

Atypical Neuroleptics: Metabolic Risks and Alternatives

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Atypical Neuroleptics: antipsychotics built with comfort in mind

What are they?

- Clozaril (clozapine)
- Risperdal (risperidone)
- Zyprexa (olanzapine)
- Seroquel (quetiapine)
- Geodon (ziprazidone)
- Abilify (aripiprazole)



What's so great about the atypicals?

Remember Haldol? Pure Dopamine blockade

- Pseudoparkinsonism--EPS
- Akathesia—"ants in your pants"
- Tardive Dyskinesia—permanent involuntary movements
- Hyperprolactinemia—amenorrhea and gynecomastia, impotence
- Neuroleptic Malignant Syndrome
- Blunted ability to feel pleasure



What's so great about the atypicals?

The atypicals are a major change.

- They block dopamine where you want it blocked—the limbic system—while preserving dopamine activity in the
- nigrostriatal tract—less stiffness and tremor
- Tubuloinfundibular—less prolactinemia



What's so great about the atypicals?

Abilify (aripiprazole) is the newest atypical

- blocks dopamine receptors while having a partial agonist activity



What's so great about the atypicals?

- Improved tolerability = compliance
- Fewer nasty neuromuscular side effects
- They tend to have an antidepressant effect rather than blunting emotions
- Being used for a host of other conditions like
 - Bipolar illness
 - Dementia with agitation
 - Delirium
 - Aggression in Brain injured patients and kids with severe behavior problems



The Bad News

A recent Canadian study found that weight gain in excess of 7% of baseline occurred in

- 56% of patients on Seroquel (quetiapine)
- 24% of patients on Zyprexa (olanzapine)
- 24 % of patient on Risperdal (risperidone)



Canadian Journal of Psychiatry, Vol 48, No 10, November 2003

The Bad News

- A study of 56,849 VA patients on antipsychotics were monitored
- 4132 (7.3%) developed diabetes
- Excess risk did not appear until after a year of treatment
- Risk with Zyprexa (olanzepine) compared to a conventional antipsychotic was 1.15



Leslie D, Rosenheck R. American Journal of Psychiatry 2004; September

The Bad News

In 2004, the FDA required a product label change for drugs in this class warning about an increased risk of hyperglycemia and diabetes.



www.fda.gov/medwatch/safety/2004

The Bad News

- Most patients can tolerate short-term treatment with an atypical, but long-term use requires clinicians to monitor lipids and glucose
- Most patients gain weight on these drugs—sometimes huge amounts
- Even patients who do not gain weight often suffer hyperglycemia and dyslipidemia
- Increased risk of stroke in elderly on Risperdal and Zyprexa Sink; JAMA. 2005;293(5)



Assessment of risk factors:

- Age
- Sedentary lifestyle
- History of gestational diabetes
- Family history of diabetes
- Ethnicity (Native-American, Hispanic, African-American at increased risk)



Assessment of risk factors: other medications

- Remeron (mirtazepine)
- Tricyclics
- Lithium
- Depakote (valproic acid)



Assessment of risk factors: physical exam

- Blood Pressure
- Body Mass Index (BMI)
- Waist circumference—truncal obesity is a risk factor
 - greater than 40" in men
 - greater than 35" in women



Assessment of risk factors: Lab

- Fasting blood sugar
 - Greater than 100 is impaired
 - Greater than 126 is diabetes
- Triglycerides
 - Greater than 150
- Lipids
 - HDL less than 40 in men
 - HDL less than 50 in women



Ongoing Management: ADA Guidelines, 2004

- Each visit
 - BMI
- At 3 months
 - Blood pressure and waist circumference
 - FBS
 - Lipids
- Annually
 - Blood pressure and waist circumference
 - FBS
- At least every five years
 - Lipids



Prepare the patient

- Warn the patient about the potential for weight gain and other medical risks
- Nutritional education
- Ask the patient to exercise
 - At least 20 to 30 minutes of aerobic activity 6 days a week
 - Weight-bearing exercise to build muscle mass will help control weight



