Childhood OCD- “Hiccup of the brain” (J Rapoport)

JR Oesterheld, MD

Tufts University School of Medicine

Gayathri Tadepalli, MD

University of Cincinnati College of Medicine

Questions 1,2,3

Answer True or False

1. In children with OCD, insight into the OC behaviors is required.

2. It is not necessary to differentiate OC behaviors from normal developmental OC behaviors or normal rituals of childhood.

3. CBT is not effective in treatment of childhood OCD.

Questions 4, 5

4. Co-morbid diagnosis of OCD include all of the following except:
   - a. ADHD and ODD
   - b. Major depression and anxiety
   - c. Somatoform disorders
   - d. Motor tics

5. Criteria for PANDAS includes:
   - a. Motor and vocal tics
   - b. Obsessive and compulsive disorder of childhood onset
   - c. Tourette Disorder
   - d. Sudden onset of OCD after a streptococcal infection

Question 6

6-The following medications are used in the treatment of OCD, except:

A. Clomipramine

B. Fluoxetine

C. Desipramine

D. Fluvoxamine

Preview

- Differentiate OCD from normal childhood rituals
- DSM-IV criteria
- OCD symptoms
- OCD Instruments- especially CYBOCS
- OCD Co-morbidity
- Course of OCD
- CBT
- Pharmacotherapy
- POTS
- PANDAS

Teaching Points

- Youth are sometimes quite secretive about OCD symptoms
- Although clomipramine and SSRIs can be effective in treatment, in a recent POTS, CBT has been shown to be more effective, but in this trial the best treatment is both CBT and sertraline

Introduction

- Must differentiate normal developmental OC behaviors or normal rituals e.g., cracks in sidewalks (rituals related to belief in power of wishing (Evans et al 2002) and normal collecting behaviors, e.g., hrs sorting baseball cards
- Prevalence in community samples: teens 1-3.6% (Apter 1996)
- Must distinguish vernacular “obsessive” and “compulsive” from clinical syndrome

Introduction-2

- Boys have more severe or earlier onset: boys 9 years, have family member with TS or OCD; girls with onset later at 11 years (Swedo 1989, Leonard 1992)
  - Younger boys have more severe symptoms (Flament 1985). These boys present more with comorbidities, tics, and disruptive behavior disorders. Earlier onset, is associated with increased genetic loading with family history of tics (Lenane et al 1990, Pauls et al 1995)
  - Rates equalize in teens (Leonard 2006)

DSM-IV Criteria

Either obsessions or compulsions

Obsessions

- 1-recurrent and persistent thoughts, impulses, or images that are experienced as intrusive and inappropriate and that cause marked worry or distress
- 2-not simply excessive worries about real-life problems
- 3-attempts to ignore or suppress them or neutralize them with some other thought or action.
- 4-recognize they are a problem of ones own mind and not imposed from without (not children)

DSM-IV Criteria

Compulsions

- 1-repetitive behaviors (hand washing, ordering, checking or mental acts (praying, counting, repeating words) one is driven to perform
- 2-behaviors ward off distress or prevent dreaded situation(not children)

DSM-IV Criteria

- B-Is recognized as excessive or unreasonable (not children)
- C-More than 1 hr a day or interfere with normal routine
- D-Not part of another Axis 1 condition
- E-Not caused by a substance or general medical condition

Compulsions and Obsessions

- In general, compulsions relieve anxiety
- In children, generally they are not aware of any anxiety component or that the obsession are ego-dystonic or senseless

Etiology

- Evidence of genetic transmission- twin studies show genetic influences in the range of 45-65% (van Grootheest et al 2005)
- Higher rates of OCD seen in first degree relatives (Nestadt et al 2000)
- Areas of brain implicated
  - Basal ganglia
    - Increase size of caudate nuclei (Calabrese 1993)
    - Functional deficits in cortico-striato-thalamo- cortical circuit underlie OCD
    - Neurochemicals implicated
      - Serotonin decrease

Symptoms of Youth OCD

- Obsessive thoughts and washing- some time in 85%
- Repeating rituals in 50%:need to be perfect/ just so
- Checking in 46%, (e.g., doors, windows, appliances)
- Ordering, arranging and symmetry in 17%,
- Scrupulosity in 13%
- Takes 4-6 months before parents aware of sxs, secretiveness leads to long time before diagnosis (Leonard 1993)

