Outreach Education

ADHD: Putting Evidence Into Practice©

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February 13, 2009

Program Handouts

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ADHD: Putting Evidence Into Practice

Patti Varley, MN, ARNP, BC
Friday Feb. 13, 2009
Seattle Children’s

Genetic Study Summary

- Adult relatives of children with ADHD have elevated rates of ADHD
- Child relatives of adults with ADHD have elevated rates of ADHD
- Molecular genetic findings are similar for children and adults


MTA Study

- 14-month, multicenter, randomized, controlled study
- 579 children, aged 7 to 10 years; ADHD/Combined
- 4 treatment groups
  - Medication management (titration followed by monthly visits)
  - Intensive behavior treatment (parent, school, and child components, with therapist involvement gradually reduced over time)
  - Combined treatment: medication management and behavioral treatment
  - Standard community care

MTA Study: Comorbid Disorders

- Oppositional defiant disorder – 39.9%
- Anxiety disorder – 33.5%
- Conduct disorder – 14.3%
- Tic disorder – 10.9%
- Affective disorder – 3.8%
- Mania/hypomania – 2.5%

MTA Cooperative Group. Arch Gen Psychiatry 1999;56:1073-1086

MTA Results

- All groups improved
- Combined treatment and medication management were significantly better than behavioral treatment and community care
- Combined treatment and medication management did not differ in any direct comparisons
MTA Results

- Combined treatment was superior to behavioral treatment and/or community care; medication management was not.
- Combined treatment and medication management were better than community care; behavioral treatment was not.
- Mean total methylphenidate daily dose at treatment end point:
  - Medication management: 37.7 mg/d in 3 doses
  - Combined treatment: 31.2 mg/d in 3 doses
  - Community care: 22.6 mg/d in 2 doses

MTA Conclusions

- Medication management was superior to behavioral treatment and routine community care for ADHD symptoms.
- Combined treatment was equal to medication management for core ADHD symptoms and may have modest advantages for non-ADHD symptoms and positive functioning outcomes.

MTA: Parent and Teacher Satisfaction With Treatment

- Despite greater symptom reduction in the medication management group than in the behavioral treatment group, the satisfaction ratings by parents and teachers were higher for the behavioral treatment group.
- Parent evaluations of the relative effectiveness of the 4 different treatments in reducing “referring problems” (vs. symptoms) were equivalent across the 4 treatment groups.

MTA: Percent “Normalized”* at 14-Month End Point

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent Normalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>88</td>
</tr>
<tr>
<td>Combined</td>
<td>68</td>
</tr>
<tr>
<td>Medication</td>
<td>56</td>
</tr>
<tr>
<td>Behavioral</td>
<td>34</td>
</tr>
<tr>
<td>Community Care</td>
<td>25</td>
</tr>
</tbody>
</table>

MTA: 24-Month Follow-Up

- Patients (N = 521) were allowed to change treatment groups after the 14-month treatment phase.
- Four naturalistic subgroups emerged based on medication treatment:
  - Med/Med
  - Med/No Med
  - No Med/Med
  - No Med/No Med
- Data on behavioral treatment were not collected.

MTA: 24-Month Results

- Groups with greatest improvement at end of treatment phase (combined and medication management) deteriorated, but the other 2 groups (behavioral and community care) did not.
- Changes in medication use mediated 14- to 24-month changes in ADHD symptom ratings:
  - Med/No Med showed largest deterioration
  - Med/Med and No Med/No Med showed modest deterioration
  - No Med/No Med showed improvement.
MTA: 24-Month Results

- No significant differences in 14- to 24-month growth rates among the groups
- Changes in medication use mediated growth effects
  - Med/Med showed reduced height gain (5.69 cm)
  - No Med/No Med actually grew faster than predicted by population norms (6.16 cm)


MTA: 24-Month Conclusions

- Continued use of stimulant medication was associated with maintenance of effectiveness but continued mild growth suppression*

*MTA 36-month follow-up data are currently in press.

