DEPRESSION AND ANXIETY IN THE PEDIATRIC POPULATION

Kelly Blankenship, DO
Michigan State University/ Pine Rest Program Director,
Child & Adolescent Psychiatry Fellowship
Michigan State University Assistant Professor of Psychiatry

Financial Disclosures

- None
Agenda

- Depression
  - Case Presentation
    - Prevalence
    - Diagnostic Criteria
    - Risk Factors
    - Clinical Presentation
    - Screening
    - Suicidal Ideation
    - Treatment
- Anxiety
  - Case Presentation
    - Diagnostic Criteria
    - Clinical Symptoms/Risk Factors
    - Treatment

Case Presentation

- Moly is a 14 year old female presenting to your office with a chief complaint of significant weight loss over the past 3 months
- She has lost 20 pounds since her last visit to your office 5 months ago
- Molly is quiet but appears irritated and lets her mother do most of the talking
- Molly rolls her eyes when mother discusses concern over Molly’s 20 pound weight loss over the past 3 months. Her mother reports that she and her husband separated 6 months ago. Mother has primary custody as dad ‘walked out on the family’. Mother is working long hours so the family rarely eats together. Mother reports being unsure regarding her daughter’s diet. She reports that Molly ‘won’t talk to me’ about her weight loss and eating.
When you ask about any concerning behavior mother has noticed, she reports Molly rolling her eyes and being more ‘of a teenager’ lately. When you ask what that means, mother replies with ‘you know normal teenage behaviors; she’s always in her room, never wants to be with me and her siblings anymore.’ Mother goes on to tell you that over the past few months she noticed Molly has been ‘hanging out with a new crowd’. Mother reports that she has been more defiant with regards to rules as well, but again attributes this to being ‘a normal teenager’ and possibly all ‘the change’ occurring.

You start to ask Molly questions but Molly remains quiet and mother continues to answer them. Molly continues to roll her eyes as mother denies noting that Molly has been ill over the past 3 months. She denies noting any physical symptoms such as vomiting, diarrhea, fever, frequent HA or URI type symptoms.
Clinical Presentation

- You ask for mother to leave the room so you can talk with Molly alone, hopeful she will be more cooperative without her mother in the room.
- Molly shrugs her shoulders when you ask about her recent weight loss
- She tells you that she’s tired of being ‘fat’ and ‘a freak’
- She denies that she has been making herself vomit but refuses to tell you how much she is eating a day reporting ‘enough’
- She reports that she spends most of her time in her room because everyone else in the house is ‘annoying’ and ‘doesn’t get it’
- She reports that she is sleeping more but spending most of her time in her room on social media sites
- She reports having more trouble focusing at school
- She reports a decrease in energy over the past few months and reports ‘I just don’t feel like doing anything’ as another reason to stay in her room
- She reports that her new friend group ‘gets me’
- When asked what they get about her, she tells you ‘they get my struggles’. She then goes on to tell you that they act as each other’s therapist
- During physical exam you note multiple superficial laceration in different stages of healing on her left arm – when you ask her if these are self-inflicted, she reports ‘It helps me feel something’
Clinical Presentation

- When you ask about depression, she reports ‘I’m not really depressed, I just don’t think there is a point to life’. When you asked her to expand more she tells you ‘there’s really no point’. ‘Why work towards graduating high school and go to college. I’ll just end up with a job I hate. If I get married, then I’ll have to go through a divorce. It’s all pointless’.
- When you ask if she has ever thought of killing herself she reports, ‘when I feel that way I call my friends, we help each other’.
- When asked if she has ever had a plan she states ‘I would just take a bunch of pill’
- She denies she is currently feeling this way. She states the last time she felt this way was a few days ago after hearing her mother fight with her father over the phone.

Prevalence of Depression

- Prevalence of major depressive disorder is 2% in children and 4-8% in adolescents with an increase in prevalence of depression after puberty (females)
- Another 5-10% have a less severe form of depression
- Each successive generation since 1940 is at greater risk of depression and having a younger age of onset
  - AACAP Depression Practice Parameters 2007
Prevalence of Depression

- Lifetime Prevalence of Mental Disorders in US adolescents – National Comorbidity Survey Replication Adolescent (ages 13-17 years) Supplement
  - MDD or dysthymia was present in 11.7% of the youths
  - Female 15.9% and male 7.7%
  - Increased dramatically as the youths aged
    - 13-14 years 8.4%
    - 15-16 years 12.6%
    - 17-18 years 15.4%
  - Merikangas KR et al 2010

