Abstract

I recently had an adolescent patient who presented with a chief complaint of depression. He had classic symptoms of difficulty sleeping, dysthymia, and anhedonia (loss of interest in things that used to bring him joy). He was a very smart and self-aware 17-year-old, and was able to describe his symptoms easily. There were no concerns for manic episodes or psychosis, and he met diagnostic criteria for unipolar major depressive disorder. He denied suicidal ideation, and was already seeing a therapist weekly for the last several months. He had a strong family history of depression, with his father, aunts, and grandmother who also carried a diagnosis of depression. He presented with the support of his mother, asking about next steps, and specifically, pharmacotherapy. This patient is a perfect example of an adolescent who is a good candidate for initiation of antidepressant medication. Primary care pediatricians should feel comfortable with first-line agents for major depressive disorder in certain adolescents with depression, but many feel hesitant and rely on child and adolescent psychiatry colleagues for prescriptions. [Pediatr Ann. 2015;44(11):466-468,470.]

This article is aimed at giving primary care pediatricians practical tips for the initiation and management of antidepressants, as well as advice on when to ask specialists for help. This article does not discuss the screening or diagnosis of pediatric depression, but it is worth saying that pediatric and adolescent depression is a common, treatable problem. It is estimated that 3% to 8% of adolescents suffer from depression. In many instances, patients have their first major depressive episode in the adolescent period between ages 15 and 24 years (Figure 1). This diagnosis is relatively common, and for certain patients, initiation of antidepressant medication by a primary care pediatrician can be an important step in their recovery.
Although this article focuses primarily on pharmacotherapy for depression, it is important to say that psychotherapy and psychoeducation, regular exercise, healthy diet, and good sleep hygiene, as well as family therapy and support organizations can be paramount in helping an adolescent conquer depression. Lastly, it is important to approach adolescent depression in an integrative fashion, seeking the help of therapists, social workers, and/or case managers when possible. This is especially important, because many patients have significant social stressors that may not be addressed by medication, including bullying, abuse, or family discord. Combination therapy with psychotherapy and pharmacotherapy has been shown in some studies to be superior to pharmacotherapy alone, particularly in the first few months of treatment, with improvements in function as well as decrease in suicidal ideation.6,7

FIRST-LINE AGENTS

The first-line agents for major depressive disorder in adolescents are the selective serotonin reuptake inhibitors (SSRIs). There is consistent evidence for several SSRIs medications, and fewer side effects than older agents such as tricyclic antidepressants. The most well-studied agent is fluoxetine. Important issues to consider prior to starting medications are patient or family preference, known allergy to fluoxetine, and drug-drug interactions. Additionally, SSRIs medications may inhibit hepatic cytochrome P450 enzymes that metabolize other medications. Medication interactions include benzodiazepines, warfarin, clozapine, and monoamine oxidase inhibitors among others. Thankfully, many pediatric patients are otherwise healthy, and if they are taking other medications, many resources exist for providers to determine the risk of drug-drug interactions.

SECOND-LINE AGENTS

The evidence for fluoxetine is strong, with some studies showing that 70% of pediatric depressive episodes remit with initiation of fluoxetine.5 However, for those 30% of patients that have continued symptoms, escitalopram, citalopram, and sertraline are also SSRIs that are reasonable options. Venlafaxine is also a reasonably well-studied alternative.6,7 It is interesting to note that some SSRI medications, such as paroxetine, have not been shown to be effective in pediatric depression, despite being an SSRI.8

If several options above have failed to improve the patient’s depression, seeking the help of a child and adolescent psychiatrist is a good next step. Other agents, including buproprion or duloxetine, may be tried but have less evidence in pediatrics, and buproprion has an unfortunate side effect of appetite suppression that may be detrimental in growing adolescents. Tricyclic antidepressants are rarely used for treatment of depression in adolescents because of limited data showing efficacy and more severe side effects including autonomic symptoms.

FOLLOW UP AND DOSE ADJUSTMENT

Once you have decided on a medication, start at a low dose and titrate upward. Therapeutic effects can take 1 to 8 weeks to materialize; therefore, many physicians recommend waiting 2 to 4 weeks before increasing the dose or switching to a different medication. Some psychiatrists recommend even faster titration, every 1 to 2 weeks. If switching between SSRIs, the clinician should taper the patient off slowly, with 1 to 2 weeks between dose adjustments. The reason for a relatively slow taper is because SSRIs have a relatively long half-life. See Table 1 for dose adjustments for common SSRI medications.

