The Carlat Child Psychiatry Report

VOLUME 1, NUMBER 5 WWW.THECARLATCHILDREPORT.COM DECEMBER 2010

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IN THIS ISSUE

Use of Antipsychotics in Children and Adolescents

Management of Antipsychotic Induced Weight Gain

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Dr. Fisher has disclosed that she has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Antipsychotics are effective at many things, including inducing weight gain. For example, a study of 90 adolescents started on atypical antipsychotics for a variety of diagnoses found significant weight gain in 70% of patients, on average about 12 pounds (Mareno C et al, *Bipolar Disord* 2010;12(2):172–184). In addition to the metabolic risks, obesity confers additional risks of low self esteem and behavior problems, asthma, irregular or early menarche, polycystic ovarian syndrome, slipped capital femoral epiphyses, obstructive sleep apnea, gallstones, and increased mortality 20 and 32 years later (Jain A, *What works for obesity?* London: BMJ Publishing Group; 2004). Furthermore, adolescents hate weight gain, and it is one of the reasons they often give for not complying with prescribed medication.

Lifestyle interventions are often a hard sell, and the possibilities of a pharmacologic intervention are enticing. But do they work? Several options are reviewed below.

Stimulants

Given the fact that a large proportion of our patients with ADHD on stimulants are failing to gain weight, adding a stimulant to an antipsychotic seems like a logical approach to control weight gain. Unfortunately, most studies do not bear the practice out. Penzner et al used the naturalistic model in the SATIETY study to look at patients without mood or psychotic disorders who were started on antipsychotics to control aggression and oppositional behavior in the context of ADHD, oppositional defiant disorder (ODD), pervasive developmental disorders (PDD), or conduct disorder. Seventy-one of these patients were on stimulants and 82 were not. There was no significant difference in weight gain between groups given antipsychotics alone and those given antipsychotics and stimulants, although those on stimulants prior to starting antipsychotics were more likely to be at a lower weight to start with (Penzner et al, *J Child Adolesc Psychopharmacol* 2009;19(5):563–573).

Metformin

Metformin (Glucophage) is an oral antiglucose agent used in the treatment of diabetes. It is generally well-tolerated but may cause GI distress. Metformin is not approved for weight loss, but has shown some effectiveness when used for it.

A review of studies on metformin for obesity (not related to antipsychotic use) found six studies in adolescents, five of them randomized controlled trials (RCTs). They concluded that metformin, 500 to 1,000 mg twice daily, was effective in five out of six of trials, and resulted in 0.8 to 2.7 kg/m2 reduction in BMI

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Learning objectives for this issue: 1. Explain how to prescribe medication and other interventions for managing antipsychotic-related weight gain. **2.** Educate your patients on antipsychotic medications about oral contraceptives to prevent pregnancy. **3.** Explain the common side effects in children taking antipsychotics. **4.** Understand some of the current findings in the literature regarding psychiatric treatment. This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

Management of Antipsychotic Weight Gain

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(3.2 kg/m2 for the open label study) (Rogovik et al, *Drugs* 2010;70(3):335–346).

Another study reports a case of an adolescent girl maintained on clozapine (Clozaril) who was treated with metformin, 500 mg twice daily, resulting in a five-pound weight loss. However, total weight gain after treatment with clozapine for 10 months was 49.6 pounds and her weight had remained on "a steady trajectory upwards," so the case report is more significant for the deceleration of weight gain after starting metformin than weight loss itself (Weaver et al, *J Child Adolesc Psychopharmacol* 2010;20(2):153–157).

In a 16 week RCT of weight control in adolescents on antipsychotics using metformin doses up to 2,000 mg daily, a significant difference in weight gain and a decrease in waist circumference were found in the metformin group compared with the placebo group (Klein DJ et al, *Am J Psychiatry* 2006;163(12):2072–2079). In this study, too, metformin was started after the antipsychotic—it was helpful in reducing the rate of weight gain and stabilizing the weight, rather than weight reduction. It may (or may not) also prevent glucose intolerance associated with antipsychotics.