- 75% of adolescents visit a PCP every year
- 20% of these adolescents are in the midst of a depressive episodes
- 50% will continue to have depressive symptoms 6 months later
- Only 36-44% of children and adolescents who meet criteria for clinical depression will receive treatment
- Most children and adolescents will present to primary care physicians and not to mental health professionals
  - Child and adolescent psychiatry fellowship slots are decreasing nationally and not filling
  - Prediction is for the need of 12,624 child and adolescent psychiatrists in 2020 but prediction is there will be 8,312

- Wegner SE et al, SIU et al 2017, Gledhill J & Hodes M
**Diagnostic Criteria**

- **Major Depressive Disorder**
  - 2 Weeks with 5 of the following symptoms
  - Depressed mood most of the day (can be irritable mood in children and adolescents)
  - Markedly diminished interest or pleasure (anhedonia)
  - Significant change in appetite
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or excessive/inappropriate guilt
  - Decreased ability to focus or concentrate
  - Recurrent thoughts of death or suicidal ideation
  - SIGECAPS

- **Persistent Depressive Disorder (Dysthymic Disorder)**
  - Depressed mood most of the day for more days than not for at least 2 years in adults
  - In children and adolescents mood can be irritable and duration greater than 1 year
  - With 2 or more of the following symptoms
    - Poor appetite or overeating
    - Insomnia or hypersomnia
    - Low energy or fatigue
    - Low self-esteem
    - Poor concentration
    - Feelings of hopelessness

---

**Risk Factors/Symptoms**

- Interaction of genetic and environmental factors
- Single most predictive factor is significant family loading of the disease
- Parental depression
- Female gender (in adolescents)
- Highly emotional temperament (reacts quickly to everyday events, easily brought to tears, easily soothed)
- Global self-devaluations (thinking of oneself as a failure, feeble, incapable, pitiful, unlovable)
- Ruminative cognitive style- people who dwell on a particular thought
- Physical or learning disability
- Other environmental factors
  - Loss
  - Abuse or Neglect
  - Medical Illness (diabetes, cancer)
  - Bullying
  - Poor friendships

## Risk Factors/Symptoms

- Behavioral Problems
- Obesity
- Loss of a loved one
- Loss of a romantic relationship
- Family conflict
- Uncertainty about sexual orientation
- Poor academic performance
- Low SES
  - Siu A et al 2016

## Symptoms of Depression

- Sadness/anhedonia/boredom/irritability that does not respond to usual experiences that would typically bring enjoyment
- Children it can present as mood lability, irritability, low frustration tolerance, temper tantrums, somatic complaints and social withdrawal
- Change from baseline in appetite, grades, oppositional/defiant behaviors, substance use, friend group
- Seeming uninterested or discontinuing previous hobbies, clubs or sports
- Withdrawal from family and/or friends

  - [https://www.youtube.com/watch?v=pZGVgl_RZ5Y](https://www.youtube.com/watch?v=pZGVgl_RZ5Y)
  - [https://www.youtube.com/watch?v=rRzzz7npe8w](https://www.youtube.com/watch?v=rRzzz7npe8w)

  - (AACAP Practice Parameters 2007)
Screening for Depression

US preventive Services Task Force found that screening individuals 12-18 years of age may lead to earlier diagnosis and treatment for depression.

The Beck Depression Inventory for adolescents
- Child and Adolescent version
- 7 question self-report tool

The Children’s Depression Inventory
- Teacher, parent and self-report versions

Clark MS et al 2012

Plan of Care

- Home with Follow-up
  - Therapy
  - Medication management
  - Therapy and Medication Management
- Inpatient Psychiatric Unit
- Partial Hospitalization Program
Suicidal Ideation

- Do you ever wish you were dead?
- Have you ever thought about killing yourself?
- Do you have a plan? (Access to the planned method)
- Intent?
- Protective factors?
- How often and how long has the SI persisted?
- When does the SI occur?
- How long have you had these thoughts?
- Any past suicide attempts? How?
- Access to firearms?
- Do the parents feel they can keep the child/adolescent safe? (Supervision)
- SIB (cutting, burning)
- Substance Abuse

Suicidal Ideation

- 500,000 adolescents attempt suicide each year
- Risk factors include higher self-reported depression, suicidal ideation, lower family income, greater number of previous suicide attempts, history of sexual abuse, lower family cohesion
- Children are most likely to complete suicide by suffocation
- Adolescents are most likely to complete suicide by firearms
Treatment

- Psychotherapy should always be part of the treatment plan
  - Cognitive Behavioral Therapy (CBT) and Interpersonal Psychotherapy (IPT) have reported positive results in randomized controlled trials (RCTs) in adolescents
  - Attachment Based therapy
  - Family Intervention
    - (Birmaher B, Brent D 2016, Clark MS et al 2012)