- Symptoms related to developmental themes: In contrast to adult symptoms, kids, 1-contamination and 2-danger and separation associated with fear of harm to significant others or themselves (e.g. killing of parents or being kidnapped)
- In teens, sexual and religious obsessions especially pre-intimacy (Scahill et al 2003)
- Symptoms shift over time (Rettew et al 1992)

Diagnosis

- Multiple sources of information: children tend to underreport (Stewart et al 2005)
- Estimate the extent of impairment-remember OC-behaviors can be part of MR or PDDs
- Developmental medical and family history needed
- No pathognomonic lab findings

Differential Diagnosis of OCD (Leonard et al 2006)

- Depression and Anxiety disorders
- Eating disorders
- Tic disorders
- Body dysmorphic disorder

Instruments-childhood OCD (Merlo et al 2005)

- Semi structured interviews (e.g., Anxiety Disorders Interview for Children -clinician administered with parents and children interviewed separately-45-60 mins to administer or K-SADS with one of five subscales
- Child's Leyton Obsessional Inventory: with cards sorted 3 times for type, resistance and interference (Berg 1988)
- Drug sensitive Scales-C-YBOCS, NIMH OC scale (Goodman 1992)

CYBOCs

- Checklist of symptoms and 10 item clinician-driven questionnaire with 4 degrees of severity- 2 subscales Obsessions (20 points) and Compulsions (20 points)= 40 points, integrate parent, child and clinician observations
- Total 0-7 subclinical
- Total 8-15 mild *10=remission
- Total 16-23 moderate *16= entry
- Total 24-31 severe
- Total 32-40 extreme
- Good interrater reliability (Yucclen et al 2006)

Co-morbidity of childhood OCD

- Sole diagnosis (26%)
- Major depression (26%)
- Anxiety disorders: simple phobia (17%), SAD (7%),Over anxious disorder (16%)
- Motor tics (30%) may have younger age of onset
- Reading and language delays (24%)
- ODD (11%), more in preadolescent boys
- ADHD (10%)--but 30% in preadolescent boys (Swedo 1989)

Youth with OCD v OCD+ tics

- OCD+tics have higher rates of symmetry, just so, sensory (touching, rubbing) staring, blinking, also more familial, more common in boys and in early onset
- OCD with no tics have more contamination and cleaning sxs

(Holzer et al 1994, Leckman et al 199)

ADHD+OCD

- Impact of ADHD is on compromised school performance is considerable (Geller et al 2003)
- Concentrating on school and doing homework common problems (Piacentini et al 2003)
- More problems in social functioning, school and depression (Sukhodolsky et al 2005)
- In a survey of youth with OCD, 25% patients have co-morbid ADHD (Masi et al 2006)
- ADHD+ OCD was significantly associated with a higher rate of males, an earlier onset of OCD, a greater psychosocial impairment, and a heavier co-morbidity:bipolar disorder, tic disorder, and oppositional defiant disorder/conduct disorder (Masi et al 2006),

  with tic disorder precedes OCD (Leonard 2006)

Course of Pediatric OCD

- When reviewing history, look for micro episodes early on
- Usually insidious onset
- Can be a waxing and waning course

Results of OCD symptoms

- Academic difficulties
- Social problems
- Difficulties with parents/sibling

Family accommodation in OCD

- Family involvement in rituals related to severity of OCD, externalizing disease and parental OCD sxs
- If parents try to do response prevention without the children having a toolkit, they may spiral into more conflict (Piacentini 1999, March 2003)

Meta-analysis of long term outcome of Childhood OCD(Steward 2003)

Is pediatric OCD a separate and distinct disorder?

