Attention-Deficit / Hyperactivity Disorder: Challenges to Clinicians

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A highly prevalent and complex disorder with multiple causes

- Genes
- Environment
- Biochemical anomalies
- Modulating factors
Diagnostic challenges - 1

- A syndromal diagnosis
  - 6/9 inattention + 6/9 overactivity/impulsivity symptoms, ≥6 months, ≥2 situations, impairment
  - ? Cut-off
- Subjected to informant’s expectation /background/knowledge /mental state
- Sub-threshold cases
Prevalence study, Chinese, grade 7-9, DISC-IV

- N=541 (261 boys, 280 girls)
- Symptom criteria = 4.4% (5.7%, 3.2%)
- + Impairment criteria = 3.9% (5.4%, 2.5%)
- % reduction in prevalence = 11% (5%, 21%)

Prevalence of DSM-IV disorders in Chinese adolescents and the effect of an impairment criterion: A pilot community study in Hong Kong
Impairment criteria

6 domains of daily living
- Caretakers get annoyed or upset
- Doing things / going places with family
- Doing things / going places with friends
- Schoolwork or grade
- Teachers get annoyed or upset
- Child feels annoyed or upset

1 severe or 2 intermediate impairment
No laboratory or radio-imaging diagnostic test
Diagnostic challenges - 2

- Poor consistency among informants
  - Poor correlation between parent ratings and teacher ratings
  - Similar discrepancy between child and adult
  - Cultural / mindset variables
    - ASEBA
Diagnostic challenges - 3

- Differential diagnoses
  - May get confused with other conditions e.g. ODD, learning difficulty, cognitive deficiency, anxiety disorders, bipolar affective disorder
High comorbidities

- ODD
- Tic
- Dyslexia
- Depression
- Motor Clumsiness
- Conduct Disorder
- Anxiety
- Depression
Treatment challenges - 1

- Limited choice / availability of effective treatment
  - Most HA pharmacy provide only Ritalin ± Concerta / Strattera as 1\textsuperscript{st} line medication treatment
  - Psycho-social treatment program
  - School based support and intervention
Treatment challenges - 2

- **Long term benefit of medication treatment**
  - Superiority over non-medicated comparison groups reduce at 24 months and almost disappear at 36 months

- Peter S Jensen et al. 3-year follow up of the NIMH MTA Study. J. Am. Acad. Child Adolesc. Psychiatry, 46:8, August 2007
Treatment challenges - 3

- Adverse effect or long term hazards associated with medication treatment
Growth suppression

Weight

8/11 studies reported significant differences,

- 20mg MPH > 30-40 mg; Ss cont’d thro’ summer < Ss d/c (Safer 1972)
- MPH < expected at yr 1 & 2; Ss cont’d thro’ summer < Ss d/c (Scatterfield 1979)
- Placebo > MPH (Conners 1980)
- MPH (%tile) < baseline after 1-4 years; does related (Mattes 1983)
- MPH d/c for summer > MPH cont’d at yr 1 but NS at yr 2 (Klein 1988)

Growth suppression

Height

- 4/10 studies reported significant findings
  - MPH (%tile) < control (Safer 1972)
  - MPH (%tile) < baseline after 2-4 years, dose related (Mattes 1983)
  - MPH < expected at yr1 but NS at yr 2 (Scatterfield 1979)
  - MPH cont’d thro’ summer < d/c at yr 2 (Klein 1988)

Growth suppression

- Stimulant medications lead to delays in expected growth in height and weight
- Most obvious in the heavier and taller (vs light & short) children (vs adolescent)
- Ht & wt deficits increase with length of time on medication
- Deficits attenuate over time (even if maintained on medication)
- ? Part of ADHD or attributed to medication
- Mechanism: CNS, hepatic growth factor, cartilage effect, receptor up/down-regulation

Growth suppression

Management strategies:
- Explanation, education & explore expectation
- Monitoring
- Adjustment in dose regimen
- Meal arrangement
- Drug holiday
- Change to non-stimulant

Balance pros and cons of inadequate treatment vs growth deficit
 Tic

- Worsening by stimulant?
- Clonidine and Atomoxetine significantly improve comorbid tic symptoms
- Methylphenidate does not associate with worsening of tic. Some suggestion that they may improve tic

