozapine gave any efficacy advantage and recommended against the practice.

To reason in the other direction, it is clear that risperidone has its best benefit/adverse effect profile at low doses. Combining risperidone with another antipsychotic could move that profile in an unfavorable direction.

But clinicians are stuck. In most patients, no matter what the pharmacotherapy, response is incomplete. It is understandable that doctors try "harder," and increasing dose and polypharmacy seem the only way. When only first-generation drugs were available, this routinely lead to excessive doses with more adverse effects, poorer adherence, and no evidence for better efficacy. Are we now repeating this mistake with polypharmacy? This clozapine/risperidone report is well done, and the failure to observe an advantage for the combination should be a decisive influence on this common practice.

References:

Carpenter WT, Zito JM, Vitrai J, Volavka J. Hypothesis testing: is clozapine's superior efficacy dependent on moderate D2 receptor occupancy? Biol Psychiatry. 1998 Jan 15;43(2):79-83. Abstract

View all comments by William Carpenter

Related News: Trial Fails to Support Polypharmacy in Refractory Schizophrenia

Comment by: Herbert Meltzer (Disclosure)
Submitted 16 February 2006 Posted 17 February 2006
☑ I recommend the Primary Papers

The paper by Honer et al., which reported a lack of benefit from augmentation of clozapine by risperidone in patients with schizophrenia who were partial responders to clozapine, is consistent with our previous report which had the same design but was of somewhat shorter duration (Anil Yagcioglu et al., 2005), with the exception that we found that improvement in psychopathology after the addition of placebo was superior to risperidone. A second paper from our double-blind, randomized trial has been submitted which showed that improvement in cognition with placebo was often, but not always, greater than that with risperidone as well. Honer et al. explicitly stated that their results were consistent with ours. We proposed, based upon my hypothesis that more potent blockade of 5-HT2A than D2 receptors contributed to the beneficial effects of clozapine (Meltzer et al., 1989), that the reason for the superior response to placebo in our trial was that risperidone, by adding D2 receptor blockade to clozapine, interfered with the beneficial effects of being part of a clinical study with its increased clinical contact and supportive nature. The results of our study and that of Honer contrast with a third study (Josaissen et al., 2005), which found risperidone addition improved psychopathology more than placebo.

The New England Journal of Medicine editorial from John M. Davis is a very disappointing commentary on this important confirmation of our research in a key area because it has a number of serious errors in fact and gratuitous criticism of industry-funded studies which, at least in this case, are easily refutable. Davis stated that our study and that of Josiassen et al. were industry-funded, as contrasted with the Honer et al. study, which was funded by the Stanley Medical Research Foundation, of which Davis has been a long-time adviser. The implication is clear that the industry-funded studies are biased. Davis then continues his effort to raise doubt about industry-funded studies by contrasting the results of his several meta-analyses of industry-funded clinical trials, which found advantages of atypical over

typical antipsychotic drugs, with that of the NIMH-funded CATIE study, which did not (Lieberman et al., 2005).

In fact, our study was clearly marked as having been funded by the Stanley Medical Research Foundation, the William K. Warren Medical Research Foundation, and the Janssen Pharmaceutical Company, manufacturer of risperidone. The Josaissen study was industry-supported. Instead of evaluating the three studies for their merits, or even reading the paper carefully (in the case of our study), Davis would have us doubt their validity because they were industry-supported. This is unacceptable in my view. His call for more industry and non-industry studies is a smoke screen for his real message, that industry-funded studies are biased. I and my coauthors can vouch for the fact that none of the three funders of our pioneering research exerted the least influence on the design, performance, or write-up of our work. Janssen was informed of the results of the study as called for in our contract and made no effort, nor should it have, to restrain or modify the message. This, in fact, has been consistent with my entire experience with major pharma and biotech companies. If Professor Davis has had more negative experiences with industry in this regard, he should make them public. As it is, he offers incorrect information to raise doubts about industry-funded research at a time when it is already under attack in the area of clinical trials and when continued investment on its part in clinical research in psychiatry is urgently needed, in my view. What we need is more thoughtful consideration of the merits and shortcomings of all clinical trials regardless of funding source. The clinical investigators and funder of the CATIE trial are now finding that merely because their study was government-funded, it is not being taken by many as the last word in informing us about antipsychotic drug treatment in schizophrenia.