Once started on SSRI medication, checking in monthly is a good start to screen for any side effects and to check efficacy of the current dose. Common side effects of SSRIs include gastrointestinal symptoms (loose stools or constipation, change in appetite, nausea, belly pain), dry mouth, sweating, sleep disturbance, headache, rash, and sexual dysfunction. Additionally, SSRIs can be activating, causing patient symptoms of agitation and restlessness. “Disinhibition” may also occur, with risk-taking behaviors or increased impulsivity. Fluoxetine seems to be slightly more activating than other SSRIs medications. This disinhibition may be related to concerns about increased suicide risk with initiation of SSRIs, and suicidal ideation must be assessed at every follow-up visit.

Some side effects may be transient, so if they are mild and tolerable, physicians can continue medication for 2 to 5 days to see if the side effects resolve. More serious side effects are rare, but include serotonin syndrome, hypomania, akathesia (severe restlessness), and discontinuation syndrome, which may occur with abrupt cessation of antidepressants.

In addition to screening for side effects after initiation of medications, pediatricians should assess efficacy to determine next steps. A commonly used rating scale for pediatric depression is the Patient Health Questionnaire.9 This rating scale can be administered easily in a primary care office. Once stabilized, monthly check-ins with the pediatrician are reasonable as well as symptom check.
lists periodically (every 3 months is a reasonable regimen).

Short-term prognosis for children and adolescents with unipolar depression is good—approximately 60% respond to initial treatment. Most patients need to be on antidepressant medications for 6 to 12 months. However, some patients with more severe depression may need longer than 12 months of medication. It is important to note that remission often occurs with abrupt cessation of antidepressant medications.

**BLACK BOX WARNING FOR SSRI MEDICATIONS: INCREASED SUICIDALITY**

Pediatricians often hesitate to prescribe antidepressants because of the black box warning for increased suicidality with SSRI medications. In 2004, the US Food and Drug Administration (FDA) reviewed 24 clinical trials including 4,400 youth with depression, anxiety, or obsessive-compulsive disorder. They analyzed suicidal thoughts in short-term treatment with SSRIs (4-16 weeks). Although no suicides occurred in these patients, the FDA found that 4% of patients treated with SSRIs had increases in suicidal thoughts, compared to 2% of patients treated with placebo.

Suicidal ideation is certainly a symptom that needs to be assessed at every visit, and because it is a symptom, rates of prescribing SSRIs have reduced substantially since the black box warning was instituted. At the same time, there has also been an increase in completed suicides in youth. There is no proven causal relationship, but many feel that antidepressants (Figure 2) can be effective in preventing suicide in children and adolescents.

**WHEN TO GET HELP FROM A CHILD PSYCHIATRIST**

The patient described at the beginning of the article is an ideal candidate for treatment of depression by a primary care pediatrician. The patient was amenable to therapy, had a good network of support from friends and family, was healthy otherwise, and without comorbid substance abuse, eating disorder, or other health problems, and was not suicidal. Patients who are actively suicidal may need inpatient treatment and consultation with a psychiatrist. Other issues that may need consultation include:

1. High risk for suicidal behavior and/or history of suicide attempts;
2. Presence of substance abuse;
3. Presence of eating disorder;
4. Presence of manic or psychotic symptoms;

---

**TABLE 1. Dose Adjustments for Common SSRIs**

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Starting Dose (mg/day)</th>
<th>Incremental Increase (mg/day) Every 2-4 Weeks</th>
<th>Incremental Taper (mg/day) Every 1-2 Weeks</th>
<th>Effective Dosage Range (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>10</td>
<td>5-10</td>
<td>10</td>
<td>10-40</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>10-20</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10-60*</td>
</tr>
<tr>
<td>Sertraline</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25-200</td>
</tr>
</tbody>
</table>

Abbreviation: SSRIs, selective serotonin reuptake inhibitors.
*For fluoxetine the dose range varies based on diagnosis—10 to 40 mg for depression and 10 to 60 mg for anxiety.

---

Figure 2. A young patient receiving medication from her physician.
5. No improvement after 6 to 8 weeks of treatment;
6. Recurrent/chronic depression lasting more than 2 years;
7. Severe functional impairment;
8. Psychiatric comorbidities;
9. Complicated psychosocial factors, ie, dysfunctional family dynamics; and
10. Inadequate response to initial therapy or clinician discomfort in managing antidepressant medications.

**ALTERNATIVE THERAPIES FOR MAJOR DEPRESSIVE DISORDER**

Patients may suggest use of St. John’s Wort or fish oil to treat depression. However, for both of these alternative therapies, there are limited data for their efficacy in both pediatric patients and adult patients. Additionally, St. John’s Wort can have drug-drug interactions and, in particular, can interact with oral contraceptive pills.

**CONCLUDING REMARKS**

Pediatric depression is a common problem and primary care pediatricians can feel comfortable initiating antidepressant medications in certain low-risk patients. For the patient with clear unipolar depression, low suicide risk, and no improvement with psychotherapy alone, an antidepressant prescription from a primary care pediatrician is a reasonable next step in the process toward recovery. See Table 2 for a few take-home points.

**REFERENCES**