An open label study found no significant weight loss after eight weeks on metformin, but the study was small and the metformin was added after the fact (Shin et al, *J Child Adolesc Psychopharmacol* 2009;19(3):275–279). Studies in adults on antipsychotics have been mixed, with some finding significant benefit and some finding no benefit. (For example, see Jain op.cit or Maayan L et al, *Neuropsychopharmacol* 2010;35(7):1520–1530.)

It may make sense to start metformin, particularly in patients with additional risk factors for metabolic syndrome. Weight loss may not be the most important outcome: rather, deceleration of weight gain and weight stabilization, decreased triglycerides, and potentially (although not demonstrated) reduction in the risk of metabolic syndrome. It would be nice to see a RCT of metformin started concurrently with antipsychotics to see if weight gain can be prevented.

Orlistat

Orlistat (marketed over the counter as the weight-loss drug Alli) is now the single FDA-approved anti-obesity agent available in the U.S. and is approved for patients 12 and over. It impairs fat absorption by inactivating gastric and pancreatic lipases. A meta-analysis of orlistat and sibutramine (which was recently pulled from the market) for weight reduction in obese adolescents (but not those on antipsychotics), found two RCTs comprising 573 adolescents, dosed daily with orlistat 120 mg for three and six months. The authors calculated a modest reduction of 0.83 kg/m2 in BMI, consistent with other analyses. The effect size was 0.24, and therefore of questionable clinical significance. There were no significant differences in serum lipids, glucose, or insulin. The patients suffered relatively frequent GI side effects, no doubt from the presence of undigested fat in the lower GI tract (Viner RM et al, *Obes Rev* 2010;11(8):593–602).

Conjugated Linoleic Acid

A natural fatty acid found primarily in meat and dairy products, conjugated linoleic acid (CLA) may be of use in the treatment of obesity. Adult studies have been mixed. In an RCT of pediatric patients ages six to 10 with obesity, 28 kids were given 3 g of a proprietary mixture of CLA called Clarinol daily for around seven months. Thirty-one kids were given a fat based placebo (sunflower oil). The study authors found a reduced accretion of fat mass in the CLA group—that is, the children gained weight, but not as much as the placebo group did, and not as much as their weight trajectory would have predicted. There was no effect on fasting glucose, lipids, or insulin. One subject had an elevation in liver enzymes (Racine LM et al, *Am J Clin Nutr* 2010;91(5):1157–1164).

Fiber supplements

In a review of an Italian study of 53 obese children ages five to 18, those who were given two to three grams of glucomannan fiber daily were found to have decreased excess bodyweight, cholesterol, and triglycerides after four months. This review also reported a second positive study on glucomannan in 60 children under age 15 (Rogovik op.cit).

Lifestyle interventions

With the fairly modest effects of the pharmaceuticals described previously, most experts agree that "lifestyle interventions" are the mainstay of obesity treatment. (They also enhance the weight loss achieved with pharmaceutical interventions.) It appears that both low-carbohydrate and low-fat diets are effective and safe for adolescents. Additional interventions we can make as clinicians are as follows (Rao G, *Am Fam Physician* 2010;81(12):1449–1455):

1. Before starting antipsychotics, make sure our patients understand that they increase hunger and that they should plan accordingly, using the following suggestions:

    a. eat breakfast daily

    b. limit sweet beverages (soda, fruit juice, etc) to one serving daily

    c. limit fast food to less than once a week

    d. eat dinner together as a family

    e. limit TV viewing

    f. get daily exercise

    g. switch to low calorie snacks

2. Regularly measure weight, BMI, and waist circumference.

3. Assist our patients in making and maintaining these choices by referring to specialists as needed: nutritionists, physical therapists, personal trainers, and/or counselors specializing in weight loss. The USDA has two excellent websites as well: www.mypyramind.gov and www.nutrition.gov, which includes an interactive program to analyze the individual's diet.