References:

Honer WG, Thornton AE, Chen EY, Chan RC, Wong JO, Bergmann A, Falkai P, Pomarol-Clotet E, McKenna PJ, Stip E, Williams R, MacEwan GW, Wasan K, Procyshyn R; Clozapine and Risperidone Enhancement (CARE) Study Group. Clozapine alone versus clozapine and risperidone with refractory schizophrenia. N Engl J Med 2006;354:518-20. Abstract

Anil Yagcioglu AE, Kivircik Akdede BB, Turgut TI, Tumuklu M, Yazici MK, Alptekin K, Ertugrul A, Jayathilake K, Gogus A, Tunca Z, Meltzer HY 2005. A double-blind controlled study of adjunctive treatment with risperidone in schizophrenic patients partially responsive to clozapine: efficacy and safety. J Clin Psychiatry 2005; 66:63-72. Abstract

Meltzer HY, Matsubara S, Lee JC. Classification of typical and atypical antipsychotic drugs on the basis of dopamine D-1, D-2 and serotonin2 pKi values. J Pharmacol Exp Ther. 1989 Oct;251(1):238-46. Abstract

Davis JM. The choice of drugs for schizophrenia. N Engl J Med 2006;354: 518-20. Abstract

Josiassen RC, Joseph A, Kohegyi E, Stokes S, Dadvand M, Paing WW, Shaughnessy RA. Clozapine augmented with risperidone in the treatment of schizophrenia: a randomized, double-blind, placebo-controlled trial. Am J Psychiatry. 2005 Jan;162(1):130-6. Abstract

Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005 Sep 22;353(12):1209-23. Epub 2005 Sep 19. Abstract

View all comments by Herbert Meltzer

Related News: **Trial Fails to Support Polypharmacy in Refractory Schizophrenia**

Comment by: **William Honer**
Submitted 15 May 2006 Posted 16 May 2006
☑ I recommend the Primary Papers

Our paper (Honer et al., 2006) and the associated editorial by Dr. John M. Davis (Davis, 2006) concerning augmentation of risperidone with clozapine drew some commentary in this Forum, and recently, three letters to the Editor of the New England Journal of Medicine. The April 27 issue of the NEJM also includes our response, and a response from Dr. Davis. The first of the letters, from Grass and colleagues (Grass et al., 2006) concerns the broader issues of the confidence with which we can conclude that risperidone augmentation of clozapine offers no benefit, and the degree to which the results of this approach to antipsychotic polypharmacy can be generalized to other combinations of antipsychotic drugs. Basically, our conclusion in the paper is that the difference between risperidone and placebo augmentation of clozapine is unlikely to be associated with a moderate-to-large effect size, such as would be observed with switching a group of patients from typical antipsychotics to clozapine. Smaller differences cannot be excluded. However, as clarified by Dr. Davis in the recent issue, one of the two previous, smaller placebo-controlled studies showed relative benefit for placebo versus risperidone augmentation, at least for positive symptoms (Anil Yagcioglu et al., 2005). The NEJM letters from Meltzer and colleagues (Meltzer et al., 2006) and from Gerson (Gerson, 2006) concern the Davis editorial which accompanied our paper. Dr. Meltzer's concerns about the editorial are also presented in his commentary in the Forum, and Dr. Davis has graciously apologized for his errors in the current response in the Journal, and clarified that monitoring of white cell counts provides a safe approach for patients taking this medication.

We still face the broader issue of antipsychotic polypharmacy, which appears reasonably prevalent despite a very small evidence base. Our trial was initially designed with the hope that risperidone, being a high-affinity dopamine D2 antagonist, would be an optimum drug to augment the low D2 affinity of clozapine. This was not the case, and strictly speaking our results cannot be generalized beyond this combination of medications. Much larger studies would be needed if a non-inferiority design were to be used. For example, subjects currently treated with antipsychotic polypharmacy could be randomized to continuation or to substitution with placebo for all but one antipsychotic drug. A preliminary, uncontrolled study indicated this strategy was successful in most, but not all cases (Suzuki et al., 2004). Perhaps new findings concerning the consequences of antipsychotic polypharmacy for cognitive function (Kawai et al., 2006) and the economic costs (Stahl and Grady, 2006) will also contribute to improving evidence-based practice.