Cognitive Behavior Therapy

Uses therapeutic techniques to improve coping skills, communication and peer relationships

It also combats negative emotions and thought processes

Links cognitive distortions to depressed mood

https://www.youtube.com/watch?v=0ViaCs0k2jM

Clark MS et al 2012, Godhii & Hodes 2015
Interpersonal Therapy

- Focuses on interpersonal context in which depressive symptoms occur and the connections between relationships, emotions and affect
- Thought to possibly work well in this age group because of importance of peer group and family relationships and their influence on depression and response to treatment
- Focuses on areas of: grief, role transition, interpersonal role disputes and interpersonal deficits
  - Gledhill J & Hodes M 2015

Treatment

- Psychopharmacology
  - Fluoxetine- FDA approved to treat Major Depressive Disorder in children and adolescents (8-18 years of age)
  - Escitalopram- FDA approved to treat adolescents with Major Depressive Disorder (12-18 years of age)
  - Sertraline, Citalopram, Duloxetine and Bupropion are often used off-label to treat depression in the pediatric population if patient has failed or is not able to tolerate FDA approved treatments
Treatment

- Psychopharmacology
  - Half life of sustained release buproion, citalopram, paroxetine and sertraline (lower doses than 200 mg) may have shorter half lives in adolescents than adults
    - Withdrawal symptoms could occur with non-compliance
  - Randomized controlled trials of tricyclic antidepressants showed these were no more efficacious than placebo
    - Side effect profile
    - Can be fatal in overdose
      - (Birmaher B, Brent D 2016)
      - (Emslie G, Croarkin P 2016)

Medication Management

Are SSRIs associated with an increased risk of developing SI or suicidal behavior
- Black Box Warning
- Number needed to treat 10
- Number needed to harm 112
  - (Birmaher B, Brent D 2016)
  - (Emslie G, Croarkin P 2016)
Recent increased controversy over the use of SSRI in children and adolescents following a publication of meta-analyses suggesting antidepressants are not effective, minimally effective or no more effective than placebo.

Review published in May of 2017 reporting:
- Meta-analyses that include large number of industry-sponsored trials distort the picture of efficacy of SSRIs in children and adolescents
- Industry trials often have high placebo response rate, methodological and implementation challenges that suggest they should be considered failed trials not negative trials thus mostly uninformative regarding medication efficacy.
Two studies funded by the National Institute of Mental Health (NIMH), exhibited many methodological strengths, had low placebo response rate and meaningful-group differences that support antidepressant efficacy

- Walkup JT 2017

Treatment for Adolescents with Depression Study (TADS)

- 439 adolescents between the ages of 12-17 years of age were randomized to 4 Arms- Fluoxetine alone (10-40 mg/day), CBT alone, CBT + Fluoxetine, Placebo
- Fluoxetine and placebo groups were blinded, CBT groups were not
- Fluoxetine with CBT 71% response rate
- Fluoxetine alone 60.6% response rate
- CBT alone 43.2% response rate
- Placebo 34.8% response rate
Comparing CBT and SSRIs

- Fluoxetine and CBT were superior to fluoxetine alone, CBT alone and placebo
- Fluoxetine alone was superior to CBT
- CBT did not separate from placebo
- Clinically significant decrease in suicidal thinking was present in all groups with the CBT + Fluoxetine group showing the greatest reduction
- Adolescents in this study tended to have more severe depression and higher rates of comorbidities than in past studies
- CBT did show a decrease in suicidal thinking
  - TADS 2004

Paroxetine

- Not FDA approved to treat depression in children and adolescents
- Re-analysis of data was done due to the restoring invisible and abandoned trails (RIAT) initiatives put in motion in 2013
- Re-analysis of data from the SmithKline Beecham’s study 329 which compared the efficacy of paroxetine and imipramine with placebo in the treatment of adolescent depression
- 275 adolescents with major depression were randomized to receive Paroxetine (20-40 mg), imipramine (200-300 mg) or placebo for 8 weeks
Paroxetine

- Paroxetine and Imipramine were not statistically or clinically significantly different from placebo.
- There were clinically significant increases in harm, including suicidal ideation and behavior in the paroxetine group.
- There was significant cardiovascular problems (tachycardia, postural hypotension and prolonged QT) in the imipramine group.
  - Noury JL et al 2015

Pediatric Anxiety
Case Presentation

- CC: Jade is 6 y/o new patient presenting to your office with a chief complaint of frequent stomach aches.
- HPI: Stomach aches started in August of this year (around when school started). There is no associated N/V/D with these and BM are daily and normal. The stomach aches seem to be worse in the mornings. She has missed 10 days of school so far this year due to stomach aches.

