

Kids and Antidepressants: Do They Play Nice Together?

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Objectives

- Distinguish between adult, adolescent, and childhood depression
- Outline suicide data in order to describe the impact of using antidepressants in children and adolescents
- Summarize clinical trial data for antidepressants used to treat child and adolescent depression

Prevalence

- 2.5% of US children
- 8.3% of US adolescents (1/20)
- Approximately 2.6 million youth age 6-17yo
- Over 10 million, roughly 7% of antidepressant prescriptions are now written for children

Am Acad Child Adolescent Psychiatry 1996;35(11):1427-39
CMAJ 2004;171(8):837-838
JAMA 2004;292(6):807-820

Depression Comparison

DSM_IV Symptoms of Major Depressive Disorder	As Frequently Seen in Youth
Depressed mood most of the day	Irritable or cranky mood; Preoccupation with nihilistic song lyrics
Decreased interest/enjoyment in once-favorite activities	Loss if interest in sports, video games, and activities with friends
Significant weight gain/loss	Failure to gain weight as normally expected; anorexia or bulimia; frequent complaints of physical illness
Insomnia or hypersomnia	Excessive late-night TV; refusal to wake for school in the morning
Psychomotor agitation/retardation	Talk of running away from home, or efforts to do so
Fatigue or loss of energy	Persistent boredom
Low self-esteem; feelings of guilt	Oppositional and/or negative behavior
Decreased ability to concentrate; indecisive	Poor performance in school; frequent absences
Recurrent suicidal ideation or behavior	Recurrent suicidal ideation or behavior

Child Rating Scales

- Children's Depression Rating Scale, Revised (CDRS-R)
 - 17 item scale
- Reynolds Adolescent Depression Scale (RADS)
 - 30 item scale
 - Self rated
- Suicidal Ideation Questionnaire-Junior High School Version (SIQ-Jr)
 - 30 item scale, grades 10,11,12
 - 15 item scale, grades 7,8,9

Treatment Options

- Selective Serotonin Reuptake Inhibitors (SSRI)
- Tricyclic (TCA)
- Venlafaxine
- Bupropion
- Nefazodone
- Mirtazapine
- Monoamine Oxidase Inhibitors (MAOI)
- Duloxetine

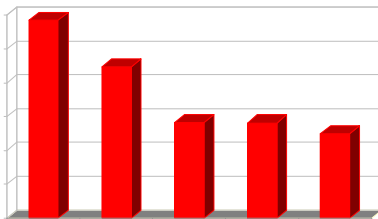
FDA Approved

- Fluoxetine
 - Depression, ages 7-17yo
 - OCD, ages 7-17yo
- Sertraline
 - OCD, ages 6yo and older
- Fluvoxamine
 - OCD, ages 8yo and older
- Phenelazine
 - Depression non-endogenous, 16yo and older

FDA Approved

- Amitriptyline
 - Depression, 12yo and older
- Clomipramine
 - OCD, 10yo and older
- Doxepin
 - Depression, 12yo and older
- Imipramine
 - Enuresis, 6yo and older

Top 5 Selected Antidepressants Dispensed* to 1-17 Year Olds, 2002



February 2, 2004, meeting of the Psychopharmacologic Advisory Committee and the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee. Drug Utilization for Selected Antidepressants Among Children & Adolescents in the U.S., Rigoni G

Response to Antidepressants

First Few Days	1-3 weeks	2-4 weeks (up to 8 weeks)
<ul style="list-style-type: none"> ■ Increased agitation/anxiety ■ Improvement in insomnia, sleep ■ Appetite improves 	<ul style="list-style-type: none"> ■ Increased activity, sex drive ■ Self-care habits improve ■ Concentration and memory normalize ■ Sleeping and eating patterns normalize 	<ul style="list-style-type: none"> ■ Relief of depressive mood ■ Begin to experience pleasure ■ Feel less hopeless ■ Thoughts of suicide subside

Psychotropics Made Simple. 1998:18.

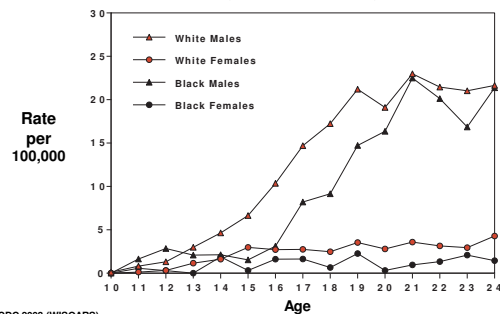
Suicide

- Suicidal Ideation Questionnaire-Junior High School Version (SIQ-Jr)
- Suicide attempted by up to 35%
- Depression is a serious medical illness and potentially lethal
- 17% of adolescents think about suicide per year
- 12% females and 5% males attempt suicide per year
- Every 1% increase in antidepressant prescriptions there is a 23% decrease in adolescent suicides per 100,000

J Affect Disorders 2003;76(1-3):211-221.
Arch Gen Psychiatry 2003;60:978-982.