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Combined Oral Contraceptives: A General Overview

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Dr. Powell has disclosed that she has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Given the teratogenicity of certain psychiatric drugs like mood stabilizers and antipsychotics, it is logical and responsible to offer contraception to patients for whom these drugs are prescribed. However, actually doing so can be complicated.

Ideally, a patient has a psychiatrist managing her mental health care and a primary care physician or gynecologist overseeing her reproductive health needs, including contraceptive management, cervical cancer screening, and routine testing for sexually transmitted diseases. In reality, however, patients may not visit their PCPs or gynecologists regularly, or may not even have a primary care doctor. Psychiatrists may be placed in the situation where they either prescribe their patients birth control or the patients go without.

While there are a variety of contraceptive options for patients to choose among, this article will address combined oral contraceptives (COCs). All sexually active patients should be strongly encouraged to use condoms for STD protection, regardless of what other methods of pregnancy prevention they use.

Assessing the appropriateness of combined oral contraceptives (COCs)

Deciding whether a patient is a candidate for COC therapy depends on the patient's medical history—in particular if she has a contraindication to estrogen. The World Health Organization has developed medical eligibility criteria for initiating contraception, which can be downloaded at http://bit.ly/bP9K8N. Contraindications to estrogen therapy include personal history of a venous thromboembolism (VTE) or pulmonary embolus, a known thrombogenic mutation, personal history of breast cancer, smoking in women aged 35 years or older, uncontrolled hypertension, and migraine headaches with aura or other neurologic symptoms (World Health Organization. *Medical Eligibility Criteria for Contraceptive Use.* 4th ed. Geneva, Switzerland: World Health Organization; 2009). Please note that this is not a comprehensive list and you should be familiar with full WHO guidelines before prescribing hormonal contraceptives.

In addition, it is important to consider your patients' limitations and opinions in regard to taking birth control pills. For example, certain patients may have difficulty remembering to take a pill every day. You should educate these patients about long-term contraceptive options such as Depo Provera, Implanon, and intrauterine devices. Some patients have inaccurate ideas about contraception, eg, they may think that COCs cause weight gain or affect future fertility. Multiple studies have documented that there is no association between a low-dose estrogen COC and weight gain (Pitts SAB and Emans SJ, *Curr Opinions in Pediatr* 2008;20(4):383–389).

You should see a patient three months after starting an OCP to check blood pressure, discuss side effects, and check in on compliance. If the patient is doing well, you can see her on a yearly basis (Zieman M et al, *A Pocket Guide to Managing Contraception.* Tiger, Ga: Bridging the Gap Foundation; 2007).

Differences among COC brands/types

COCs differ in the following ways: 1) The amount of estrogen; 2) the amount and type of progestins; 3) monophasic vs multiphasic formulations; and 4) ratio of active pills to inactive pills.

When starting a patient on a COC, begin with a 35 mcg or lower estrogen concentration, because starting higher than this can lead to an increased risk of VTE. Choosing the type of progestin in a COC depends on the clinical history of the patient. Second generation progestins—norgestrel and levonorgestrel—provide excellent potency and stabilization of the endometrium. Common preparations include Aviane, Lo-Ovral, and Seasonale. However these provide no anti-androgenic effects, so are not the best choices for patients with acne, polycystic ovarian syndrome, and/or hirsutism. For these patients, it is best to choose a COC with a third or fourth generation progestin. Third generation progestins—norgestimate and desogestrel—are found in Ortho-Cyclen, Ortho Tri-Cyclen, Kariva and Mircette, among other pills.

