Treatment of ADHD
Tallinn 2015-10-02
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Assessment first!

- The crucial question:

Do I have the right patient for this treatment?
Making the diagnosis- look at all pieces that makes it up

Family history
Adhd 80%

Course
Adhd continuous&fluctuating

Symptom criteria
Adhd inatt&hyperactive

Response to treatment
Making the diagnosis – be cautious and consider…

Adhd is normally distributed
  Less extreme =
    + numbers
    - diagnostic clarity
    - response to medication

Multiple informants
give you a better indication of your position
Adhd – how does it affect functioning? = how severe?

At home

At school

With friends

At activities
Do I have the right patient for this treatment?

- Life circumstances?
- Comorbidity? IQ??
- Severity?
- Substance (ab)use
- Diagnosis?
- Family history of cardiac problems before age 40

If yes – GO!
ADHD treatment

- Psychoeducation
- Adaptation at school + home
- Medication, severe=early, mild=wait
Adhd – the medicines

- Atomoxetine
- Stimulants:
  - Methylphenidate
  - Amphetamines
- Alfa-agonists:
  - Clonidine
  - Guanfacine
The Mechanisms of Action of Stimulants

**Presynaptic Neuron**

- **AMPH** blocks uptake into vesicle
- **AMPH** diffuses into vesicle causing DA release into cytoplasm
- **AMPH** is taken up into cell causing DA release into synapse
- **Synapse**

**Storage vesicle**

**Cytoplasmic DA**

**DA Transporter Protein**

Wilens TE. J Clin Psychiatry. 2006. 67, (suppl 8) 32-37
How many patients with ADHD respond to stimulants?

ADHD population

Methylphenidate 70%

Methylphenidate OR Amphetamine 90%

Amphetamine 70%

Stimulants are very effective in reducing ADHD
lisdexamphetamine vs placebo vs mph (concerta)

Figure 2  ADHD-RS-IV mean total scores at baseline and endpoint (±SD), and LS mean changes (±SE) from baseline to endpoint (full analysis set). **p < 0.001 based on difference in LS mean change (active drug-placebo). Endpoint is the last on-treatment, post-baseline visit of the dose-optimization or dose-maintenance period (visits 1-7) with a valid ADHD-RS-IV total score. A decrease from baseline in the ADHD-RS-IV total score indicates an improvement in ADHD symptomatology.

Coghill et al Article in press
Stimulants and side effects

- Loss of appetite & weight
- Insomnia
- Dysphoria & irritability
- Headache & abdominal pain
- Tics & dyskinesia
- Tachycardia & hypertonia
- Psychotic symptoms
Stimulants and impact on Growth-Weight

Wilens et al 2005 JAACAP
Stimulants and monitoring..

- Growth – accept -0.5 sd in age-adjusted height

- Heart
  - blood pressure = usual age adjusted limits
  - Pulse rate;
    - resting 90 but in office 100-110.
    - In doubt make Home assessment!
Stimulants and dosing

C Medikinet

C Ritalin

T Concerta

C Equasym

Tailor the dosing

• What is the individual need
  • Worst in the morning?
  • Only for school??
  • Afternoons?
  • Can´t eat enough??
  • Handle the rebound???

• Dosing
  • Preschool 0,75 mg/kg
  • Adolescents & adults 1-1,3 mg/kg range – 2 mg/kg but sometimes higher
  • Tips:
    • short acting before waking up for calm mornings or
    • split doses of concerta for calm evenings without rebound
    • Extra short acting for special occasions
    • Lower/shorter duration during weekends
Amphetamine

- 2nd line
- Sometimes better and less dysphoria
- Greater risk of abuse with short acting
  - use lisdexamphetamine.
  - Prodrug with duration 13 hrs
  - 30-50-70 mg
Atomoxetine- 2nd line

The pros

- 24 hrs duration
- Non stimulant=no abuse
- Can be combined with a stimulant
- For comorbid adhd
  - Anxiety & sleep
  - Disruptive

The cons

- Somewhat lower effect
- Somewhat more side effects
- Interactions on Cyp2D6
  - Fluoxetine makes ++atm
  - QTc risk if atm is added to antipsychotics
Alfa-agonists 2nd line
clonidine and guanfacine

The pros
- Very good combo with stimulant
- Works best for hyperactivity & aggression & sleep
- 1st line for tics
- Best tolerated
  - SE: sedation, headache, ortostatic BP

The cons
- Somewhat less effective
- Clonidine very sedative
  - Super for sleep and relax
  - Not for school
- Guanfacine expensive
## Side effects of ADHD meds

<table>
<thead>
<tr>
<th>Side effect</th>
<th>MPH</th>
<th>AMPH</th>
<th>ATMX</th>
<th>α-2 AGONIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite decrease</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>nausea</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>irritability</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Somnolens</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>insomnia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Emotional lability</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>sadness</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tics</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>vertigo</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>tachycardia</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>+blood pressure</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Combining meds?

- Stimulant + alfaagonist
  - Approved combo in the US
  - No interactions
  - Added benefit but side effects doesn´t add up

- Stimulant + atomoxetine
  - Some evidence,
  - no interactions,
  - added benefit + side effects

- Atomoxetine + alfa agonist
  - No studies,
  - Pharmacodynamically questionnable

- Stimulant + neuroleptic
  - 3-4line if adhd,
  - works for severe aggression and tics (risp, ari) or severe sleep (que)
  - Metabolic side effects of neuroleptic are not balanced by the stimulant-monitor!!

- Stimulant + melatonin
  - 1st line and
  - Good for sleep
  - No interactions and few side effects
Treatment refractory ADHD

- 30% either doesn’t respond to or tolerate a stimulant
- Try 2nd line = alfaagonists or atomoxetine
- Reassess!!
  - Comorbidity?
  - Prodromal disorder (schizophrenia, personality)
  - Drug ab(use)