“Behavioral Use” von Antipsychotika: Entwicklungen und pro-con Debatte

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### Severity of Adolescent ODD & CD

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Serious(^b)</th>
<th>Moderate(^b)</th>
<th>Mild(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major depressive episode/dysthymia</td>
<td>35.6 (5.2)</td>
<td>31.0 (6.4)</td>
<td>33.4 (6.7)</td>
</tr>
<tr>
<td>Bipolar disorder(^c)</td>
<td>30.5 (5.8)</td>
<td>26.5 (12.1)</td>
<td>43.1 (10.7)</td>
</tr>
<tr>
<td>Any mood disorder</td>
<td>32.4 (4.5)</td>
<td>29.8 (7.4)</td>
<td>37.8 (7.7)</td>
</tr>
<tr>
<td><strong>Anxiety disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agoraphobia(^d)</td>
<td>22.1 (7.4)</td>
<td>25.9 (15.5)</td>
<td>52.0 (15.9)</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>32.0 (8.6)</td>
<td>21.0 (8.9)</td>
<td>47.1 (9.0)</td>
</tr>
<tr>
<td>Social phobia</td>
<td>23.9 (5.1)</td>
<td>23.8 (9.3)</td>
<td>52.3 (9.0)</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>19.6 (5.1)</td>
<td>16.8 (11.6)</td>
<td>63.7 (10.6)</td>
</tr>
<tr>
<td>Panic disorder(^e)</td>
<td>35.4 (12.6)</td>
<td>21.2 (10.3)</td>
<td>43.4 (10.9)</td>
</tr>
<tr>
<td>Posttraumatic stress disorder</td>
<td>27.7 (7.0)</td>
<td>23.8 (11.1)</td>
<td>48.5 (10.4)</td>
</tr>
<tr>
<td>Separation anxiety disorder</td>
<td>25.0 (8.1)</td>
<td>25.5 (8.9)</td>
<td>49.5 (10.9)</td>
</tr>
<tr>
<td>Any anxiety disorder</td>
<td>18.4 (3.4)</td>
<td>19.6 (10.3)</td>
<td>62.0 (9.6)</td>
</tr>
<tr>
<td><strong>Behavior disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention-deficit/ hyperactivity disorder</td>
<td>35.4 (8.2)</td>
<td>40.6 (14.0)</td>
<td>24.0 (10.6)</td>
</tr>
<tr>
<td>Oppositional-defiant disorder</td>
<td>43.8 (7.8)</td>
<td>24.3 (6.8)</td>
<td>31.9 (8.9)</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>59.8 (8.4)</td>
<td>21.1 (9.4)</td>
<td>19.2 (8.6)</td>
</tr>
<tr>
<td><strong>Eating disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any behavior disorder</td>
<td>33.6 (5.1)</td>
<td>30.2 (9.4)</td>
<td>36.2 (9.6)</td>
</tr>
<tr>
<td><strong>Substance disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse(^g)</td>
<td>26.4 (5.7)</td>
<td>21.4 (8.2)</td>
<td>52.1 (9.2)</td>
</tr>
<tr>
<td>Drug abuse(^g)</td>
<td>33.8 (6.1)</td>
<td>19.2 (7.3)</td>
<td>47.0 (7.1)</td>
</tr>
<tr>
<td>Any substance disorder</td>
<td>29.1 (5.0)</td>
<td>19.2 (6.7)</td>
<td>51.7 (7.1)</td>
</tr>
<tr>
<td><strong>No. of disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any disorder</td>
<td>18.8 (2.9)</td>
<td>22.9 (9.8)</td>
<td>58.2 (9.5)</td>
</tr>
<tr>
<td>Exactly 1 disorder</td>
<td>8.5 (3.8)</td>
<td>19.1 (12.4)</td>
<td>72.4 (12.1)</td>
</tr>
<tr>
<td>Exactly 2 disorders</td>
<td>12.1 (2.5)</td>
<td>25.3 (10.9)</td>
<td>62.5 (10.4)</td>
</tr>
<tr>
<td>≥3 Disorders</td>
<td>43.1 (6.2)</td>
<td>28.3 (7.1)</td>
<td>28.6 (7.0)</td>
</tr>
</tbody>
</table>

NCS-RA: n=6,483  
Atypical Antipsychotic Use Increasing Dramatically in Youth

- Atypical antipsychotics: In 2002 = 93%, in 2004 = 99%
- ~10% of mental health visits in 2002 involved SGA treatment
- Most likely if > 9 yrs, BPD OR=56, Psychosis OR=37, Disruptive Behavior OR=10, Anxiety OR=5; ~14% in Psychosis, 17% PDD