Case Presentation

- In addition to the missed school days, the school nurse has called mother several days reporting that Jade is in her office due to stomach aches
- Mother reports that she doesn’t seem to have problems with stomach aches on the weekends or in the evenings.
- Her diet has not changed and she has no prior history of any medical or GI problems
- There are no family history of concerning medical problems. Mother does mention a significant family history of anxiety and depression.
Case Presentation

- There have been no recent travels by Jade or anyone else out of the country
- No food allergies or sensitivities
- During the examination Jade sits close to her mother and often hides her head
- When you make eye contact with Jade, she quickly looks away
- When you ask Jade questions she looks to her mother to answer and does not speak
- When you start your physical exam she looks to her mother for reassurance to let you begin
- Physical exam and vitals are WNL

In further discussion mother reports that Jade has always been ‘shy’ and describes her as a ‘slow to warm’ child
- She reports that Jade does not like to talk to people unless she knows them well
- Mother reports that at school she is starting to ‘open up’ to the teacher and students. Mother reports that initially she would not talk to the teacher
- Mother reports that she does well on the bus because her 8 y/o sister sits with her
Case Presentation

When you ask about any other concerning behavior, mother reports that she likes her hair ‘to be just so’, stating her pony tails has to be exactly in the middle of her head
- Mother also reports that she will become very upset if the line of her socks are not perfect on her toes
- Mother reports that she has missed the bus several mornings because she is having a ‘tantrum’ because her hair and socks are not ‘just right’

Anxiety Prevalence

- Most common mental illness among children and adolescents
- Nearly 1/3 of adolescents have a diagnosable anxiety disorder
- 8.3% of adolescents have a severe anxiety disorder
- 50% of clinically referred adolescents have an anxiety disorder
- Anxiety disorders are associated with negative mental health outcomes including mood disorders, substance misuse, reduced educational achievement

Prevalence

Onset of Anxiety d/o

- Separation anxiety d/o and specific phobia (7-9 years old)
- Unspecified Anxiety d/o (10-13 years old)
- Social Phobia (15-16 years old)
- Agoraphobia, Obsessive-compulsive d/o, Post-traumatic stress disorder, Panic and Generalized anxiety d/o (median age of 28 years)

Merikangas KR 2005

Risk Factors

- Parental anxiety
  - Inherited and learned
- Invalidating Parenting
  - Parents minimize their child’s experience of anxiety by dismissing or criticizing their feelings
- Overprotective parenting
  - Could model fear of potential trigger and prevent their children from practicing coping skills and facilitate avoidance of stimulus
  - Dillon-Naftolin 2016
Risk Factors

- Behavioral Inhibition
  - Behavioral withdrawal in challenging or fearful situations
- Low SES
- Anxiety Sensitivity
  - Anxiety sensations are indicators of a physical concern
  - This can lead to being afraid to be afraid which can lead to Panic attacks
- Female Gender
  - Appears to begin at age 5 and increase throughout adolescence
    - Merikangas KR 2005

Symptoms of Anxiety Disorders

- Fear, worry, indecisiveness- children and adolescents may not recognize that the fear is unreasonable
- Often children will look for others to make decisions or answer questions
- They may have difficulties separating from caregivers
- In younger children anxiety can manifest as crying, irritability and angry outbursts- these symptoms can be misunderstood as oppositional or defiant behavior
- Tantrums may be an effort to avoid the anxiety provoking stimulus
  - (AACAP Practice Parameters Anxiety Disorders 2007)
Some adolescents can discuss feeling anxious, scared, worried.

Other complain of stomachache, headache, fatigue, muscle tension, general pain, palpitations, syncope, dizziness, paresthesia, numbness, trembling, poor concentration, insomnia, urinary frequency, dry mouth.

Adolescents are usually able to discuss symptoms.

Children may struggle to describe the feeling of anxiety.

Frequent somatic complaints (headaches, chest pain, urinary frequency and stomach aches).

Some evidence to suggest a common influence in the nervous system for anxiety, generalized sensitivity and low pain threshold.

Medically unexplained pain referred to as functional somatic symptoms (FSS).

As the number of FSS symptoms and functional impairment increase so does the likelihood of anxiety and/or depression.

- One study found that patients who endorse symptoms of muscle pain, headache or stomach pain are 2.5-10 times to screen positively for panic disorder, GAD or MDD.
- Great Smoky Mountain study found that 70% of the girls complaining of headaches and stomachaches were also diagnosed with anxiety disorders.

