Assessment of potential cardiovascular risks of methylphenidate in comparison with sibutramine: do we need a SCOUT (trial)?

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Abstract
With the recent approval of methylphenidate (MPH) for treating attention-deficit/hyperactivity disorder (ADHD) in adults, the number of patients exposed will increase tremendously. The ongoing debate on the cardiovascular safety of MPH has triggered two large retrospective cohort studies in children and adolescents as well as in young to middle-aged adults. These studies looked into serious cardiovascular events (sudden cardiac death, acute myocardial infarction and stroke) as primary endpoints and concluded that MPH was safe after a mean duration of 2.1 years of follow-up in children and adolescents and mean duration of 0.33 years of current use in adults. The results are encouraging with respect to the short- and medium-term use of MPH. Without the inherent limitations of retrospective cohort studies, a prospective randomized, double-blind, placebo-controlled, multicenter trial in individuals stratified for cardiovascular risk factors would allow for an optimized risk assessment. With many millions of patients treated per year and drawing parallels to the lately discovered risks of sibutramine, another sympathomimetic with an overlapping mode of action and similar side effects on heart rate and blood pressure, we hypothesize that such a trial might be a dedicated risk mitigation strategy for public health. A critical assessment of cardiovascular side effects of MPH appears particularly warranted, because ADHD is associated with obesity, smoking and poor health in general. We summarize recent findings with the focus on cardiovascular risks of MPH in humans; we additionally analyze the limited number of rodent studies that have addressed cardiovascular risks of MPH.