Suicide Rates During Adolescence

— UNITED STATES, AGES 10-24, 2001 —



CDC 2003 (WISQARS)
FDA Presentation by Dr. David Shaffer, Columbia University

Suicide Risk Factors

- Previous suicide attempts
- Close family member who has committed suicide
- Past psychiatric hospitalization
- Recent losses
- Social isolation
- Drug or alcohol abuse
- Exposure to violence in the home or the social environment
- Handguns in the home

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Warning Signs

- Suicidal talk
- Preoccupation with death and dying
- Signs of depression
- Behavioral changes
- Giving away special possessions
- Making arrangements for unfinished business
- Difficulty with appetite and sleep
- Taking excessive risks
- Increased drug use
- Loss of interest in usual activities

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Selective Serotonin Reuptake Inhibitors In Childhood Depression: Systematic Review Of Published Versus Unpublished Data

Whittington CJ, et al. Lancet 2004;363:1341-45

Outcomes

- Efficacy outcomes
 - Remission and response
 - Mean depression level
- Safety outcomes
 - Serious adverse events
 - Discontinuation attributable to an adverse event

Results Fluoxetine

- More likely than placebo to bring about remission by the end of 7-8 weeks (NNT 6)
- More likely to observe a clinically meaningful treatment response (NNT 5)
- Small reduction in CDRS-R, standardized mean difference -0.43 (CI -0.65 to -0.20)
- Fewer serious adverse events (<1% vs 3.6%)
- No increased risk of suicidal behavior (3.6% vs 3.8%)
- No increased risk of attempted suicide (2.4% vs 1.9%)

Risk/Benefit Profile: Favorable

Results

Paroxetine

- More likely than placebo to bring about remission by the end of 8 weeks (NNT 7)
- Similar in treatment response (38.1% vs 43.3%)
- No reduction in HAM-D, mean standardized difference -0.21 (CI -0.51 to 0.08)
- Greater risk of adverse events (12% vs 4%)
- Possible increased risk of suicidal behavior (3.7% vs 2.5%)

Risk/Benefit Profile: Unfavorable

Results

Sertraline

- More likely than placebo to bring about response by the end of 10 weeks (NNT 10)
- Small reduction in depressive symptom standardized mean difference -0.28 (CI -0.49 to -0.08)
- No difference in remission (48.1% vs 50.6%)
- Possible increase in adverse events (3.7% vs 3.3%) when rate of discontinuation is taken into account (9.0% vs 2.7%)
- Possible increased risk of suicidal behavior (2.6% vs 1.1%)

Risk/Benefit Profile: Unfavorable

Results

Citalopram

- Efficacy data was limited
- At end of 8-12 weeks, little reduction in CDRS-R, standardized mean difference -0.34 (CI -0.64 to -0.04)
- Small increase in treatment emergent adverse events (79.0% vs 70.1%)
- Increased risk of suicidal behavior (7.1% vs 3.6%)

Risk/Benefit Profile: Unfavorable

Results

Venlafaxine

- Efficacy data was limited
- At end of 6 weeks, published data shows no reduction in CDRS, standardized mean difference 0.25 (CI -0.44 to 0.93)
- At the end of 8 weeks, unpublished data also shows little reduction in CDRS, standardized mean difference -0.29 (CI -0.5 to -0.07)
- Increased risk of suicidal behavior (7.7% vs 0.6%)

Risk/Benefit Profile: Unfavorable

Conclusions

- Whittington meta-analysis
 - Fluoxetine, favorable results
 - Paroxetine, unfavorable results
 - Sertraline, unfavorable results
 - Citalopram, unfavorable results
 - Venlafaxine, unfavorable results

Lancet 2004;363:1341-45.

FDA Warning

- October 15, 2004, black box warning
- "increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) or other psychiatric disorders
- At least weekly face-to-face contact during the first 4 wks of tx, then every other wk for 4 wks, then at 12 wks, and as clinically indicated
- Additional contact by telephone may be appropriate between face-to-face visits
- Adults should be observed similarly

Consequences of Black Box

- Limit access to necessary, appropriate, and effective treatment
- Increased patient counseling
- Increased psychotherapy
- Increased patient care contact

Consequences of Depression

- Problems
 - School
 - At home
 - Friends
- Four of ten will have a second episode within two years
- Substance abuse
- Over half will eventually attempt suicide

J Am Acad Child Adolesc Psychiatry 1994;33(6):809-818
British Journal of Psychiatry 2001;179:218-223

Conclusion

- Activation
 - Term used to describe anxiety or agitation with initiating an antidepressant
- Using antidepressants has decreased suicide rates in children and adolescents
- Antidepressant use should be taken seriously by the public and medical professionals
- Anyone looking for clear and simple answers here will be frustrated
- Accurate diagnosis and careful treatment will save many more lives than might be lost through the use of these drugs

Child and Adolescent Depression Questions???



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