The fourth generation progestin, drosperidone, is found in Yaz and Yasmin. Because drosperidone is an analog of spironolactone, it should be avoided in patients who are taking ACE inhibitors or have underlying medical conditions, such as renal disease, that can contribute to elevated potassium levels (Hatcher RA et al eds. *Contraceptive Technology.* 19th ed. New York, NY: Ardent Media, Inc; 2007).

COCs come in monophasic and multiphasic formulations. Monophasic formulations contain active pills that all contain the same concentration of hormones, while multiphasic formulations contain active pills with varying levels of hormones. This difference in formulation explains the difference between Ortho Cyclen and Ortho Tri-Cyclen, for example. Monophasic formulations are recommended if patients wish to modify cycle length by occasionally eliminating the week of placebo pills to skip or delay a menstrual period (Zieman op.cit).

Traditionally, a pill pack would contain 21 days of active hormone-containing pills and seven days of inactive, or placebo, pills. This allowed women to have a period during the last week of the pill pack.

Newer trends in COCs have been to increase the ratio of active pills to inactive pills so that women will experience fewer menstrual periods per year. For example, Seasonale is designed to have women menstruate only four times per year. While safe and desirable for many patients, extended cycling can cause increased breakthrough spotting between periods. Also, some patients find it disconcerting to not have a menses every month because it may increase anxiety about possible pregnancy.

Risks and side effects of COCs

Among the greatest concerns related to COC therapy is increased incidence of venous thromboembolism (VTE). Depending on the age and medical profile of the patient, other serious risks include myocardial infarction, stroke, hypertension, and benign liver tumors (Hatcher op.cit).

VTE risk is associated primarily with the dose of estrogen contained in COCs, which is why it is so important to assess risk factors for estrogen use when starting COCs. In the general population, a woman's risk of developing a VTE is four to eight in 100,000 women per year. This risk increases to 10 to 30 in 100,000 women per year when a patient is on a low-dose COC.

However, when explaining this increased risk to patients, it is important to remind them that the risk of VTE when on a COC is still significantly lower than the risk during pregnancy, which is 60 in 100,000 women per year (Zieman op.cit). It is crucial to counsel patients about this increased VTE risk and symptoms to watch for. You can use the ACHES mnemonic to

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Q&A With the Expert

Expert Interview

Side Effects of Antipsychotics in Children

Jeanette Jerrell, PhD

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Dr. Jerrell has disclosed that she receives grant and research support from Bristol Myers Squibb to study adverse events from aripiprazole in children. She also serves the company as a safety advisor related to this medication. Dr. Fisher reviewed this article and found that there is no evidence of commercial bias in this educational activity.

CCPR: Dr. Jerrell, you have done a lot of research over the years on adults and children taking antipsychotic medications. Can you tell us a little bit about your background in this field?

Dr. Jerrell: I have been working with adult clients with schizophrenia in some capacity for most of my career. Early on, my research focused on psychosocial treatments and then antipsychotic medications, but I've always focused on cost effectiveness comparisons. Then, around the early 2000s, psychiatric investigators really started looking into the cardiometabolic effects of taking antipsychotic medications in adults.

CCPR: And how did this segue into studying the same issues in children?

Dr. Jerrell: I had done observational database studies using our state Medicaid database for adults with schizophrenia, and at a certain point, with all the children and adolescents who were being prescribed psychiatric medications, I thought that the adverse effects of antipsychotics in this young patient population were worth examining.

CCPR: And what did you learn?

Dr. Jerrell: For the children's studies, I requested a 10 year data file to study, because I really didn't expect to find many kids in the South Carolina Medicaid database that were prescribed antipsychotics. I certainly didn't expect the more than 4,000 kids that I did find who were taking antipsychotic medications during this decade. Then, we started looking at specific side effects and the results really became interesting.

CCPR: Did you find a high incidence of those same cardiometabolic effects in children that you had seen in adults?

