ADHD Medications and the Heart

Still a concern after all these years...

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History

• February 9, 2006: Drug Safety and Risk Management Advisory Committee of the FDA voted 8-7 to recommend a black box warning regarding the CV risks of stimulant drugs used to treat ADHD

• Unexpected action as FDA had not requested a review of labeling for this class of drugs

• FDA had asked for recommendations of approaches to studying CV risks
Drugs under review

• Amphetamines (Adderall and other brands)

• Methylphenidate (Ritalin, Concerta and other brands)

• Drugs that had been well documented in clinical trials to be effective in management of ADHD starting in 1950s

• ~2.5 million children on these medications in 2006
CV effects according to advisory committee

• Thoroughly described in medical literature to “…substantially increase the heart rate and blood pressure.”

• FDA’s Adverse Event Reporting System included 25 cases of sudden death in children and adults, some with evidence on autopsy of undiagnosed congenital heart disease, such as hypertrophic obstructive cardiomyopathy.
Cardiovascular effects of ADHD medications

• With appropriate dosing for effect
  • HR increase 3-10 beats/minute
  • SBP increased 3-8 mmHg
  • DBP increases 2-14 mmHg

• Study looking specifically at methylphenidate showed heart rate effect by weeks with no further increase, SBP gradually increased throughout 6 months of monitoring, DBP and EKG did not change significantly.
“The majority of the group accepted my argument that the propensity of sympathomimetic agents to raise blood pressure and heart rate, the history of serious adverse effects associated with two members of the class (ephedra and PPA) and the rapid increase in exposure, particularly in adults, warranted strong and immediate action.”
Recommendation for EKG prior to starting ADHD medication

• April 2008: American Heart Association statement that is reasonable, although not mandatory, for clinicians to consider ordering an EKG before beginning treatment of ADHD with stimulants or other medications

Joint Statement from AHA and AAP
Endorsed by AACAP, ACC, Society for Developmental and Behavioral Pediatrics, and others

- Data show that children with heart conditions have a higher incidence of ADHD
- Need to carefully assess patients for heart disease prior to using medications for ADHD
- Patient and family history and physical exam
- EKG prior to treatment is reasonable but not mandatory with prescribing physician the best person to make the assessment about where there is a need for an ekg.
Children without cardiac disease

• 3 large studies demonstrate no difference in the risk of serious cardiovascular events (sudden cardiac death, acute myocardial infarction, or stroke) between children and young adults receiving stimulant ADHD pharmacotherapy and nonusers.

• Sudden deaths occur in about 2 children for every million taking ADHD medications; fewer than the 8-62 deaths per million in the general population.
Children with cardiac disease

• ADHD is common in children with CHD
• Limited data available
• There are no data to suggest that specific forms of CHD carry an increased risk of sudden unexpected death in patients on ADHD medications
• Risk may be higher in other pediatric cardiac disease (LQTS)
FDA current position

- Findings from largest cohort study did not show an association between ADHD medications and adverse cardiovascular events
- Recommends physicians prescribe medications “according to the professional prescribing label”.
- Monitor for heart rate and blood pressure effects
- Should not be used for patient with “serious heart problems” or if increase in HR or BP would be “problematic”
- Cardiology consultation if cardiac concerns
Cardiac Evaluation prior to starting ADHD medication

- History, comprehensive with cardiovascular focus
- Family History
- PE
Personal history with cardiovascular focus

- Any cardiac disease
- Rheumatic fever
- Fainting or dizziness especially during exercise
- Seizures
- Chest pain
- Shortness of breath with exercise
- Unexplained change in exercise tolerance
- Palpitations
- High blood pressure
- Current medications
Family history

• Sudden or unexplained death
• Event requiring resuscitation in child or young adult
• Cardiac arrhythmias
  • WPW
  • LQTS
  • Brugada
  • ARVD
• Cardiomyopathy (hypertrophic, dilated, restrictive)
• Marfan Syndrome
Physical Exam

• Vital signs

• Complete cardiovascular exam

• Physical findings associated with Marfan Syndrome
Additional testing

• If no history or PE findings suggestive of CV disease, no further testing is recommended prior to initiation of pharmacotherapy

• If a concerning history or physical exam: EKG and/or Pediatric Cardiac consultation

• If known congenital heart disease, discussion/consultation with patient’s cardiologist is warranted.

• Routine screening with EKG on all patients is NOT recommended
  • No specific EKG findings associated with increased risk of adverse cardiac event
  • EKGs have significant number of false positives
Summary

• ADHD is common and failure to treat has risks
• Stimulant medications are known to have benefit in the management of ADHD
• There is no evidence that there is an increased risk of a sudden cardiac event (death, MI, stroke) occurring in patients in patients without underlying cardiac disease
• There is no current evidence that specific cardiac diagnoses are absolute contraindications to ADHD pharmacotherapy
• An EKG is NOT required before starting ADHD medications unless there is something in the history or on PE is concerning for CV disease.
• Risk/benefit needs to be discussed and documented