If the patient develops Metabolic Syndrome or Pre-Diabetes

- Monitor more closely; e.g., fatty liver disease
- Treat the abnormality
 - Metformin for mild elevations in FBS
 - Statins for dyslipidemia
- Evaluate whether the patient can be taken off the drug or switched to another neuroleptic



If the patient develops Metabolic Syndrome or Pre-Diabetes

Unless you are treating schizophrenia, you have four options:

- Management with mood stabilizers alone
- Reduce the dose of the atypical you are using
- Switch to a less risky atypical
- Switch to a conventional neuroleptic



If the patient has any diagnosis besides schizophrenia

- Option 1: Use a mood stabilizer. These drugs remain first-line treatment for bipolar mood disorders
 - Lithium—most effective for classic mania
 - Depakote—mixed, rapid cycling
 - Tegretol
 - Lamictal—bipolar depression
 - Trileptal—like Tegretol
- Neurontin helps seizures and chronic pain but does nothing for mood disorders
- Topamax has little proven efficacy



If the patient has any diagnosis besides schizophrenia

SLOWLY taper and discontinue the antidepressants if the patient is prone to mania or even hypomania



If the patient has any diagnosis besides schizophrenia

- Option 2: Reducing the dose of the atypical. Often relatively low doses can control symptoms
 - 0.5 to 1.0 mgs of Risperdal
 - 5 to 10 mgs of Zyprexa
 - 200 to 300 mgs of Seroquel
- Cut these numbers in half for elderly patients



If the patient has any diagnosis besides schizophrenia

- Option 3: Switch to a less risky atypical
- greatest risk is with Clozaril followed by Zyprexa and Seroquel
 - Risperdal—somewhat less
 - Geodon—less still
 - Watch for EKG changes
 - Avoid doses below 40 mgs BID
 - Abilify—does not usually cause weight gain but shares the class warning
 - Can cause agitation



If the patient has any diagnosis besides schizophrenia

- Option 4: Switch to a conventional neuroleptic
 - Stelazine 1 to 2 mgs
 - Navane 1 to 2 mgs
 - Haldol 0.5 to 1 mgs
 - Mellaril 100 mgs
 - May cause more weight gain than Haldol but be better tolerated
- Understand the risks inherent in conventional neuroleptics. Ask someone who uses them if you are not familiar with their use.



If the patient has schizophrenia

Most to least effect on weight:

- Risperdal 3 to 6 mgs daily
- Geodon at higher doses 80 to 120 twice daily
- Abilify at higher doses 20 to 30
- Mellaril
- Loxitane
- Haldol



Take Home Message

If you use an atypical, use the lowest effective dose and monitor for

- Weight gain
- Metabolic Syndrome
- Dyslipidemias
- Diabetes can occur event without weight gain



Take Home Message

Do not use an atypical as long-term monotherapy for conditions other than schizophrenia unless you have a really good reason

- Mood stabilizers are still the first line treatment of bipolar illness
- Be sure your dementia/OBS patients are treated with the lowest dose and really need it.



Disease Management: *Healthy TogetherSM* Program

- Healthy TogetherSM ... *Breathe Easy!*
 - Asthma (Pediatric & Adult)
 - COPD
- Healthy TogetherSM ... *Take Control!*
 - Diabetes
- Healthy TogetherSM ... *Take Heart!*
 - Congestive Heart Failure
 - At Risk Cardiac (CAD)
- Healthy TogetherSM ... *A Healthy Perspective!*
 - Depression
- Healthy TogetherSM ... *Healthy Additions!*
 - Prenatal/Maternity



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Resources

- Telephonic Referrals to our toll-free number at **1-888-545-1710**
- Forms available on Website- apshealthcare.com
- Forms to be faxed to APS **1-888-245-1928**
- ACS **1-800-251-1268**
- The Office of Medicaid **307-777-7531**