- N=16 samples of kids, n=521: follow-up 1-15 yrs
- Age of onset 10, mostly male, very co-morbid, short follow up
- Pooled date shows 41% had full OCD at follow-up, 60% full or subthreshold OCD
- Predictors of full OCD= earlier onset, duration of OCD at baseline and hospitalization
- Non-predictors=gender, yr of

FDA approval for drugs

- Adults-clomipramine, fluoxetine, fluvoxamine, paroxetine, sertraline
- Youth- clomipramine (10 yr and older), fluoxetine (8 yrs and older), fluvoxamine (8 yrs and older), sertraline (6 yrs and older)
- Need 10-12 weeks at highest tolerated doses (no evidence that super-doses needed in youth)
- In practice, all SSRIs used

Common side effects of SSRIs

- Less than 13% dropouts due to side effects
- Sedation, GI, insomnia, anorexia, tremor, sexual side effects and activation (March 1998, Riddle et al 2001)

Black Box warning

- Recent addition of Black Box warning for suicidality for all antidepressants in youth
- Recent review of sertraline in OCD studies (n=4) shows NNT and NNH overwhelming in favor of treatment (March 2006)

Childhood OCD-Medication-Meta-analysis

- Meta-analysis of all DBPC medication trials in pediatric OCD including paroxetine (Geller et al 2003)
- 12 studies met criteria for inclusion with 1044 children included and 8-12 weeks of treatment
- Overall ES of 0.46 (modest effect)--- end up with continuing impairment despite some improvement
- Clomipramine superior to each SSRI (which were indistinguishable from each other)

Take home (Reinblatt and Walkup 2005)

- All SSRIs appear equally effective
- Choice made on side effects, pharmacokinetic profiles and DDIs
- Check for sexual side effects and check growth
- Go slow as titrate upward
- 12 mo of treatment better than 6 mo

Treatment Resistant OCD in Youth (Reinblatt and Walkup 2005)

- If partial response, add CBT
- Switch SSRIs
- Augmentation, esp risperidone with schizotypy and tics
- Augmentation with CMI, buspirone, Li, pindolol, another SSRI or SNRI, clonazepam
- SSRI and CMI
- IV CMI and psychosurgery

CMI

- First medication to be studied for OCD
- 3 studies support efficacy:
  - Flament et al 1985, 10wk DB cross-over of 23 youth 3mg/kg
  - DeVeaugh-Geis et al 1992 led to FDA approval
  - Leonard et al 1989 DB crossover between CMI 93-5mg/kg/dy and DMI

CMI

- Ask about sudden death in first-degree relatives
- In youth, CBC, LFTs, creatinine, EKG, BP and HR
- Start at 25mg and gradually increase by 25 mg each 10 days-2 weeks, get EKGs and at least one plasma level of CMI and desmethylCMI before next level and aim for 3mg/kg/day and not higher than 5mg/kg/day.

- Watch for anticholinergic, seizures, antihistaminic bld pressure and heart rate changes

CMI metabolism

CYP2C9,19,3A (DCMI) CYP2D6

- CMI→ desmethylCMI → OHmetabolites

SSRI added to CMI

- CMI is serotonergic; desmethylCMI (DCMI) is active metabolite and it is noradrenergic
- Usual ratio active metabolite= DCMI/CMI=2.2-2.8
- If you use paroxetine, fluoxetine-> increased DCMI relative to CMI because block hydroxylation with less CYP2D6 inhibition with sertraline
- If you use citalopram- not a significant DDI
- If you use fluvoxamine--- because it is relatively modest inhibitor of CYP2D6 while potent inhibitors of other sites of CMI->DCMI: increased CMI with increased CMI relative to DCMI: need tiny amounts of CMI, start with 10 mg tid

How successful are we treating kids with OCD

- The CY-BOCS not extremely sensitive to change at highest severity
- 25% decrease=5 pts
- 32% decrease=8.5 pts (fluvoxamine study, Hollander et al 2003)
- A 25% or 35% decrease is generally taken as efficacy and a score of 10 as full remission

How successful are we treating youth with OCD with medication?

- Most pts enter with 24 and 24-8=16 (which still makes them moderate severity) and therefore a 65-75% response rate of those treated will yield a moderately symptomatic successfully treated group of patients
- 47% of children achieved a full remission, and an additional 25% achieved a partial remission on paroxetine (Wagner 2003)

Co-morbidity effects outcome of medication intervention

- Trial of paroxetine and OCD: the response rates in patients with co-morbid ADHD, tic disorder, or ODD with response rates of 56%, 53%, and 39% v. 71% overall (Geller et al 2003)