Dillon-Naftolin E 2016.
Symptoms of Anxiety Disorders
Generalized Anxiety Disorder

- Unreasonable expectations about their own performance and excessively critical of themselves
- Perfectionist tendencies
- Need excessive reassurance
- Excessively self-conscious
- Worry about “adult” matters
- Persistent worry about negative consequences
  - (Connolly S, Suarez L 2016)

Symptoms of Anxiety Disorders
Social Anxiety Disorder

- Fear doing something “wrong” in social situations
  - Worry about scrutiny by others
  - Difficulty answering questions in class, reading aloud, initiating conversations, attending parties or other social events
  - Can exhibit crying, tantrums, freezing, clinging, shrinking or refusal to speak in social situations
  - Often shy or withdrawn
  - Often lack assertiveness, can have rigid posture and limited eye contact
  - Children may have restricted social skills, longer speech latency, few or no friends, limited involvement in peer activities
  - (Connolly S, Suarez L 2016)
Symptoms of Anxiety Separation Anxiety Disorder

- Significant distress when separated from caregiver
- Significant worry surrounding their health or family member’s health or location
- Worry that an event will occur that will lead to prolonged separation (getting lost)
- Refusal to go places
- Refusal to sleep alone
- Nightmares regarding separation
- Physical symptoms when separation is anticipated
  - (Connolly S, Suarez L 2016)

Screening

- The Screen for Child Anxiety Related Emotional Disorders (SCARED)
  - 41-item measure for ages 9-18 years
- Spence Children’s Anxiety Scale
  - Pre-school to adolescence
- Multidimensional Anxiety Scale for Children
  - Ages 8-19 years
    - Dillon-Naftolin 2016
Treatment of Anxiety

- Child and Parent Psychoeducation
- Exposure based Cognitive Behavioral Therapy
- Parental anxiety management strategies
- Parental skills training
  - (AACAP Practice Parameters - Anxiety Disorders 2007)
  - (Connolly S, Suarez L 2016)

Cognitive Behavioral Therapy

- Teach children to recognize unwanted symptoms of anxiety
  - Recognize cognitive processes associated with increase in anxiety
- Use these cues to trigger need to use anxiety management strategies
  - Training in behavioral relaxation
  - Performance-based practice opportunities
    - Kendall & Hedtke 2006
Pharmacological Treatment

- Selective Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)
  - Duloxetine- FDA approved for generalized anxiety disorder (GAD) in children and adolescents ages 7-17 years
    - Start at 30 mg
    - Max 120 mg/day

Pharmacological Treatments

- Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Fluoxetine- FDA approved to treat Obsessive Compulsive Disorder in children and adolescents ages 7-18 years
  - Fluvoxamine- FDA approved to treat Obsessive Compulsive Disorder in children and adolescents ages 8-18 years
  - Sertraline- FDA approved to treat Obsessive Compulsive Disorder in children and Adolescents ages 6-18 years
  - Clomipramine FDA approved to treat Obsessive Compulsive Disorder in children greater than 10 years of age
  - (Emslie G, Croarkin P 2016)
National Institute of Mental Health (NIMH) conducted a randomized, controlled trial of 488 children ages 7-17 years with a primary diagnosis of separation anxiety disorder, generalized anxiety disorder or social phobia.

4 groups:
- 14 sessions of CBT
- Sertraline up to 200 mg qday
- CBT + Sertraline
- Placebo

Administration of rating scales at baseline, 4, 8 and 12 weeks.

According to the CGI-I:
- CBT + Sertraline group rated as very much improved or much improved 80.7%
- CBT alone group was 59.7%
- Sertraline group was 54.9%
- Placebo group was 23.7%

Combined therapies were superior to both mono-therapies.
CBT vs SSRI

- Pediatric Anxiety Rating Scale- similar results
- CBT did not start to separate from placebo until week 8-12
- Sertraline arms separated from placebo at week 4
- NNT
  - 1.7 for combination therapy
  - 3.2 for sertraline alone
  - 2.8 for CBT alone
  - Walkup JT et al 2008

- Responders to the CAM study continued to attend 6 monthly booster sessions in their assigned study arm
- Those assigned to sertraline continued to take it
- These participants were re-evaluated at 24 and 36 weeks post randomization
- Those in the placebo arm were offered active CAMS treatment
  - If they did not respond by week 12 results were not included
CBT vs SSRI

- 80% of initial responders maintained or exhibited enhanced response at weeks 24 and 36
- Combined group continued to maintain superior results to the CBT and sertraline arms on some outcomes with attenuation over time
- CBT and sertraline group continued to remain indistinguishable over time
  - Piacentini J et al. 2014

References


References cont