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# The α- and β-adrenergic antagonist controversy with sympathomimetic agents

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## To the Editor

We read with great interest the Letter to the Editor by Richards et. al. (1), published in response to our article on synthetic cathinones, or "bath salts" (2). While we applaud the authors attempt to shed some light on the controversial use of selective β-adrenergic receptor antagonists as treatment for toxicity produced by sympathomimetic agents such as the synthetic cathinones, several statement and claims made by Richards et al., require further clarification. Richards et al., state that they… "routinely utilize intravenous labetalol, a mixed α- and β-blocker, in the treatment of methamphetamine, cocaine and "bath salt" patients, with excellent results." Importantly and underemphasized by these authors is the fact that labetalol possess α-adrenergic receptor antagonistic properties. Additionally, we outlined the important role activation of α- and β-adrenergic receptors play in the cardiovascular and hyperthermic responses seen to sympathomimetic agents such as the synthetic cathinones.

Previously, we had shown in a preclinical model that β-adrenergic receptor antagonists devoid of α-adrenergic receptor antagonistic properties were not affective in attenuating the hyperthermia induced by the sympathomimetic agent, 3,4-methylenedioxymethamphetamine (MDMA, 3). In this same study, we demonstrated that carvedilol, an $\alpha_1$- and $\beta_{1,2,3}$-adrenergic could attenuate MDMA-induced hyperthermia and subsequent rhabdomyolysis (3). Subsequent to our findings with carvedilol, Hysek et al., (4) demonstrated in healthy human subjects that carvedilol could reverse MDMA-mediated increases in blood pressure, heart rate and body temperature. Hysek et al., (5) had previously demonstrated in healthy human subjects that the non-selective β-adrenergic receptor antagonist (devoid of α-adrenergic receptor activity), pindolol, inhibited MDMA-induced

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increases in heart rate but was ineffective at preventing the increase in mean arterial blood pressure. These studies indicate that β-adrenergic receptor antagonism without α-adrenergic antagonism is ineffective at reversing the hemodynamic and hyperthermic effects of MDMA. Thus, the positive outcomes seen by Richards et al., through the use of labetalol is predictable and consistent with recommendations by the American Heart Association/ American College of Cardiology Foundation Guidelines (6) supporting the use of a combined α- and β-adrenergic receptor antagonist, such as labetalol or carvedilol, as a treatment option for myocardial infarction and unstable angina induced by cocaine and methamphetamine.

Based on these preclinical and human data and the current Guidelines (6), we would suggest physicians avoid a non-discriminating approach to selecting β-blockers in treating patients with sympathomimetic exposure and use a combined α- and β-adrenergic receptor antagonist such as labetalol or carvedilol (6). All β-blockers are not created equal as Richards et al, letter may have inadvertently suggested.

## References

1. Richards JR, Laurin EG, Albertson TE. Beta-blocker use for toxicity from “bath salts”. J Emerg Med. 2015; 48(2):e45–6. [PubMed: 25453853]
2. Banks ML, Worst TJ, Rusyniak DE, Sprague JE. Synthetic cathinones (“bath salts”). J Emerg Med. 2014; 46(5):632–42. [PubMed: 24565885]
3. Sprague JE, Moze P, Caden D, Rusyniak DE, Holmes C, Goldstein DS, Mills EM. Carvedilol reverses hyperthermia and attenuates rhabdomyolysis induced by 3,4-methylenedioxymethamphetamine (MDMA, Ecstasy) in an animal model. Crit Care Med. 2005; 33(6):1311–6. [PubMed: 15942349]
4. Hysek CM, Schmid Y, Rickli A, Simmler LD, Donzelli M, Grouzmann E, Liechti ME. Carvedilol inhibits the cardiostimulant and thermogenic effects of MDMA in humans. Br J Pharmacol. 2012; 166(8):2277–88. [PubMed: 22404145]
5. Hysek CM, Vollenweider FX, Liechti ME. Effects of a β-blocker on the cardiovascular response to MDMA (Ecstasy). Emer Med J. 2010; 27:586–87.
6. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE Jr, Chavey WE, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wemger NK, Wright RS. 2012 ACCF/AHA focused update incorporated into the ACCF/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013; 61(23):e179–347. [PubMed: 23639841]