Dr. Jerrell: Yes, very much so. In one study, we found that cardiac events including arrhythmias, ischemic, and pulmonary events were more likely to occur in children prescribed multiple antipsychotic medications than in those who were prescribed only one antipsychotic (McIntyre RS and Jerrell JM, *Arch Pediatr Adolesc Med* 2008;162(10):929–935).

CCPR: And were these instances very high among the children on these medications?

Dr. Jerrell: Relatively speaking, they were. The cardiovascular event incidence rates were only about eight to nine percent in the antipsychotic treated group, but that's still higher than in the child and adolescent control group, which was about three percent.

CCPR: And were there any long-term sequelae of these events? Did anyone die, for example?

Dr. Jerrell: In the data we examined, there were very few deaths in either the control group or the antipsychotic treated groups. And that is noteworthy because many of these kids were on antipsychotic medications for an average of about seven years.

CCPR: What did you learn about metabolic effects?

Dr. Jerrell: There was a significantly higher risk of incidence of weight gain or obesity and diagnosis of type 2 diabetes in children treated with antipsychotics (McIntyre and Jerrell ibid). For example, in the control group, obesity and weight gain was diagnosed in 8.6% of the children, whereas it was diagnosed after the start of an antipsychotic medication in 13.9% of the children. Similarly, type 2 diabetes mellitus was diagnosed in 1.9% of children in the control group and in 3.1% of those started on antipsychotics.

CCPR: So there was a clear risk that if a child took an antipsychotic, he or she was more likely to have weight gain or diabetes?

Dr. Jerrell: Yes, and it was significantly higher if they were prescribed more than one antipsychotic medication, which many kids were.

CCPR: Were there any medications that were implicated more than others?

Dr. Jerrell: Our results were not drug-specific, primarily because risperidone (Risperdal) was the most commonly prescribed antipsychotic medication, either as monotherapy (39.5% of those in the antipsychotic treated group), or as one of the "multiple antipsychotics" prescribed to 42.3% of the treated group.

CCPR: What have you learned about neurological side effects?

Dr. Jerrell: Similar to the neurological adverse effects found in the few randomized controlled trials that have been done with kids, we found diagnoses of seizures, sedation, and involuntary movement disorders, such as extrapyramidal symptoms and akathisia types of issues were more common in antipsychotic-treated cohorts. [For example, see Vitiello B et al, *Eur Neuropsychopharmacol* 2009;19(9):629–635.] Exposure to risperidone, multiple antipsychotics (which was usually risperidone plus something else), or an antipsychotic co-prescribed with an SSRI antidepressant consistently elevated the risk of developing a range of these neurological side effects (Jerrell JM et al, *J Child Neurology* 2008;23(12):1392–1399). In terms of SSRIs, although we know that Prozac inhibits the metabolism of Risperdal, we didn't do a subanalysis of specific SSRIs taken with specific antipsychotics, so I can't say if this drug combination is associated with a higher incidence

of neurological adverse events.

CCPR: In your research on antipsychotic side effects, you have specifically included children with developmental disabilities and mental retardation. I certainly see a lot of these kids in my practice. What have you learned about them?

Dr. Jerrell: We thought it was important to study these kids, because they're being seen by psychiatrists and, quite often, doctors have to base their care decisions for these children on research from treatment groups that are not representative of the developmentally disabled. The results showed what you would expect—that these kids already have impaired brain functioning, which is also reflected in a higher risk of having neurological side effects when exposed to antipsychotic agents (Jerrell JM, et al, *J Child Neurology* 2008;23(12):1392–1399). However, we did not find any differences for cardio-metabolic effects among the developmentally disabled (McIntyre and Jerrell ibid).

CCPR: You also have looked specifically at African American kids. Any difference there?

Dr. Jerrell: Slightly fewer than 50 percent of the kids in this study were African American, and when we examined the results for this subgroup, we found that they don't respond any differently to antipsychotics than anyone else, but they do demonstrate the same risk for adverse events (Jerrell JM, *J Natl Med Assoc* 2010;102(5):375–383). Typically, fewer African American kids enter randomized controlled trials, so this study was useful for gaining more information on a particular subgroup of patients.

