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Stimulant medication cessation in the setting of non-compaction cardiomyopathy

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Stimulant Discontinuation for ADHD Treatment in a Patient with Non-Compaction Cardiomyopathy

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Objectives

- To understand the importance of monitoring and screening for cardiovascular risk factors in patients prescribed stimulants for treatment of Attention Deficit/Hyperactive Disorder (ADHD).
- To recognize that cardiac issues can impact stimulant prescribing and may result in life threatening complications.
- To develop an appreciation of the repercussions of complications and untreated ADHD symptoms from discontinuation of stimulants.
- To recognize the importance of collaborative care across specialties in treating patients.

Introduction

- Non-compaction cardiomyopathy (NCM) is largely a genetic condition due to failure of left ventricular compaction resulting in extensions of bundles of muscle (trabeculations) into the chamber. This impairs the ability of cardiac muscle to contract or relax adequately (4).
- Diagnosis for NCM can occur at any age. Patients may be asymptomatic though there is a risk of complications including cardiac arrest, blood clots and heart failure (4).

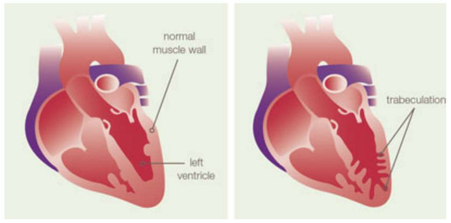

Figure 1: Comparison of normal heart (left) and heart with left ventricular non-compaction cardiomyopathy (right) (4).

- ADHD is defined as a persistent pattern of inattention and/or hyperactivity/impulsivity that interferes with functioning which is inappropriate for an individual's developmental level (1).
- ADHD contributes to academic, social and occupational functioning and is prevalent in 4.4% of adults in the United States (3).
- Psychostimulants and non-stimulant medications may be used to treat symptoms of ADHD.
- Stimulant medications may impact heart rate, heart rhythm, blood pressure and QTc which can increase risk of cardiovascular complications including sudden death. (Figure 2).
- Cardiovascular safety of ADHD medications in adults is not completely understood with variance of results.
- In adults aged 25 – 64 years old, the US Food and Drug Administration (FDA) did not find an increased risk of myocardial infarction, stroke or sudden cardiac death with stimulant use for ADHD (FDA).
  - FDA does not recommend stimulant use in patients with heart problems, problematic elevated blood pressure or heart rate.
- Development of cardiomyopathy in patients using stimulants is rare in younger age groups. The highest rates occurred in individuals age 65 or older (5).
- Use of stimulants (lisdexamfetamine, metyhlphenidate and atomoxetine) was not associated with a higher rate of heart failure or cardiomyopathy over 3 years of use (5).
- Pre-existing cardiovascular conditions reduces likelihood of use of stimulant therapy for treatment of ADHD. (2).
- There are no established monitoring guidelines for patients on stimulant medications for ADHD.

Patient Presentation

31-year-old female with a past medical history of ADHD, low BMI and clubbed feet. She was evaluated on an outpatient basis with the following timeline:

- Referred to HFH Behavioral Health Services in 2016 and diagnosed with ADHD (combined type).
- Prior medications trials included dextroamphetamine-amphetamine IR and XR formulations (though benefitted only with IR). Started on dextroamphetamine-amphetamine IR 20mg twice daily.
- At follow up 4 months later she was noted to be tachyardic to 120 beats per minute. Dose adjusted to dextroamphetamine-amphetamine IR 10mg twice daily.
- EKGs showed right axis deviation, possible left atrial enlargement, non-specific T-wave abnormality and QTc of 483ms (on repeat 1 month later was 425ms).
- Referred to Rheumatology
  - Full evaluation done with workup only notable for speckled pattern ANA. Remaining studies unremarkable. Lupus felt to be unlikely.
- Referred to Cardiology
  - Initial workup included ECHO which showed EF of 34.7%, left wall hypokinesis, mild diastolic dysfunction of LV, upper normal right ventricular size and moderately reduced RV systolic pressure.
  - Event monitor for 7 days which only showed sinus tachycardia.
  - Eventually started on carvedilol 3.15mg twice daily and lisinopril 2.5mg daily.
- Later diagnosed with Generalized Anxiety Disorder and started on buspirone 7.5mg twice daily, but this was discontinued 2 weeks later due to emotional lability.
- Trialed other stimulants included atomoxetine (discontinued due to drowsiness) as well as methylphenidate. Initially did well on methylphenidate at 72mg with improvement in both tachycardia and ADHD symptoms, but tachycardia later returned and persisted despite decreases in dosage.
- Given cardiac issues all stimulants were then discontinued. Since then has had symptoms of ADHD, struggles with employment stressors and learned that she is unable to have children due to cardiac issues.