Seizure

- Comorbidity of seizure & ADHD greater than expected
- ↑Risk for EEG abnormalities in ADHD children (6.1% vs. 3.5%) and subsequent seizure
- In a group of Pediatric epileptic patient (n=175) 24% meet ADHD pred inattentive criteria, 11% for ADHD combined, and 2% for pred hyperactive-impulsive subtype

Dunn D W et al. (2003). ADHD and epilepsy in childhood. Dev Med Child Neural 45:50-54
Seizure

- Some AED may exacerbate behavioral symptoms (e.g. barbiturates, topiramate)
- Consider valporate, carbamazepine (improve mood & beh problems), levetiracetam, lamotrigine, clobazam (does not impair cognitive/executive function)

Seizure

- Some ADHD medications may lower seizure threshold
- Case report about new onset seizure in MPH treated patient
- Improve ADHD symptoms in controlled trials of MPH in epileptic patients
- In a recent meta-analysis, seizure risk in medicated (MPH, atomoxetine) ADHD patients is not statistically different from placebo or population seizure risk

Seizure

- MPH or atomoxetine if the ADHD s/s ≥ moderate + seizure ≤ once/month
- 2nd line: trial of clonidine or guanfacine
- 3rd line: TCA or modafinil
- Melatonin may be considered for sleep problems

Suicide behavior

Meta-analysis

- Suicidal-related behavior
- 0.37% (5/1357) in Atomoxetine group vs. 0% in placebo group
- Nil committed suicide

Mark E Bangs et al, Meta-Analysis of Suicide-Related Behavior Events in Patients Treated with Atomoxetine. J. Am. Acad/ Child Adolesc Psychiatry, 47:2, February 2008
Sudden death

- FDA review (2006) of isolated reports of sudden death (19 under 18-year-old, 6 adult cases) in patients taking medications to treat ADHD ⇒ inconclusive

- Retrospective cohort study (2009) identify 7 cases of death from 18637 patient-year (1993-2006) who were prescribed methylphenidate, dexamfetamine, and Atomoxetine. Mortality rate similar to general population

Drug abuse / addiction

Controversy

Stay awake for studying/exam

Misuse & diversion

A review (21 studies, 113,145 subjects) found 5-9% past year prevalence of stimulant misuse in grade/high-school-age children (5-35% in college students)

A study of 161 students on MPH found that 16% of the 73 survey respondents had been asked by other students to trade, sell, or to give them their stimulant medication

Drug abuse / addiction

- Men reports more misuse
- White and Hispanics 3\times the rate in African American and 2 \times the rate in Asian American (Teter 2006)
- Motivation: to concentrate (58%), alertness (43%), get ‘high’ (43%), others (14%) (Teter 2005)
- Oral (96%), intra-nasal (38%) (Teter 2006)
- Comorbid with CD &/or SA
  - Divert (83% had CD, 83% had SA)
  - Misuse (58% had CD, 75% had SA)

Drug abuse / addiction

- “Vitamin R”, “R-ball”, “Skippy”
- Oral / snorting / i.v.
- Toxic effects: irritability, agitation, euphoria, lethargy, dizziness, restlessness, hallucination, delusion, seizure; tachycardia, hypertension, arrhythmia, vomiting, abd pain
- Withdrawal s/s: lethargy, apathy, depression, paranoid
- Severe obstructive lung disease have been described in chronic i.v. methylphenidate abuser
Drug abuse / addiction

DDx: intoxication with other substances

Management:
- Activated charcoal
- Agitation
- Delirium
- Seizure
- Psychotic symptoms
- Arrhythmia
- Hypertension
- Fever

Prevention
Treatment challenges - 4

- Compliance problem
  - Irregular drug intake
  - Over use of drug holiday
  - Premature drop out of treatment
  - More of a problem if comorbid with ODD, CD, familial psychopathology, inadequate parental supervision
Treatment challenges - 5

- Expectation from patient/family
  - Increase service demand
  - Ready availability of ADHD information over the web/media (some are misleading)
  - Reduced reserve/functions of the family
Treatment challenges - 6

- Continuity of care
  - A developmental problem which commonly extends into adult life
  - Transition to adult service
  - Expertise and availability of adult assessment & treatment service
The way ahead

- Increase demand
- Limited resource
- Restructuring of service provision
- Set priority
- Collaboration
- Training
THANK YOU