CCPR: Did you learn anything about hyperprolactinemia and prolactin levels in children and adolescents taking antipsychotics?

Dr. Jerrell: Unfortunately, Medicaid data do not capture lab values, so I can't speak to changes in prolactin levels per se. And even if they did, I'm not sure how many doctors would be ordering prolactin levels on their adolescent patients, when these results don't correlate highly with sexual and reproductive problems. So, we were dependant on diagnostic codes entered for some type of sexual or reproductive problem. We did not find a difference in the development of sexual or reproductive conditions between the antipsychotic treated cohort and the control group. However, females, adolescents, and those with comorbid metabolic or endocrine conditions did experience more sexual or reproductive problems, which are commonly thought to result from hyperprolactinemia (Jerrell JM et al, *J Adolesc Health* 2009;45(1):70–76).

CCPR: What is the take-home message from your research? What should practicing psychiatrists like myself keep in mind when prescribing antipsychotics?

Dr. Jerrell: Well, I'd like to emphasize that co-prescribing multiple antipsychotics appears to significantly raise the risk of many adverse side effects, as opposed to canceling out each other's side effects, as some people have thought in the past. That's a myth I'd like to dispel. Of those prescribed multiple antipsychotics, only about one third of kids were cross-tapered down to one drug. The rest were treated long-term on multiple medications, which frankly, is risky for individual patients, given these results.

CCPR: That's helpful, considering I think many doctors do prescribe multiple medications. Anything else?

Dr. Jerrell: Monitoring cardiometabolic indices is particularly important. Keeping track of immediate weight, blood glucose, and lipid changes, and those things over time, and monitoring the occurrence of cardiovascular events can help the practitioner know when the treatment plan or medication might need to be changed.

CCPR: Thank you, Dr. Jerrell.

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Articles in Volume 1, 2010 CCPR

Research Updates IN PSYCHIATRY

ATTENTION PROBLEMS

TV, Video Games, And Attention Problems

Researchers have often found an association between television viewing and higher rates of attention problems over time, though not all studies have supported this link. There are also concerns, but little empirical investigation, regarding video games leading to attention difficulties.

The American Academy of Pediatrics (AAP) recommends that children under age two watch no television and that children older than two engage in two or fewer hours of screen time (video games and television) per day. A recent study investigated whether time spent playing video games and watching TV predicted future attention problems.

A total of 1,323 six to 12 year olds (and their parents) tracked time spent watching TV and playing video games weekly. Attention problems were assessed by the children's teachers. At baseline, there was a small but significant correlation between attention problems and both video game playing and television watching. Time spent playing video games at baseline had a significant but small association with attention problems at 13-month follow-up; the association between TV watching at baseline and attention problems at follow-up was small and of borderline statistical significance.

Both analyses controlled for gender, grade level, and attention problems at baseline. In addition, the study found a moderate and significant correlation between current attention problems and both video game time and TV time in a sample of 210 college students (Swing EL et al, *Pediatrics* 2010;126:214–221).

CCPR's Take: A letter to the editor noted that the teacher-completed measure of attention was not well-validated, which might limit the study's validity (Ferguson CJ et al, *Pediatrics* e-letter available online). Also, other potentially influential variables such as household environment and parenting style were not included in the study. Though overall TV viewing and video game playing time were only slightly predictive of attention problems, particular types of video games and television could be more problematic.

Combined Oral Contraceptives: A General Overview

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help patients remember symptoms related to VTE complications:

Abdominal pain
Chest pain
Headaches
Eye symptoms (such as vision changes)
Swelling or pain in the legs

Other common side effects of COCs include nausea, breast tenderness, and irregular menstrual bleeding. Taking the pill at night may help with nausea, and breast tenderness and irregular spotting often resolve after the first few cycles of COCs. If these symptoms persist, you should consider switching pill formulas.