Childhood OCD-CBT

- Hierarchy-based Exposure and Response Prevention (March 1994, Scahill 1996, Franklin 1998)- 14 sessions over 12 wks with toolkit approach, self-monitoring, mindfulness (watch the Obsessions or Compulsions doing there own thing, not belong to me)- use of "fear" thermometer
- Imaginal exposure for obsessions - (in vitro)
- Habit reversal for "just-so" phenomena
- Cognitive restructuring for negative thoughts (bad thought leads to catastrophic results)
- Self observation, extinction, operant conditioning, and modeling have been used in adolescence. Behavioral rewards
- Flooding, graded exposure, and response prevention (March et al 1994)
- Family and group forms of treatment which are equally effective (Barrett et al 2004)
- Underutilized technique (Lewin et al 2005)

POTS- The Pediatric OCD Treatment Study

- 12 week 4 arms: sertraline alone, sertraline +CBT, CBT alone and placebo alone n=112
- Randomized parallel groups
- Entry criteria CYBOCS=16: mean of 24.6 with only ADHD meds allowed
- Sertraline-fixed flexible upward titration from 25-> 200 mg/d over 6 wks
- Outcome measure of remission CYBOCS + or < than 10

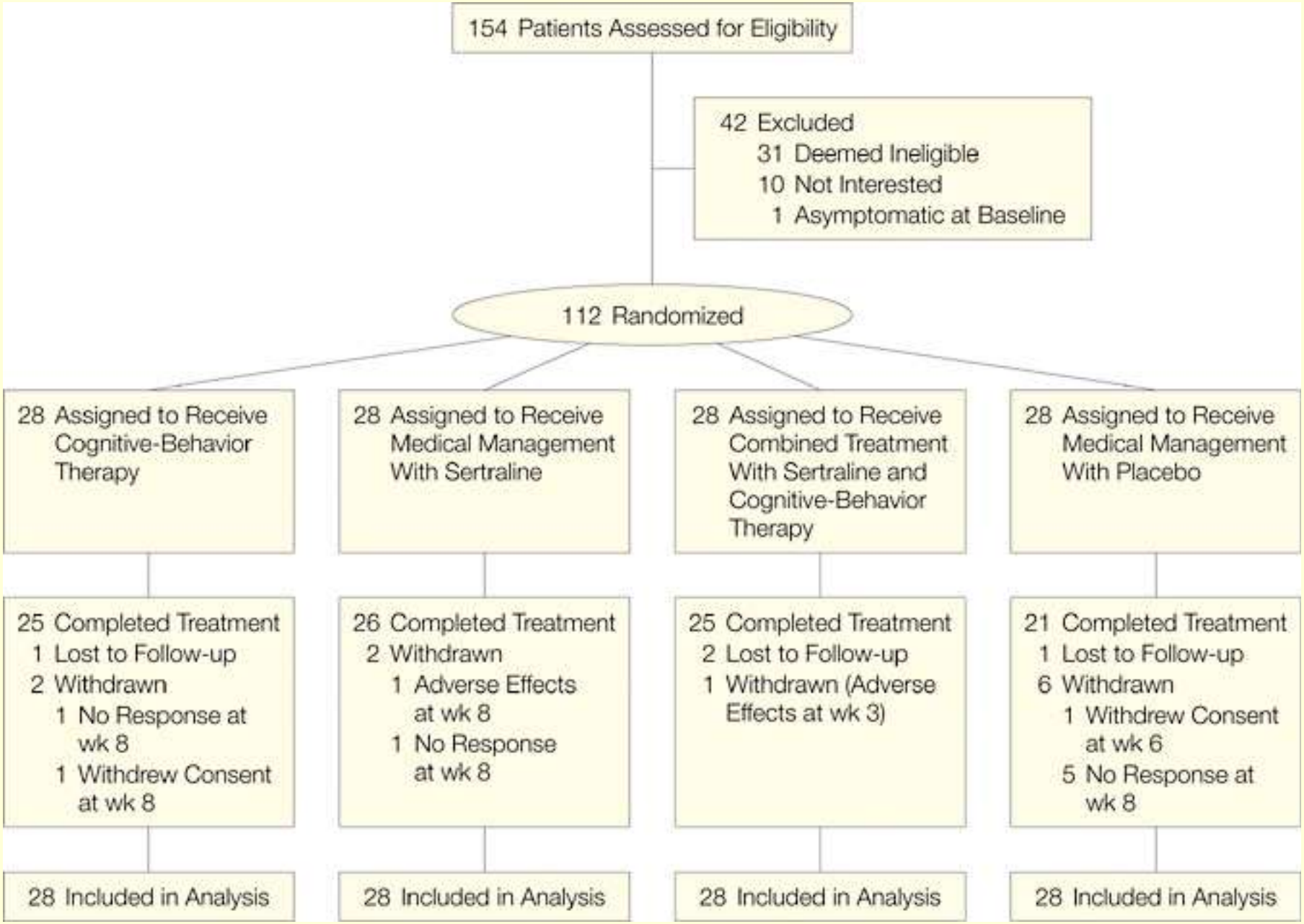
154 Patients Assessed for Eligibility
42 Excluded
31 Deemed Ineligible
10 Not Interested
1 Asymptomatic at Baseline
112 Randomized
28 Assigned to Receive Cognitive-Behavior Therapy
28 Assigned to Receive Medical Management With Sertraline
28 Assigned to Receive Combined Treatment With Sertraline and Cognitive-Behavior Therapy
28 Assigned to Receive Medical Management With Placebo
25 Completed Treatment
1 Lost to Follow-up
2 Withdrawn
1 No Response at wk 8
1 Withdrew Consent at wk 8
26 Completed Treatment
2 Withdrawn
1 Adverse Effects at wk 8
1 No Response at wk 8
25 Completed Treatment
2 Lost to Follow-up
1 Withdrawn (Adverse Effects at wk 3)
21 Completed Treatment
1 Lost to Follow-up
6 Withdrawn
1 Withdrew Consent at wk 6
5 No Response at wk 8
28 Included in Analysis
28 Included in Analysis
28 Included in Analysis
28 Included in Analysis