Cardiovascular Risks Of Stimulant Medications

Table 1. Classification of Recommendations and Level of Evidence

Classification of recommendations

- Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective and should be performed. Benefit>>>risk.
- Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
  - Class IIa: weight of evidence/opinion is in favor of usefulness/efficacy. It is reasonable to perform procedure/administer treatment. Benefit>>>risk. Additional studies with focused objectives needed.
  - Class IIb: usefulness/efficacy is less well established by evidence/opinion. Procedure/treatment may be considered. Benefit≥≥risk. Additional studies with broad objectives needed; additional registry data would be helpful.
- Class III: conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful. Risk≥benefit. No additional studies needed. Procedure/treatment should not be performed/administered because it is not helpful and may be harmful.

Level of evidence

- A: data derived from multiple randomized clinical trials or meta-analyses
- B: data derived from a single randomized trial or nonrandomized studies
- C: Only consensus opinion of experts, case studies, or standard of care

Figure 2: From (6) for "Cardiac Effects of Medications Used to Treat ADHD."
D: dopamine
NE: norepinephrine
NT: neurotransmitter
HR: heart rate
BP: blood pressure
S: serotonin.

Medications	Mechanism of Action	Cardiac Effects and Comments	Recommendations for Cardiovascular Monitoring: Class I, Level of Evidence C	Recommendations for Cardiovascular Monitoring: Class IIa, Level of Evidence C
Methylphenidate (Ritalin, Ritalin SR, Concerta, Metadate, Methylin, Focalin, Daytrana)	Release and/or inhibit reuptake of catecholamines (eg, D and NE) increase level of these NT at the synapse[94]	Increased HR and BP, no ECG changes[107]	BP, HR	ECG on first visit
Amphetamine (Dextroamphetamine, Dextrostat, Adderall, Vyvanse)	Release and/or inhibit reuptake of catecholamines (eg, D and NE) increase level of NT at the synapse[94]	Increased HR and BP, no ECG changes[107]	BP, HR	ECG on first visit
Atomoxetine (Strattera)	Selective norepinephrine reuptake inhibitor[122]	Increased HR and BP in adults and children, palpitations in adults, no ECG changes[122,154,155]	BP, HR[91,155]	ECG on first visit[91,155]

Discussion

- Etiology of NCM is unclear and it is unknown if stimulant medications contributed to patient's presentation.
- Given risk of increasing heart rate which may exacerbate cardiac issues, stimulant medications were held.
- It is important to monitor patients on stimulant medications for cardiovascular complication throughout their treatment.
- Stimulant use for treatment of ADHD requires evaluation of risks and benefits at initiation, continuation and discontinuation of medications.
- There is no specific set of guidelines available for prescribing stimulants. However, if a patient is noted to have cardiovascular risk factors then further evaluation, medication adjustment and cardiology consultation should be considered.
- Further research is needed to understand the cardiovascular risk of patients in the setting of stimulant use to make appropriate risk-benefit decisions.

Current Recommendations For Stimulant Use

- No widely accepted recommendations for screening/monitoring in setting of stimulant use for treatment of ADHD.
- Given the varying opinions, it is important to:
  - Obtain thorough medical, social and family history (especially of sudden death in young individuals, arrhythmias, prolonged QT, hypertrophic cardiomyopathy, genetic cardiac conditions, Marfan syndrome, etc.)
  - Physical exam
  - Vitals (heart rate and blood pressure) should be checked prior to starting stimulant medications and routinely during treatment.
  - Routine EKG for screening is not required for each patient. However, it should be obtained if cardiac risk factors or clinically warranted due to symptoms.
  - Consider cardiology consultation if indicated by history, physical exam and work-up.

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