Medication Management of Depressive Disorders in Children and Adolescents

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First Line Medications

SSRIs

Prozac (Fluoxetine): 5-60 mg

Zoloft (Sertraline): 12.5-150 mg

Paxil (Paroxetine): 5-40 mg

Celexa (Citalopram): 10-40 mg

Luvox (Fluoxamine): 25-200mg

TADS-Treatment for Adolescents with Depression Study Team

- Multicenter, randomized clinical trial sponsored by NIMH
- Aim to evaluate the short and long term effectiveness of four treatments of adolescents with major depressive disorder

  -Fluoxetine, CBT, Fluoxetine+CBT, placebo

JAMA, Aug 2004

TADS-Treatment for Adolescents with Depression Study Team

- Demographics:

-439 adolescents (12-17 y) with current MDD

-54.4% girls, 73.8% white, 12.5% AA 8.9% Hispanic

-86% experiencing first episode

- Co morbidity:

-15.3% anxiety, 13.7% ADHD, 13.2% ODD, 10.7% social phobia, 10.5% dysthymia

TADS-Treatment for Adolescents with Depression Study Team

- **Compared to Fluoxetine alone and CBT alone, Fluoxetine+CBT was superior**
- **Fluoxetine alone was superior to CBT alone**
- **Rates of response**

  -Fluoxetine+CBT- 71.0%

  -Fluoxetine alone-60.6%

  -CBT alone- 43.2%

  -Placebo- 34.8%
- **SI was present at baseline in 29% and improved in four treatment groups**

JAMA, Aug 2004

Antidepressants with FDA approval

- For depression: Prozac (Jan-’03)
- For OCD: Zoloft (age 6)

  Luvox (age 8)

- Fluoxetine:

  -2002 (Emslie), 20mg fixed daily dose better than placebo

  -2003 (Hughes and Emslie), placebo controlled pharmacokinetic study-response was variable

- Sertraline

  -2003 (Wagner)-RCT-376 patients mean dose was 131mg/day-safe and effective for children and adolescents

  7 pts on meds had serious AE- SI & aggression

  -2001 (Nixon) six month open trial-mean dose 125mg in adolescents with MDD and dysthymia

- Paroxetine

  -2001 (Keller) RCT mean dose was 28mg/day compared to TCA and placebo

  Significantly more AE than placebo

  -2003 (Braconnier) double blind study compared to Clomipramine

  No placebo group, high discontinuation

- Citalopram

  -2004 (Wagner) Double blind study, compared to placebo, mean dose 24mg/day-significant improvement for depression

  AE: rhinitis, nausea, abdominal pain

  SE and discontinuation similar to placebo

First SSRI not effective

- Change to a different agent in same class
- Choose based on SE
- Reassess for co morbidity

Characteristics of SSRI resistant depression

- Comorbidity-anxiety, ADHD, substance abuse
- Family Discord
- Greater initial impairment

If two SSRIs fail change class

- If co morbid anxiety

  -If need alerting, consider Venlafaxine

  -If need sedation, consider Mirtazepine

  -If need activation consider Bupropion

  -If above fail consider Clomipramine

Buspirone

- May be helpful for anxiety and augmentation of depression

MDD with psychotic features

- Lack of data to support a choice, but newer atypicals preferred

MDD with ADHD

- Begin with a stimulant for 2 weeks

  -If both respond, continue ADHD algorithm

  -If ADHD only responds, start MDD algorithm

  -If neither respond, proceed with MDD algorithm

Tricyclics

- Used in children and adolescents for a wide range of symptoms (MDD, ADHD, enuresis)
- Studies have not shown efficacy in children and adolescents
- Concerns about safety and side effects

  -CV side effects, esp. in overdose

  -sedation, weight gain, dry mouth

FDA Warning

- Oct 31, 2004

-AACAP talking points

-www.parentsmedguide.org

-The American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry have prepared a fact sheet to help patients and families make informed decisions about obtaining the most appropriate care for a child with depression.

What prompted the FDA warning?

- In 2004, the FDA reviewed 23 clinical trials involving more than 4,300 child and adolescent patients who received any of nine different antidepressant medications.
- No Suicides occurred in any of these studies.

What prompted the FDA warning?

- The FDA found that “adverse events” (thoughts of suicide or description of potentially dangerous behavior) were reported by approximately 4 percent
- In 17 of 23 studies, medication neither increased suicidal thinking nor induced new suicidal thinking
- All studies combined showed a slight reduction in suicidality over treatment

What prompted the FDA warning?

- It’s important to recognize that suicidal thoughts are a common part of depressive illnesses
- Research demonstrates that over 40% of children and adolescents with depression think about hurting themselves.

What prompted the FDA warning?

- Treatment that increases communication about these symptoms can lead to more appropriate monitoring which decreases the actual risk of suicide.

Did the FDA prohibit the use of antidepressant medications by children and adolescents?

- No
- Close monitoring by parents and physicians for worsening of depressive symptoms or unusual changes in behavior.
- The “black box” states the antidepressants are associated with an increased risk of suicidal thinking and/or behavior in a small proportion of children and adolescents.

Do antidepressants increase the risk of suicide?

- There is no evidence that antidepressants increase the risk of suicide
- The FDA reported an increase in spontaneous reports of suicidal thoughts and/or behavior among children receiving medication, but there is no evidence that these suicidal thoughts or behaviors leads to an increased risk of suicide

Do antidepressants increase the risk of suicide?

- CDC 1992 to 2001, rate of suicide among American youth ages 10-19 declined by more than 25%
- CDC reports nearly 1 in 6 adolescents think about suicide in a given year

What factors other than depression increase the risk of suicide?

- Previous suicide attempt
- Presence of serious mental disorder
- Loss of or separation from parent
- End of a romantic relationship
- Physical or sexual abuse

Does talking about suicide signal increased likelihood of SIB

- Psychiatrists and other mental health professionals have found that when a young person talks about suicidal thoughts, it often opens the door to discussion regarding the need to take special safety precautions or protective measures

Can my child keep taking the antidepressant being prescribed?

- Research suggests increased risk of suicidal thoughts in the first 3 months of treatment
- One antidepressant medication Fluoxetine, or Prozac is formally approved by the FDA for treatment

How can I help monitor my child?

- Monitor for evidence of improvement over 6-8 weeks
- Weekly follow-up for the first month
- Then every other week for the next month