Table 2. Mean CYBOCS Score, by Treatment Group and Week (n = 28)

Week	CY-BOCS Score, Unadjusted Mean (SD)*			
	Cognitive-Behavior Therapy	Sertraline	Combined Treatment	Placebo
Baseline	26 (4.6)	23.5 (4.7)	23.8 (3.0)	25.2 (3.3)
4	20.6 (6.5)	18.5 (7.5)	18.1 (6.8)	22.4 (5.4)
8	18.1 (7.9)	16.9 (8.2)	14.4 (8.1)	22.5 (4.4)
12	14.0 (9.5)	16.5 (9.1)	11.2 (8.6)	21.5 (5.4)

Abbreviation: CY-BOCS, Children's Yale-Brown Obsessive-Compulsive Scale.
*Last observation carried forward used to impute missing values.

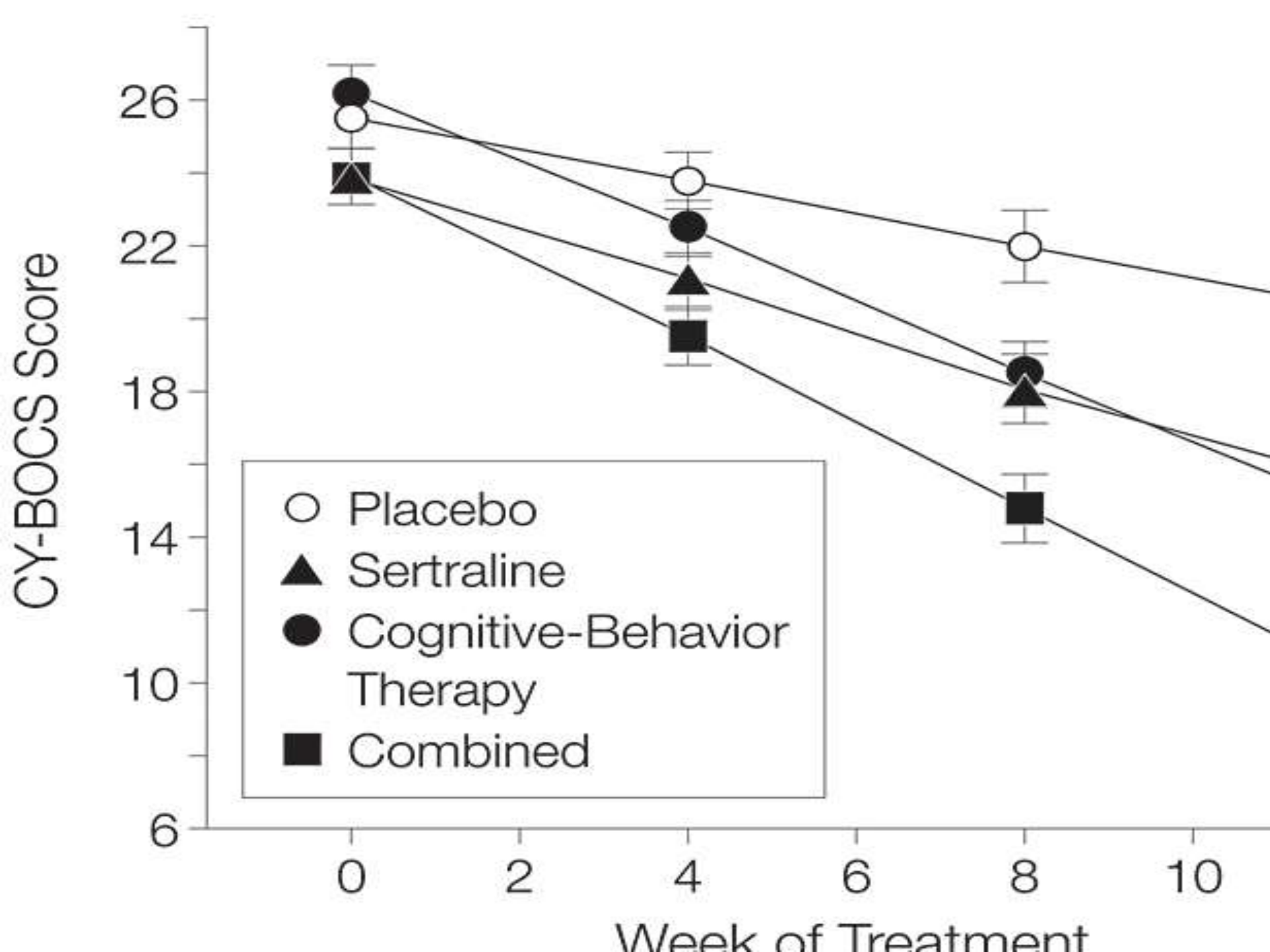
CY-BOCS Score
26
22
18
14
10
6
0
2
4
6
8
10
Week of Treatment
Placebo
Sertraline
Cognitive-Behavior Therapy
Combined

Table 3. Treatment-Emergent Adverse Events in Medication-Treated Patients*

Adverse Event	No. (%)		
	Sertraline (n = 28)	Combined Treatment (n = 28)	Placebo (n = 28)
Decreased appetite	5 (18)	4 (14)	0
Diarrhea	6 (21)	0	1 (4)
Enuresis	2 (7)	2 (7)	0
Motor overactivity	1 (4)	6 (21)	1 (4)
Nausea	7 (25)	5 (18)	1 (4)
Stomachache	8 (29)	4 (14)	2 (7)

*Data are for events occurring in at least 5% of sertraline-treated patients and with an incidence of at least 2 times that seen in placebo-treated patients in either the sertraline-alone or the combined-treatment group. Medication-related adverse events were not recorded for patients treated with cognitive-behavior therapy alone.

Total of 7 sert pts had behavioral activation

