

Avoidance of β -blockers in patients who use stimulants is not supported by good evidence

Tyler Wilson MD, Ian Pitcher MD, Paxton Bach MD MSc

■ Cite as: *CMAJ* 2022 January 31;194:E127-8. doi: 10.1503/cmaj.211347

Physicians often hesitate to prescribe β -blocker therapy for patients who actively use stimulants, even for indications such as heart failure with reduced ejection fraction and tachyarrhythmias, worrying that potentially harmful interactions will outweigh well-established benefits.¹ The American Heart Association guidelines for the management of non-ST elevation myocardial infarction (NSTEMI), published in 2014, advise against using β -blockers in acute myocardial infarction with signs of acute stimulant intoxication, unless patients are also receiving a coronary vasodilator.² Outside of acute stimulant intoxication, however, these guidelines state that patients presenting with NSTEMI and recent stimulant use should receive the same care as patients who do not use stimulants. A Canadian guideline on heart failure makes no specific recommendations for or against the use of β -blockers in patients who use stimulants.³ We argue that in the absence of guidance to the contrary, doctors should reconsider their tendency to withhold β -blockers from patients who use stimulants.

Hesitancy to prescribe β -blockers for patients who use stimulants is primarily informed by our understanding of pharmacodynamics. Cocaine and crystal methamphetamine promote release of neurotransmitters such as norepinephrine and epinephrine. Subsequent stimulation of β -1 receptors increases heart rate and cardiac contractility, and β -2 receptors promote smooth muscle relaxation. Alpha-1 receptors, on the other hand, induce vasoconstriction.^{1,4} Until recently, experts have opined that in the context of stimulant use, β -blockers may lead to “unopposed α -receptor stimulation,” which could result in vasoconstriction with no compensatory smooth muscle relaxation.¹ This in turn could lead to cardiac ischemia, hypertension and subsequent cardiovascular complications.

Concerns about unopposed α -receptor stimulation were originally supported by a small study published in 1990, in which 15 participants underwent cardiac catheterization and were given intranasal cocaine followed by intracoronary propranolol.¹ The authors observed increased coronary artery vasoconstriction after administration of propranolol, but no change in systemic blood pressure. A single patient developed acute ST elevation and symptoms of myocardial ischemia, which were reversed with sublingual nitroglycerin. The generalizability of this study was limited by its small size, the use of the nonselective β -blocker

Key points

- Patients who use stimulants such as crystal methamphetamine and cocaine often have cardiovascular conditions for which β -blockers are part of the standard of care.
- Many clinicians are hesitant to prescribe β -blockers in the setting of active stimulant use owing to a perceived risk of “unopposed α -receptor stimulation.”
- Evidence does not support a high risk of harms from the combination of β -blockers and stimulants, and the best available evidence suggests long-term β -blockers are safe in the context of stimulant use.
- Until there is clear evidence of harm, patients with stimulant use disorder and concurrent cardiac comorbidities deserve to be offered the standard of care, including discussion on the risks and benefits of β -blocker therapy.

propranolol (which is infrequently prescribed for cardiac conditions) and its intracoronary administration. In a follow-up study, 15 participants underwent cardiac catheterization and were given intranasal cocaine followed by intravenous labetalol, a β -blocker with additional α -blocking properties.⁵ In this study, no worsening coronary vasoconstriction was seen and, in fact, labetalol decreased systemic blood pressure.

Since this initial experiment, several other studies have looked at both the treatment of acute stimulant toxicity and long-term β -blocker therapy in patients with ongoing stimulant use. A 2016 systematic review that included 50 studies comprising 1744 patients examined the treatment of acute hyperadrenergic symptoms from cocaine with β -blockers.⁶ Only 7 cases of potential adverse drug effects, including changes in blood pressure or new cardiac symptoms, were identified in this review; however, the causal association with β -blockers was unclear. No adverse events were attributed to β -blockers with α -blocking properties such as carvedilol or labetalol. A 2018 systematic review identified 5 retrospective cohorts examining 1794 patients presenting to the emergency department with cocaine-associated chest pain.⁷ There were no differences in the rates of in-hospital all-cause mortality or nonfatal myocardial infarctions associated with the prescription of β -blockers to people using cocaine.