The follow-up of the MTA sample will continue as the participating children go through adolescence and enter adulthood.

PATS – Greenhill, et al

- Preschoolers with ADHD RCT with methylphenidate

"The Preschool ADHD Treatment Study, or PATS, provides us with the best information to date about treating very young children diagnosed with ADHD," said NIMH Director Thomas R. Insel, MD. "The results show that preschoolers may benefit from low doses of medication when it is closely monitored, but the positive effects are less evident and side-effects are somewhat greater than previous reports in older children."

PATS Results

- Largest Study To-Date
- Positive Response
- Lower Doses
- Higher Side Effects
FDA Warning
(Not BLACKBOX)
August 2006
Followed Advisory Panel 2-9-2006 recommendations
- 8-7 vote for the FDA to display a BLACK BOX warning about possible cardiovascular risks though - "We didn’t find the sudden death data very persuasive"
- 15-0 for FDA to create "Medication Guides" explaining possible risk
  - Possible Cardiovascular risks
  - Psychiatric side effects, including psychosis

EKG Monitoring
- Recommendation to routinely do baseline EKG made 5-6-08 by the AHA
- Changed shortly thereafter to a class IIB recommendation, by clinician choice

American Heart Association 5/2008
Now a Class IIa recommendation that children with ADHD get a careful cardiac evaluation, including an EKG before starting stimulant, which means it is reasonable to consider an EKG, but at the physician's judgment. It is not Mandatory.

ADHD Motor Vehicle Driving
Study of 16 to 22 year olds
-35 with ADHD (not on medication)
-36 controls
Significantly more drivers with ADHD
- drove without a license
- had licenses revoked or suspended
- had multiple crashes (2+)
- had multiple traffic citations (3+), especially for speeding
Subgroups of ADHD with co morbid oppositional defiant or conduct disorder were at highest risk

ADHD and Psychoactive Substance Use Disorders (PSUD)
- 4-year follow-up of a clinically referred sample of boys 6 to 17 years old at baseline (ADHD N=140; control n-120)
  - no difference in the rate of alcohol or drug abuse between groups (15% vs. 15%), mean age-early adolescence
  - Risk for PSUD mediated by conduct disorder and bipolar disorder with or without ADHD

Trials Suggest Improved Driving on Methylphenidate
**ADHD Pharmacotherapy and Substance Abuse**

**Overall Rate of PSUD**

<table>
<thead>
<tr>
<th>Percent of Group</th>
<th>Unmedicated ADHD (N=45)</th>
<th>Medicated ADHD (N=117)</th>
<th>Control (N=344)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>11%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>

Wilen, 2003

- Adults with ADHD (N=139) vs. controls (N=268)
  - Significantly greater lifetime rate of PSUD than controls (55% vs. 27%)
  - Age of onset of PSUD in subjects with ADHD averaged 3 years earlier than controls (late adolescence/early adulthood)
  - ADHD was a significant risk factor independent of co-morbid diagnoses

Biederman et al., JAACAP 1997-36:21
Biederman et al., BioPsychiatry 1998:44:269

**Medication for ADHD**

I. Primary - Stimulants
   a) Methylphenidate (Ritalin**, Metadate ER**, Concerta**, Methylin**)
   b) Dextroamphetamine (Dexedrine***, Dextrostat***)
   c) Amphetamine/Dextroamphetamine (Adderall***)
   d) Dexmethylphenidate (Focalin)**
   e) Vyvanse**

II. Secondary
   a) Atomoxetine (Strattera)
   b) Alpha-2 Agonists
      1) Clonidine (Catapres*)
      2) Guanfacine (Tenex*)
   c) Other Antidepressants
      1) Bupropion (Wellbutrin*)
      2) Venlafaxine (Effexor*)
   d) Tricyclic Antidepressants
      1) Imipramine (Tofranil*)
      2) Nortriptyline (Pamelor*)
      3) Desipramine (Norpramin*)
   e) Stimulant
      1) Pemoline (Cylert)** (taken off the market)
   f) Other
      1) Modafinil (Provigil*)