POTS Outcome

- Mean daily dose CBT+sertraline=133 mg and sertraline alone= 176 mg
- Effect size of CBT=0.97 and sert alone 0.67 and combined treatment 1.4
- Remission rate (CYBOCS=10) for combined 53.6%; CBT alone 39.3%; sertraline 21.4% and placebo 3.6%
- Conclusion: start with either CBT or CBT+ an SSRI

Sydenhams Chorea

- Concept of molecular mimicry
- Group A beta hemolytic streptococcal (GABHS) common in skin and throat-> strep peptides-> B lymphocyte response
- Only specific serotypes (e.g., class 1 strain)-> rheumatic fever
- Only susceptible hosts acquire rheumatic fever (Rh F) (autosomal recessive with limited penetrance-about 3% population)
- Sydenhams chorea =neuropsychiatric manifestations of Rh F where antigens cross-over and coat basal ganglia
- Can there be a form without chorea? Controversial entity=pediatric autoimmune neuropsychiatric disorders associated with streptococcus (PANDAS)

(Sweedo et al 1998)

Table 1. The five clinical criteria of the PANDAS subgroup

(1) Presence of obsessive–compulsive disorder and/or tic disorder (meeting DSM-IV criteria).
(2) Prepubertal symptom onset.
(3) Episodic course characterized by acute, severe onset and dramatic symptom exacerbations.
(4) Neurological abnormalities (e.g. choreiform movements) present during symptom exacerbations.
(5) Temporal relationship between GABHS infections and symptom exacerbations.

