Adulthood Self-Reported Cardiovascular Risk and ADHD Medications: Results From the 2004–2005 National Epidemiologic Survey on Alcohol and Related Conditions

To the Editor: During the past 2 decades, the number of children, adolescents, and adults receiving medications for attention-deficit/hyperactivity disorder (ADHD) has substantially increased and treatment duration has been lengthened.[1] Although placebo-controlled trials have shown that these agents can increase heart rate and blood pressure,[2] raising concerns about their cardiovascular safety,[3–5] no causal relationship between ADHD medications and serious cardiovascular events has been found among children.[6,7] However, few studies have been conducted in the adult population,[8–10] and most of them relied on new ADHD medication users.[9,10] In the largest study conducted among adults, Habel et al[8] reported that current or new use of ADHD medications with a median exposure duration of 6 months, compared with nonuse or remote use, was not associated with an increased risk of myocardial infarction, sudden cardiac death, or stroke. However, this finding needs to be replicated in a large sample of adults with a *DSM-IV* diagnosis of ADHD to examine whether a longer exposure duration to ADHD medications may increase the adulthood risk of serious cardiovascular events.[3] In addition, whether ADHD medications may increase the risk of angina pectoris has not been examined so far.

Method. On the basis of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC),[11] a nationally representative survey of US civilian noninstitutionalized adult population, we investigated the association between ADHD medications and self-reported severe cardiovascular events in naturalistic conditions. Using data from the NESARC, Bernardi et al[12] identified through a structured face-to-face diagnostic interview 807 subjects with a *DSM-IV* diagnosis of ADHD, among whom 27.6% reported having received specific medication for ADHD (N = 216). Peyre et al[13] reported that, among these participants, the median treatment duration was 2.6 years (SE = 0.92), the median age at first prescription was 15.9 years, and 36.2% (SE = 0.81) of them received an ADHD medication during the past year. Participants were asked if during the past year they had a serious cardiovascular event (including myocardial infarction, angina pectoris, and stroke) that was confirmed by a doctor. Logistic regression analyses and a propensity score method were performed to adjust for self-reported risk factors for cardiovascular diseases[14] using SUDAAN version 10 (RTI International, Research Triangle Park, North Carolina).

Results. Among ADHD participants, the 12-month incidence of self-reported serious cardiovascular events in those who received ADHD medication was 11.78% [N = 27] and 8.01% [N = 49] in those who were never treated (Table 1). There was no significant difference in serious cardiovascular events between groups (adjusted odds ratio [AOR] [95% CI]: 1.57 [0.79–2.72]; $P = .219$). In addition, there was no significant association between self-reported serious cardiovascular events and the exposure duration to ADHD medications (AOR: 1.05 [0.98–1.12]; $P = .163$) and between those who received an ADHD medication during the past year and those who received an ADHD medication before the past year (AOR: 0.72 [0.22–2.39]; $P = .531$).

After adjustments for cardiovascular risk factors were made, we found no significant association between the use of ADHD medications or the duration of use and the 12-month incidence of self-reported serious cardiovascular events in adults.

Table 1. Comparing the 12-Month Incidence of Self-Reported Serious Cardiovascular Events Among Adults With a *DSM-IV* Diagnosis of ADHD Between Those Who Received ADHD Medication and Those Who Never Received ADHD Medication in the 2004–2005 NESARC[a]

Variable	ADHD With Medication (N = 216)	ADHD Without Medication (N = 591)	Wald F[c]	P Value
Cardiovascular disease risk factors[b]				
Nonmodifiable risk factors				
Age, y, mean (SE)	35.93 (0.84)	41.01 (0.63)	23.21	< .001
Male	56.54 (3.98)	59.51 (2.37)	0.38	.543
Modifiable risk factors				
Hypertension	24.38 (3.20)	24.90 (2.07)	0.02	.893
Tobacco use in the last 12 mo	48.68 (3.95)	40.70 (2.55)	2.92	.097
Pack years,[d] mean (SE)	7.54 (0.99)	8.55 (0.82)	0.59	.447
Diabetes mellitus	10.30 (2.22)	8.03 (1.53)	0.74	.395
Physical activities (< 1 time per wk)	16.76 (3.20)	19.24 (2.12)	0.37	.545
Hypercholesterolemia	21.06 (3.29)	20.37 (1.95)	0.03	.855
Obesity (BMI > 30 kg/m^2)	33.93 (4.57)	31.36 (2.28)	0.27	.608
Serious cardiovascular events within the last 12 mo, % (SE) [n]			Wald F[e]	P Value
Myocardial infarction	1.21 (0.71) [3]	0.81 (0.34) [7]	NA	NA
Stroke	0.30 (0.30) [1]	1.26 (0.50) [8]	NA	NA
Angina pectoris	11.49 (2.53) [26]	6.94 (1.26) [42]	2.38	.132
Any serious cardiovascular event listed above	11.78 (2.53) [27]	8.01 (1.31) [49]	1.57	.219

[a]Values shown as % (SE) unless otherwise noted.
[b]Derived from the 2011 Global Atlas on Cardiovascular Disease Prevention and Control (World Health Organization in collaboration with the World Heart Federation and World Stroke Organization).[14]
[c]Wald F values were estimated using Wald F statistics ($df = 1, 65$).
[d]Pack-years of smoking history (ie, number of packs of cigarettes smoked per day multiplied by the number of years smoked).
[e]Wald F values were adjusted for a propensity score to control for differences between groups in cardiovascular disease risk factors (ie, age, sex, hypertension, tobacco use in the last 12 months, tobacco pack years, diabetes mellitus, physical activity, hypercholesterolemia, and obesity) and estimated using Wald F statistics ($df = 2, 65$).
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, BMI = body mass index, NA = not applicable, NESARC = National Epidemiologic Survey on Alcohol and Related Conditions.

Our study has several limitations. First, cardiovascular risk factors and serious cardiovascular events were self-reported, possibly underestimating their incidence. Second, the present study could be underpowered to detect a small difference between groups. Last, data on certain risk factors (eg, unhealthy diet), other serious cardiovascular events (eg, sudden cardiac death), and daily dose of medications were not available.

Therefore, the findings from this study should be interpreted with caution. As ADHD medications may increase the risk for sudden death in patients with structural cardiac abnormalities, the current guidelines[15] recommend a medical evaluation prior to starting stimulant treatment and periodic monitoring of pulse and blood pressure during treatment.

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