* non FDA approved to Rx ADHD
** FDA approval to Rx ADHD for children 6 and over
*** FDA approval to Rx ADHD for children 3 and over

**Comparison Studies Have All Been Industry Sponsored**

- Have to consider results in that context

**Recent Trials Indicate Benefit of Combining Stimulant and Atomoxetine**

- Should be reserved for cases with failure to respond to single agents
### Long-acting Oral MPH Medications

<table>
<thead>
<tr>
<th>Product</th>
<th>Concerta®</th>
<th>Metadate® CD</th>
<th>SODAS™</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formulation</strong></td>
<td>OROS®</td>
<td>Diffucaps®</td>
<td>SODASTM</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>22%</td>
<td>70%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Immediate Release</strong></td>
<td>10 mg/15 mg/20 mg</td>
<td>6 mg</td>
<td>1 mg/15 mg/20 mg</td>
</tr>
<tr>
<td><strong>Sustained Release</strong></td>
<td>14 mg/21 mg/28 mg/42 mg</td>
<td>14 mg</td>
<td>10 mg/15 mg/20 mg</td>
</tr>
</tbody>
</table>

### Products
- **Concerta® Tablets:** OROS® Delivery System
- **Metadate® CD Capsules:** Diffucaps® Delivery System
- **Ritalin® LA Capsules:** SODASTM Delivery System

### Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder
Focus, June 1, 2008; 6(3): 401 - 426.
[Abstract] [Full Text] [PDF]


Clinical Practice Guidelines American Academy of Pediatrics:

Committee on Quality Improvement, Subcommittee on Attention-Deficit/Hyperactivity Disorder

1) Pediatrics Vol. 105 No. 5 May 2000, pp 1158-1170
Clinical Practice Guideline: Diagnosis and Evaluation of the Child With Attention-Deficit/Hyperactivity Disorder

2) Pediatrics 2001 108: 1033-1044
Clinical Practice Guideline: Treatment of the School-Aged Child With Attention-Deficit/Hyperactivity Disorder

*J Atten Disord*, July 1, 2008; 12(1): 4 - 14. [Abstract] [PDF]

*J Atten Disord*, July 1, 2008; 12(1): 15 - 43. [Abstract] [PDF]

Press Release October 16, 2006
Preschoolers with ADHD Improve with Low Doses of Medication

The first long-term, large-scale study designed to determine the safety and effectiveness of treating preschoolers who have attention-deficit/hyperactivity disorder (ADHD) with methylphenidate (Ritalin) has found that overall, low doses of this medication are effective and safe. However, the study found that children this age are more sensitive than older children to the medication’s side effects and therefore should be closely monitored. The 70-week, six-site study was funded by the National Institutes of Health’s National Institute of Mental Health (NIMH) and was described in several articles in the November 2006 issue of the Journal of the American Academy of Child and Adolescent Psychiatry.
Cardiovascular Monitoring of Children and Adolescents With Heart Disease Receiving Medications for Attention Deficit/Hyperactivity Disorder: A Scientific Statement From the American Heart Association Council on Cardiovascular Disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing Circulation, May 6, 2008; 117(18): 2407 - 2423.

Reference


Inside of me there is creativity running through my body like a river, flowing into a lake. Inside of me is a purring cat happy to be petted, playful and curious. Inside of me is a castle on a hill surrounded by trees. Sometimes at war with an army of knights, sometimes in peace with the enemy. Inside of me a tree grows unharmed, branches reaching out as far as they can, roots growing down to good soil. Inside of me a key waits for someone to unlock the chest and free the treasure.

Mike Uhrich
Grade 6