PANDAS, pediatric autoimmune disorders associated with streptococcal infections; GABHS, Group A β-hemolytic streptococcus.

Table 2. Current treatment guidelines for children in the PANDAS subgroup

Sweedo et al 1998

(1) Assessment for GABHS infection by 48 h culture in a young child with abrupt onset OCD and/or tic disorder. A positive culture should be treated promptly with a standard 10-day course of antibiotics.

(2) If the abrupt onset of the OCD and/or tic symptoms occurred at least 4–6 weeks prior to the visit, then a blood test for antistreptococcal antibody titers (ASO and anti-Dnase B) should be done (along with a 48 h throat culture) to attempt to document a preceding GABHS infection. Antibiotic treatment of elevated titers is not appropriate in the absence of a positive GABHS culture.

(3) Prospective assessment for GABHS infections in a child with an episodic course of symptoms should be done. Throat cultures for GABHS should be obtained at the time of relapse of OCD and/or tic symptoms or antistreptococcal titers should be drawn 4–6 weeks later.

(4) The decision to begin antibiotic prophylaxis should be based on clinical indications in each individual child after obtaining evidence that they are in the PANDAS subgroup. The prompt diagnosis and adequate treatment of GABHS infections in this subgroup of patients is clearly indicated.

(5) Treatment with immunomodulatory therapies (like plasma exchange and intravenous immunoglobulin) should be reserved for children with acute, severe symptoms who fit the PANDAS designation. These treatments carry significant risks and should be used only for the most severely affected patients.

Common presentations to providers (Murphy and Pichichero 2002)

- Separation anxiety
- Worry
- Urinary frequency

Kurlan and Kaplan 2004 refutation of PANDAS hypothesis

- (1)level of severity of tics and OCD symptoms not defined
- (2)age of onset the same as garden variety TS and OCD. Further, there has been a case reported of post pubertal individual
- (3)abrupt onset not clinically specific since tics may not be identified gradually e.g.,at least 2 studies show 38% or 50% of kids with TS described as acute onset with no dx PANDAS
- (4) does presence of choreiform movement suggest dx is Sydenham's
- (5) GABHS as causative agent hard to show since a-carrier states,b- infection worsens any tics. There is imprecision of time course of PANDAS

Kurlan and Kaplan 2004 cont

Clinical implications

- Only get strep culture when there are clinical signs and sx (otherwise carrier state confusing)
- Antineuronal antibodies and D8/17 not reliable indicators
- Do not use prophylactic antibiotics and do not use plasma exchange and IV immunoglobulin

mAB D8/17 immunologic marker

- Believed that elevated D8/17 on B lymphocytes is a susceptibility marker for Rh F
- Found elevated in pts with PANDAS both OCD and tics (Sweedo 1997, Murphy 1997)
- Recent studies failed to provide support for the generalized use of D8/17 as a marker of susceptibility to tics and OCD in a community sample or in Acute Rh F. (Morer 2005)

Questions 1,2,3

Answer True or False

1. In children with OCD, insight into the OC behaviors is required.

2. It is not necessary to differentiate OC behaviors from normal developmental OC behaviors or normal rituals of childhood.

3. CBT is not effective in treatment of childhood OCD.

Questions 4, 5

4. Co-morbid diagnosis of OCD include all of the following except:
   - a. ADHD and ODD
   - b. Major depression and anxiety
   - c. Somatoform disorders
   - d. Motor tics
5. Criteria for PANDAS includes:
   - a. Motor and vocal tics
   - b. Obsessive and compulsive disorder of childhood onset
   - c. Tourette Disorder
   - d. Sudden onset of OCD after a streptococcal infection

Question 6

6-The following medications are used in the treatment of OCD, except:

- A. Clomipramine
- B. Fluoxetine
- C. Desipramine
- D. Fluvoxamine

Answers

- 1-F
- 2-F
- 3-F
- 4-C
- 5-D
- 6-C