Psychopharmacologic Rx of Aggression in Youth

• RIS Acute (N=10, n=698, 8.3 wks): ES= .72
• RIS Maintenance (N=3, n=391, 13.3 wks): ES= .40
• ARI Acute (N=2, n=308, 8 wks): ES= .41, .49, .62 & .79
• HAL (N=1, n= 40 inpatients, 4 wks): ES= .83
• Stimulants (N=6, n=907, 6.2 wks: ES= .60
  • MPH (N=5, n=579, 6.6 wks: ES= .63
  • AMPH (N=2, n=346, 3.5 wks): ES= .42
• Mood Stabilizers (N=6 (5 IP), n=208, 5.3 wks): ES= .47
  • VPA in OPs: ES=-.13
  • Lithium (N=4 (IP), n=164, 4.5 wks: ES= .63
  • CBZ (N=1 (IP), n=24, 6 weeks: ES= .06
• SGAs: NNT=3; Lithium: NNT=4; STIM: NNT=4

RIS vs DVPX vs PBO for ADHD (6-12 Years) + Aggression After Stimulant Optimization

RUPP Trial: Risperidone in Autism

8-Week Acute Trial: n=101
Mean age: 8.8 yrs, mean dose: 1.8 mg/d

Response criteria: ≥25% improvement in the ABC Irritability score, and a rating of “much improved” or very much improved” on the CGI-I


8-Week Relapse Prevention Trial: n=32
(14/16)

Maintenance of response criteria
Median time to relapse 34 days on PBO vs 52 days on risperidone

Aripiprazole in autistic disorder: mean change in the aberrant behaviour behaviour checklist - irritability subscale by week

Mean baseline scores (SE): Pbo = 30.8 (1.0); Ari = 29.6 (1.0)

Owen R et al., Paediatrics 2009;124:1533-1540

* p<0.05, ** p<0.005, *** p<0.001 vs placebo
Aripiprazole in autistic disorder: superiority vs placebo in the change from baseline in the aberrant behavior checklist - irritability subscale (LOCF)

Mean baseline scores (SE): Pbo = 26.9 (1.0); Ari 5 mg = 28.3 (1.0), 10 mg = 27.6 (0.9), 15 mg = 28.3 (1.0)

* p<0.05, 15 mg arm only, ** p<0.05 all arms, *** p<0.01 all arms vs placebo

Aripiprazole in Autistic Disorder: Line Item Analysis of 2 Pooled Registration Trials

Study Defined “Response” in Pediatric Autism: NNT= 2-7

Study Defined “Response” in Pediatric DBDs:
NNT= 2-5

Four additional RCTs without categorical response data
Risperidone in DBD/Subaverage IQ: Results of a 52-Week, Open-Label Study

504 children, age = 9.7 years (5–14 y)
RIS: 1.5 mg/d (0.1–4.3 mg/d)

N = 504.
N CBRF = Nisonger Child Behavior Rating Form.
*P < 0.001 versus baseline at each time point (two-sided paired t-test).
Relapse Prevention of DBD in Children and Adolescents: Time to Relapse*

Proportion Not Relapsing

Time to Relapse (days)

PLA n = 162 152 120 101 77 69 62 11 1
RIS n = 171 170 158 138 118 110 107 24 6

RIS = risperidone-treated subjects; PLA = placebo subjects.

*Kaplan-Meier estimates of time (days) from initiation of maintenance treatment to relapse. Relapse defined as deterioration (compared with the end of the continuation treatment phase) at 2 consecutive weekly visits as measured by an increase ≥2 points on CGI-S or an increase by ≥7 points on N-CBRF Conduct subscale.

Relapse Prevention with RIS Vs. PBO in Youth with DBDs and with Autism

DBD patients with relapse at 8 weeks

Approximate survival curve estimated relapse at 6 months: 30% vs 50%


Autism patients with relapse at 8 Weeks

Median time to relapse 34 days on PBO vs 52 days on risperidone


26-Week trial in youth with DBDs (n=233)

8-Week trial in youth with Autism (n=32)
Summary

- Aggressive behavior is a common, complex and difficult treatment target in child psychiatry
- Adequate diagnosis and psychosocial interventions are key first steps in the management of aggression
- Involve families closely if possible
- Make sure the patient and the environment are safe
- Treat underlying/comorbidities and psychosocial stressors
- Use lowest risk interventions whenever possible
- Antipsychotics and, to a lesser degree stimulants, and even less so, mood stabilizers have been shown to reduce aggressive behavior associated with autistic disorder and disruptive behavior disorders
- Use multimodal, multi-team member approach
Vielen Dank fuer Ihre Aufmerksamkeit!

https://www.coh-fit.com