Less information exists related to amphetamines. A 2015 systematic review of the treatment of amphetamine toxicity identified 19 studies with 227 patients, 3 of whom experienced possible adverse reactions: 1 patient had a transient, mild elevation of blood pressure, and 2 experienced recurrent chest pain.⁸

With respect to long-term therapy, a 2020 systematic review identified 3 retrospective cohort studies comparing outcomes of patients with cocaine-associated cardiomyopathy treated with and without β -blockers.⁹ The authors found insufficient evidence to infer harm, and concluded that available data suggested reduced hospital admission rates and 30-day mortality among patients treated with β -blockers. Another separate retrospective cohort study looked at 503 patients with heart failure and a comorbid cocaine-use disorder treated with carvedilol.¹⁰ Patients with heart failure with reduced ejection fraction treated with carvedilol had a lower rate of cardiovascular death and 30-day hospital readmission than those without β -blockade, despite 69% of participants reporting ongoing cocaine use at least once per week. Taken together, these results suggest that β -blockers are not only safe but effective.

In summary, although several case reports and a cardiac catheterization study have led to concerns about the use of β -blockers in people who use stimulants, a large body of higher-quality evidence has failed to show real-world risks to prescribing β -blockers in the setting of stimulant use. We argue that clinicians should include patients in decision-making, rather than unilaterally withholding β -blockers, and individualize approaches based on the risks of harm, the anticipated magnitude of benefit, and the availability of alternative treatments for a given condition.

Current evidence and guidelines support the use of β -blockers for many cardiac conditions. Given that people who use drugs already face frequent stigmatization and inequitable access to health care, it is critical that the provision of certain treatments is not made conditional on abstinence from substances without the support of strong empirical evidence to justify such a decision.

References

1. Lange RA, Cigarroa RG, Flores ED, et al. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med* 1990;112:897-903.
2. Amsterdam EA, Wenger Nanette K, Brindis Ralph G, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes [published erratum in *Circulation* 2014;130:e433-4] *Circulation* 2014;130:e344-426.
3. McDonald M, Virani S, Chan M, et al. CCS/CHFS heart failure guidelines update: defining a new pharmacologic standard of care for heart failure with reduced ejection fraction. *Can J Cardiol* 2021;37:531-46.
4. Reddy PKV, Ng TMH, Oh EE, et al. Clinical characteristics and management of methamphetamine-associated cardiomyopathy: state-of-the-art review. *J Am Heart Assoc* 2020;9:e016704.
5. Boehrer JD, Moliterno DJ, Willard JE, et al. Influence of labetalol on cocaine-induced coronary vasoconstriction in humans. *Am J Med* 1993;94:608-10.
6. Richards JR, Garber D, Laurin EG, et al. Treatment of cocaine cardiovascular toxicity: a systematic review. *Clin Toxicol (Phila)* 2016;54:345-64.
7. Pham D, Addison D, Kayani W, et al. Outcomes of beta blocker use in cocaine-associated chest pain: a meta-analysis. *Emerg Med J* 2018;35:559-63.
8. Richards JR, Albertson TE, Derlet RW, et al. Treatment of toxicity from amphetamines, related derivatives, and analogues: a systematic clinical review. *Drug Alcohol Depend* 2015;150:1-13.
9. Arenas DJ, Beltran S, Zhou S, et al. Cocaine, cardiomyopathy, and heart failure: a systematic review and meta-analysis. *Sci Rep* 2020;10:19795.
10. Banerji D, Alvi RM, Afshar M, et al. Carvedilol among patients with heart failure with a cocaine-use disorder. *JACC Heart Fail* 2019;7:771-8.

Competing interests: Paxton Bach reports receiving funds from the Michael Smith Foundation for Health Research, a grant from the Canadian Institutes of Health Research, and speakers' honoraria from University of British Columbia Continuing Professional Development, Pharmacy Leaders of Tomorrow, Eastern Health and the BC Centre on Substance Use. Dr. Bach also reports membership on a Data Safety Monitoring Board for Evaluating Microdosing in the Emergency Department and is Co-Medical Director, BC Centre on Substance Use. No other competing interests were declared.

This article has been peer reviewed.

Affiliations: Department of Medicine (Wilson, Pitcher, Bach) and of Cardiology (Pitcher), University of British Columbia; British Columbia Centre on Substance Use (Wilson, Bach), St. Paul's Hospital, Vancouver, BC

Contributors: All of the authors contributed to the conception and design of the work, drafted the manuscript, revised it critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Content licence: This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Correspondence to: Tyler Wilson, tyler.wilson@islandhealth.ca