Multiple studies have shown there is no statistically significant increased risk of depression in women on COCs. However, some patients do report increases in moodiness, depression, and other emotional states while on COCs. Such complaints deserve careful evaluation and may warrant a decrease in hormone doses or discontinuing COCs (Hatcher op.cit).

COC effectiveness

With perfect use, COCs have a 0.3% failure rate in the first year of use. However, with typical use, they have a failure rate of 8% in the first year of use (Hatcher op.cit).

Health benefits of COCs

There are many non-contraceptive benefits to COCs. Long-term users have decreased risks of ovarian and endometrial cancer. Depending on the type of progestin in a COC, certain formulations can improve acne and hirsutism. Also, many women enjoy that COC use leads to more regular menstrual cycles with less dysmenorrhea and decreased blood loss (Hatcher op.cit).

Migraine headaches and COC therapy

Migraines headaches with aura or focal neurologic symptoms are absolute contraindications to using an estrogen-containing contraceptive, regardless of a patient's age, because of the increased risk of stroke (Blake DR and Huppert J, *Contemp Pediatr* 2007;24:38–59). If a patient younger than age 35 has a history of migraine without aura or neurologic symptoms, benefits of COC therapy are thought to outweigh the risks. However, in patients age 35 or older who have a history of any migraines, COCs are not recommended (WHO op.cit).

Once a patient is placed on COC therapy, it is important to assess on follow-up visits if there are new or worsened headaches. If so, the following actions are recommended (Hatcher op.cit):

1. If patient develops new/worsening headaches that have accompanying focal neurologic symptoms, such as loss of vision, dizziness, slurred speech, flashing lights, weakness, abnormal cranial nerve exam → Discontinue COC. Refer for medical evaluation if appropriate. Consider changing to a progestin-only or non-hormonal method of birth control.
2. If patient develops headache symptoms that occur only during or worsen with menses → Consider a trial of extended cycling, such as using Seasonale.
3. If patient develops severe headache symptoms or is at high risk for stroke → Discontinue COCs. Refer for medical evaluation if appropriate. Consider changing to a progestin-only or non-hormonal method of birth control.
4. If patient develops mild headache symptoms without neurologic findings → Consider decreasing estrogen content of COCs and monitor closely.

Medications that interfere with the efficacy of COCs

Rifampin, rifabutin, St. John's Wart, ritonavir-boosted protease inhibitors, and certain anticonvulsants can lead to decreased efficacy of COCs. Anticonvulsants that interact negatively with COCs are phenytoin (Dilantin), barbiturates, carbamazepine (Tegretol), primadone (Mysoline), topiramate (Topamax), and oxcarbazepine (Trileptal).

Also, it is notable that pharmacokinetic studies show that levels of lamotrigine decrease significantly with concurrent COC use (WHO op cit). COCs may increase the effect of diazepam (Valium), chlordiazepoxide (Librium), and tricyclic antidepressants (Hatcher op.cit).

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CME Post-Test

As a subscriber to *CCPR*, you already have a username and password to log on www.TheCarlatChildReport.com. To obtain your username and password, please email CME@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this issue's CME post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning objectives are listed on page 1.

1. In the review by Rogovik et al, five out of six trials showed metformin, 500 to 1000 mg twice daily, resulted in what change in BMI (Learning Objective #1)?
   - [ ] a. an increase of 0.8 to 2.7 kg/m2
   - [ ] b. an increase of 2.7 to 3.2 kg/m2
   - [ ] c. a decrease of 0.8 to 2.7 kg/m2
   - [ ] d. a decrease of 2.7 to 3.2 kg/m2

2. When starting a patient on a combined oral contraceptive, the recommended starting dose of estrogen is which of the following (L.O. #2)?
   - [ ] a. 15 mcg or lower
   - [ ] b. 20 mcg or lower
   - [ ] c. 35 mcg or lower
   - [ ] d. 50 mcg or lower

