Effects of Stimulant Medications on Blood Pressure among a Large, Adult Canadian Cohort

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Background

- ADHD is an increasingly prevalent neurobiological disorder resulting from differences in dopamine and noradrenaline signaling.
- Stimulant medications are first-line therapy for ADHD with possible side-effects, including small but measurable differences in blood pressure (BP), that are best studied in children and adolescents despite the cumulative effects of BP elevations.
- ADHD treatment guidelines currently recommend routine blood pressure monitoring due to reported small, but measurable increases in systolic blood pressure.
- Our objectives were to assess a patient cohort of Canadian adult ADHD patients who recorded ambulatory BPs prior to and throughout titration of ADHD pharmacotherapy.

Methods

- Anonymized data from all patients provided care through PurposeMed's *Frida* Clinical Program (talkwithfrida.com) were eligible for inclusion in this analysis if they self-reported at least 3 home BP measurements and took AHDH pharmacotherapy.
- Descriptive statistics (*median, IQR*) were used to characterize the total and study patient populations. Age was grouped by decade of life and gender were used as stratifications. Co-morbidity data was not available for analysis. Change in BP over a 3-month period was estimated by applying linear regression model to study patients' blood pressure measurements to model the rate of change in blood pressures. Statistical significance was set at p-value ≤0.05 were estimated with Wilcoxon rank sum tests for pairs and Kruskal-Wallis rank some across groups, with the latter corrected using B&H correction. All analysis was completed using R-Studio (v9.3).

Table 3: Changes in systolic and diastolic BP (mmHg) over 3 months	Change in systolic BP (mmHg/3 months)	p-value	Change in diastolic BP (mmHg/3 months)	p-value
Overall	-0.83 (-1.21 to -0.45)	-	-0.33 (-0.67 to -0.04)	-
Age (years) [n; %]		0.53		0.50
18 to 29 [1,267; *41.8*]	-0.75 (-1.21 to -0.14)		-0.14 (-0.52 to 0.13)	
30 to 39 [1,160; *38.3*]	-0.68 (-1.36 to -0.07)		-0.54 (-1.04 to 0.05)	
40 to 49 [432; *14.3*]	-1.48 (-2.51 to -0.53)		-0.69 (-1.29 to 0.15)	
50 to 59 [149; *4.9*]	-0.71 (-4.92 to 0.53)		-0.71 (-1.71 to 0.91)	
60 and older [23; *0.8*]	1.07 (-4.15 to 24.3)		0.81 (-10 to 3.55)	
Gender		0.50		0.87
Female	-0.71 (-1.36 to 0.03)		-0.05 (-0.82 to 0.31)	
Male	-1.38 (-2.63 to 0)		-0.30 (-1.02 to 0.34)	
Transgender & gender diverse	1.03 (-)		0.57 (-)	
Unknown	-0.84 (-1.34 to -0.38)		-0.46 (-0.82 to -0.09)	
Medication use [n; %]				
Any stimulant [2,907; *95.9*]	-0.84 (-1.31 to -0.47)		-0.27 (-0.63 to 0)	
LisdexAMP [2,448; *80.8*]	-0.98 (-1.51 to -0.56)		-0.42 (-0.76 to 0)	
MAS-SR [481; *15.9*]	-0.56 (-1.59 to 0.53)		-0.12 (-0.93 to 0.47)	
MPH-SR [633; *20.9*]	-0.21 (-1.4 to 1.07)		-0.25 (-1.26 to 0.38)	
MPH-CR [95; *3.1*]	-0.35 (-2.08 to 2.05)		0.43 (-1.39 to 3.26)	
DextroAMP [22; *0.7*]	-2.42 (-6.33 to 4.71)		-0.83 (-6.10 to 3.06)	
Bupropion [115; *3.8*]	-0.51 (-2.22 to 1.77)		0.19 (-0.26 to 0.91)	

Results

- 3,031 of 11,947 unique patients met inclusion by having 3 or more BP measurements (median 8, IQR 5-15) that were recorded over a median time of 85 days (IQR 35-157 days). Study patients were non-significantly older (31.7 years of age) than the total patient population and there was significant gender missingness among both populations. Study patients were primarily located in ON (68.2%) with smaller proportions from AB (19.1%) and BC (12.8%).
- Systolic and diastolic BP increases significantly per age decade (118-124 mmHg). Systolic BP was significantly higher among men (123 mmHg) and gender unknown (120 mmHg) patients.
- No **significant increases in systolic or diastolic BP were measured over time in patients taking any or specific ADHD pharmacotherapy** (-2.42 to -0.21; -0.83 to 0.43 mmHg) or in stratified age decades (-1.48 to 1.07 mmHg; -0.71 to 0.81 mmHg), gender (-1.48 to 1.07 mmHg; -0.71 to 0.81 mmHg) on ADHD pharmacotherapy.

Table 1: Descriptive statistics among total and study patients with self-reported blood pressures.	All patients (N=11,947)	Patients with BP reported (N=3,031)
Age (years), median (IQR)	30.7 (26.1 to 36.9)	31.7 (27.0 to 38.4)
Gender, n (%)		
--Woman	2219 (18.6)	649 (21.4)
--Man	1281 (10.7)	378 (12.5)
--Transgender & Gender-diverse	66 (0.6)	21 (0.7)
--Unknown	8381 (70.2)	1983 (65.4)

Table 2: Self-reported blood pressures, by age & gender.	Systolic BP (mmHg)	p-value	Diastolic BP (mmHg)	p-value
Overall	120 (113 to 126)	-	77 (72 to 81.5)	-
Age (years) [n; %]		0.02		<0.001
18 to 29 [1,267; *41.8*]	119 (112 to 125)	Reference	76 (71 to 80.2)	Reference
30 to 39 [1,160; *38.3*]	120 (113 to 126)	0.04	77 (72 to 82)	<0.001
40 to 49 [432; *14.3*]	120 (114 to 126)	0.02	79 (73 to 83)	<0.001
50 to 59 [149; *4.9*]	122 (114 to 128)	0.02	78 (72 to 82.5)	0.002
60 and older [23; *0.8*]	125 (118 to 129)	0.03	76 (73.8 to 80.5)	0.71
Gender		<0.001		0.06
Female	118 (111 to 124)	Reference	76.5 (71 to 81.5)	Reference
Male	123 (118 to 128)	<0.001	78 (73 to 82)	-
Transgender & gender diverse	118 (116 to 126)	0.14	77.5 (74.5 to 86)	-
Unknown	120 (112 to 126)	<0.001	77 (72 to 81.5)	-

Conclusions

Approximately one-quarter of patients utilizing a virtual adult ADHD service provided at least 3 self-recorded BP measurements, with majority of measurements being within the normal range.

Minor age and gender-specific differences in BP were recorded that were statistically significance but not clinically meaningful.

Data missingness was a limitation of this work. Nevertheless, it is highly unlikely that clinically meaningful changes in BP would have been observed as they were not seen among the whole population or among the subset of gender-identified patients.

Next steps of this work include repeated and longitudinal analysis of this population with updated and complete gender, co-morbidity, and complete prescription-list data

Without pre-treatment risk for significant changes in BP or other higher-risk health conditions, it does not appear that routine screening of BP during the treatment of ADHD with stimulant medications is required.

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AMP = amphetamine/amfetamine; MPH = methylphenidate; SR = sustained release; CR = controlled release; LisdexAMP = Vyvanse; MAS-SR = Adderall XR; MPH-SR = Concerta; MPH-CR = Biphentin; DextroAMP = Dexedrine; Bupropion = Wellbutrin