



Billings Clinic - Montana

Advanced ADHD Psychopharm

Pediatric Mental Health ECHO
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Billings Clinic

Stimulants

- 2 categories: MPH and AMP
 - Produced in single dextro isomer or in racemic version.
- Switching between stimulants
 - 1991 study showed non-response rate dropped from 32% to 4% when able to switch between dextroamphetamine and MPH.

Stimulants

- Likely more non-responders with comorbidities.
- Studies often don't include placebo, so actual stimulant response rate might be closer to 55%.

MPH

- Active ingredient of majority of stimulant prescriptions in the US.
 - Large effect size (0.91)
- Rapid absorption, effects within 30min and 3-5hr duration of action.
 - Peak plasma concentration by 90min.

MPH

- **Dexmethylphenidate HCl (Focalin) is the d-threo enantiomer of racemic MPH.**
 - d-threo enantiomer > active than l-threo.
- **Plasma concentration increases rapidly after ingestion, reaching a maximum in fasting state 1 to 1.5hrs postdose.**

Long-Acting MPH

- Single-pulse
 - Metadate ER
 - Methylin ER
- Wax-matrix preparation to prolong release
- Slower onset of action than IR and lower serum concentrations
- 6-8hr duration, give with IR to compensate

Long-Acting MPH

- Dual-pulse
 - Metadate CD
 - Ritalin LA
 - Focalin XR

Long-Acting MPH

- Beaded MPH products, using SODAS (Spheroidal Oral Drug Absorption System)
 - Mix of IR and DR beads
- Ritalin LA mimics giving IR MPH in two doses 4hrs apart
- Focalin XR uses same SODAS technology.

Long-Acting MPH

- OROS MPH, simulating triple-pulse
- Osmotic delivery system to reduce ADHD symptoms for up to 12hrs.
- IR MPH is applied to the outside of the OROS caplet for immediate intervention.
- Slightly ascending MPH serum concentration curve.

Long-Acting MPH

- OROS MPH
 - Mimics serum concentrations produced by taking IR MPH

AMP

- Racemic
 - Adderall and Adderall XR
- Dextro isomer
 - Dextroamphetamine (Dexedrine)
 - Lisdexamfetamine (Vyvanse)

AMP

- Plasma levels peak 3hrs after po administration.
- Acidification of urine increases urinary output.
 - Taking AMP with fruit juices decreases absorption.

AMP

- Effects can be seen within 1hr of ingestion, and duration of action is up to 5hrs.
 - Duration of action longer than MPH.

Long-Acting AMP

- Adderall XR
 - Capsule preparation of IR and ER beads.
- Lisdexamfetamine dimesylate (Vyvanse)
 - Inactive parenterally
 - d-amphetamine is covalently bonded to l-lysine; bond is cleaved during digestion.
 - Treatment effects up to 12hrs.

Summary MPH

Medication	Duration of Action	Starting Dose	Typical Dose
MPH	3-5hrs	5mg BID or TID	10mg TID
Dexmethylphenidate (Focalin)	5-6hrs	2.5mg BID or TID	10mg BID
Metadate ER	Single pulse	20mg/am	40mg/am
Metadate CD	8-10hrs; dual pulse	20mg/am	30mg/am
OROS MPH (Concerta)	8-12hrs; ascending single pulse	18mg/am	36mg/am

Summary AMP

Medication	Duration of Action	Starting Dose	Typical Dose
AMP	4-6hrs	5mg BID	10mg BID
Dextroamphetamine (Dexedrine)	4-6hrs	5mg BID	10mg BID
Adderall XR	8-10hrs; dual pulse	5mg/am	30mg/am
Lisdexamfetamine (Vyvanse)	13-14hrs	30mg/am	50mg/am

Stimulants and Tics

- 1995 controlled trial involving children with ADHD and chronic tic disorder taking MPH.
 - Significant improvement in ADHD s/s without consistent worsening or increase in tic frequency for all subjects.

Stimulants and Anxiety

- 1995 controlled study tested MPH on youth with co-morbid anxiety symptoms.
 - Equally good response for +/- anxiety.
- Meta-analysis of 23 studies involving 2,959 youth with ADHD found stimulant treatment reduced risk for anxiety vs. placebo.

Stimulants and Adverse Events

- A 2005 FDA review reported 135 adverse event reports for OROS MPH out of 1.3 million cases.
 - 36 psychiatric adverse events
 - 12 instances of tactile and visual hallucinations
 - 20 cardiovascular events

Stimulants and Adverse Events

- AACAP Work Group on Quality Issues
 - Rate of sudden, unexpected death is about 0.5 per 100,000 patient-years taking mixed salt AMP and 0.19 per 100,000 patient-years for MPH.
 - In general population, 1.3-1.6 per 100,000 patient years.

Atomoxetine

- SNRI
- First drug approved by FDA to treat ADHD in both youth and adults.
- Widely used treatment algorithms recommend this as 2nd line to stimulants.
- Medium effect size (0.64).