3. Some medications may have increased effects when taken with combined oral contraceptives. Which of the following is *not* one of these meds (L.O. #2)?
   - [ ] a. diazepam (Valium)
   - [ ] b. chlordiazepoxide (Librium)
   - [ ] c. tricyclic antidepressants
   - [ ] d. lamotrigine (Lamictal)

4. In her research, Dr. Jerrell found the incidence of cardiovascular events in what percentage of kids on antipsychotics (L.O. #3)?
   - [ ] a. 3%
   - [ ] b. 8% to 9%
   - [ ] c. 13%
   - [ ] d. 39% to 40%

5. In the Swing et al study, time spent playing video games at baseline had no association with attention problems at 13-month follow-up (L.O. #4).
   - [ ] a. True [ ] b. False

To earn CME or CE credit, you must read the articles and log on to www.TheCarlatChildReport.com to take the post-test. Please see the pre-test listed below to prepare for this month's post–test. Learning objectives are noted on page 1. You must answer at least four questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be taken by December 14, 2011.

PLEASE NOTE: WE CAN AWARD CME CREDIT ONLY TO PAID SUBSCRIBERS

Your evaluation of this CME/CE activity (ie, this issue) will help guide future planning. Please respond to the following questions:

1. Did the content of this activity meet the stated learning objectives? L.O.#1: [ ] Yes [ ] No L.O.#2: [ ] Yes [ ] No L.O.#3: [ ] Yes [ ] No L.O.#4: [ ] Yes [ ] No
2. On a scale of 1 to 5, with 5 being the highest, how do you rank the overall quality of this educational activity? [ ] 5 [ ] 4 [ ] 3 [ ] 2 [ ] 1
3. As a result of meeting the learning objectives of this educational activity, will you be changing your practice performance in a manner that improves your patient care? Please explain. [ ] Yes [ ] No

4. Did you perceive any evidence of bias for or against any commercial products? Please explain. [ ] Yes [ ] No

5. How long did it take you to complete this CME/CE activity? ___ hour(s) ___ minutes
6. **Important for our planning:** Please state one or two topics that you would like to see addressed in future issues.

Combined Oral Contraceptives: A General Overview

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Prescribing patients emergency contraception

Emergency contraception (EC) can be prescribed in several ways. In the past, it was administered via high dose combined hormonal methods. This was problematic for some patients due to the nausea and vomiting that accompanied the increased estrogen dose. Today, the preferred method of EC is Plan B. Plan B contains only levonorgestrel, so it is a safe method even if a patient has a contraindication to estrogen. Plan B contains two pills, and package instructions state to take the two pills 12 hours apart from each other. However, many practitioners advise their patients to take them both at once. Plan B can be used up to five days after unprotected intercourse. However, the efficacy of Plan B decreases significantly as time from the encounter increases. If taken within 24 hours of unprotected intercourse, Plan B is 77% effective in preventing pregnancy. If taken between 49 and 72 hours, the efficacy decreases to 31%. If menstruation does not occur within 21 days of taking Plan B, patients should see their doctor for a pregnancy test. Plan B is available over the counter for patients 18 years and older. For patients younger than 18, a prescription is required (Zieman op.cit).

Alternatives to COCs to prevent conception

Patients who wish to use a combined hormonal contraceptive but have difficulty remembering to take a daily method may be interested in using the contraceptive patch (changed weekly) or vaginal ring (monthly). Depo Provera is a monthly injection that can be used in women with a contraindication to estrogen, and IUDs are now considered viable options for adolescents and can be used for five to 10 years. Another new option is a subcutaneous progesterone implant (Implanon) that is effective for up to three years.

The Carlat Child Psychiatry Report
Clearview Publishing, LLC
P.O. Box 626
Newburyport, MA 01950

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