References:

Anil Yagcioglu AE, Kivircik Akdede BB, Turgut TI, Tumuklu M, Yazici MK, Alptekin K, et al. A double-blind controlled study of adjunctive treatment with risperidone in schizophrenic patients partially responsive to clozapine: efficacy and safety. J Clin Psychiatry 2005; 66: 63-72. Abstract

Davis JM. The choice of drugs for schizophrenia. N Engl J Med. 2006 Feb 2;354(5):518-20. Abstract

Gerson SL. Clozapine alone versus clozapine and risperidone for refractory schizophrenia. N

Engl J Med. 2006 Apr 27;354(17):1846-8; author reply 1846-8. Abstract

Grass G, Hellmich M, Leweke FM. Clozapine alone versus clozapine and risperidone for refractory schizophrenia. N Engl J Med. 2006 Apr 27;354(17):1846-8; author reply 1846-8. Abstract

Honer WG, Thornton AE, Chen EY, Chan RC, Wong JO, Bergmann A, Falkai P, Pomarol-Clotet E, McKenna PJ, Stip E, Williams R, Macewan GW, Wasan K, Procyshyn R, . Clozapine alone versus clozapine and risperidone with refractory schizophrenia. N Engl J Med. 2006 Feb 2;354(5):472-82. Abstract

Kawai N, Yamakawa Y, Baba A, Nemoto K, Tachikawa H, Hori T, et al. High-dose of multiple antipsychotics and cognitive function in schizophrenia: the effect of dose-reduction. Prog Neuropsychopharmacol Biol Psychiatry 2006; (in press).

Meltzer HY, Yagcioglu AE, Akdede BB. Clozapine alone versus clozapine and risperidone for refractory schizophrenia. N Engl J Med. 2006 Apr 27;354(17):1846-8; author reply 1846-8. Abstract

Stahl SM, Grady MM. High-cost use of second-generation antipsychotics under California's Medicaid program. Psychiatric Serv 2006; 57: 127-129. Abstract

Suzuki T, Uchida H, Tanaka KF, Nomura K, Takano H, Tanabe A, et al. Revising polypharmacy to a single antipsychotic regimen for patients with chronic schizophrenia. Int J Neuropsychopharmacol 2004; 7: 133-142. Abstract

View all comments by William Honer

Related News: Children and Teens Gain Weight Quickly on Second-generation Antipsychotics

Comment by: William Carpenter, SRF Advisor (Disclosure)
Submitted 29 October 2009 Posted 29 October 2009

It has been known for years that some—not necessarily all—second-generation drugs have severe metabolic side effects. These effects are common, not rare. Metabolic changes induced will increase risk of an early death substantially unless persons receiving these treatments are immune to effects observed in the general population. In fact, cardiovascular disease, stroke, diabetes, and pulmonary disease are already associated with early death of persons with schizophrenia where mortality rates are already two to six times standard mortality rates (see SRF related news story). The fact that these populations have increased risk from other lifestyle problems (e.g., diet, sedentary lifestyle, smoking, and stress) increases the need for clinicians to minimize risk from iatrogenic sources. The importance of the report by Correll et al. is not based on surprising new data. Rather, it is the ability to bring extensive attention to this problem to the broad medical field and the public.

The increased safety and efficacy of second-generation antipsychotic drugs was debunked before the turn of the century, and the value of the CATIE and CUtLASS studies was more in their ability to spark the public discussion than in surprising new data (Lieberman et al., 2005; Jones et al., 2006). In young people, the antipsychotic drugs with serious metabolic adverse profiles should rarely be considered. Clozapine for some childhood-onset schizophrenia patients may be one of the exceptions. Antipsychotic drugs are usually prescribed with long-term use in mind. If a clinician considers this essential therapy—as it

often is in schizophrenia, less so in bipolar disorder, where effective and safer drugs are available—selection of compounds based on safety and tolerability is essential. In this regard, prescribing drugs such as olanzapine is very difficult to defend. The importance of this report being published in JAMA is underscored by the reports of Lilly directing representatives to market olanzapine to primary care providers who are less aware of the metabolic effects (see, e.g., Attorney General's Settlement).

View all comments by William Carpenter

Print this page