with physicians [6,7]. Useful discussions that might result in long-term cost-savings include switching to lower cost alternatives, using generics, and stopping or withholding interventions, drug coupons, changing pharmacies to save money, or prescribing 90-day supplies of medications instead of 30-day supplies [8]. More comprehensible information on insurance coverage and greater price transparency could facilitate identification of cost-saving options [6].

We found that dedicated social work and case management services in the ED are invaluable in helping older patients access prescribed medications at lower costs, while simultaneously addressing a myriad of psychosocial risks and other economic concerns [5]. Social workers also can provide services such as telephoning aged patients after discharge, reinforcing prescription compliance, arranging transportation, and coordinating referrals to community service agencies. Discharge planning without addressing the underlying risk factors for CRMN can drive avoidable ED utilization and hospital readmissions.

References

[1] Mazer M, Bisgaier J, Dailey E, Srivastava K, McDermoth M, Datner E, et al. Risk for cost-related medication non-adherence among emergency department patients. Acad Emerg Med 2011;18(3):267–72.

[2] Kennedy J, Coyne J, Sclar D. Drug affordability and prescription noncompliance in the United States: 1997–2002. Clin Ther 2004;26(4):607–14.

[3] Olshaker JS, Barish RA, Naradzay JF, Jerrard DA, Safir E, Campbell L. Prescription noncompliance: contribution to emergency department visits and cost. J Emerg Med 1999;17(5):909–12.

[4] Cutler RL, Fernandez-Llimos F, Frommer M, Benrimoj C, Garcia-Cardenas V. Economic impact of medication non-adherence by disease groups: a systematic review. BMJ Open 2018;8(1):e016982.

[5] L. Ouellette, R. Halasa, A. Brown, R. Beckett, D. Patel, T. Chassee, and J.S. Jones, Prescription drug assistance for elderly patients in the emergency department. Am J Emerg Med, Oct 25, 2108, [Epub ahead of print].

[6] Hunter WG, Zhang CZ, Hesson A, Davis JK, Kirby C, Williamson LD, et al. What strategies do physicians and patients discuss to reduce out-of-pocket costs? Analysis of cost-saving strategies in 1,755 outpatient clinic visits. Med Decis Making 2016;36(7):900–10.

[7] Alexander GC, Casalino LP, Land D.O. Meltzer. Patient-physician communication about out-of-pocket costs. JAMA 2003;290(7):953–8.

[8] Martin KR, Shreffler J, Schoster B, Callahan LF. Coping with prescription medication costs: a cross-sectional look at strategies used and associations with the physical and psychosocial health of individuals with arthritis. Ann Behav Med 2012;44(2):236–47.

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Another dogma dispelled? Antipsychotic treatment of sympathomimetic toxicity

To the Editor,

We would like to congratulate Connors and associates on their excellent systematic review on the use of antipsychotics for sympathomimetic toxicity, which included our emergency department studies comparing droperidol to lorazepam for agitation and experience treating amphetamine toxicity [1-4]. The authors mention a dogma that has persisted for decades regarding this issue: "Some authors discourage using antipsychotics owing to the hypothesis that these medications lower seizure threshold, predispose to cardiac dysrhythmias, and decrease heat dissipation." Emergency physicians who routinely care for agitated patients frequently disregard this opinionated contraindication. Antipsychotics represent an important treatment option, especially when multiple and escalating doses of benzodiazepines fail. Furthermore, as affirmed by the authors, it is usually impossible to ascertain if agitation is precipitated by psychiatric illness or sympathomimetic toxicity in the acute care setting, as these patients often cannot provide a cogent history. The authors' conclusion that no "significant signal of harm" was identified parallels findings from our systematic reviews and experience regarding antipsychotic treatment of amphetamine and cocaine toxicity [5,6].

Dogma, such as forbidding the use of antipsychotics for sympathomimetic toxicity (and also acute ethanol withdrawal), continue to be cited by some physicians despite contrary, limited and/or inconsistent evidence. Systematic reviews, such as the one by Connors et al., are important to gather, critique, and discuss available evidence in an objective manner in contrast to "expert opinion" with preferentially-selected references [1,5,6]. Regrettably, some experts, especially those who have previously published or lectured on the topic, may refuse to reverse or temper their opinions despite the findings of systematic reviews such as these. Fortunately for the advancement of medical knowledge and research, these individuals represent a minority.

The authors write "Pharmacological sedation options are limited to benzodiazepines, ketamine, and antipsychotic medications, though central alpha adrenergic antagonists and NMDA receptor antagonists are in the early stages of evaluation." [1]. We note the authors did not include antihistamines, which are sedating and can preclude akathisia and dystonia from antipsychotics. We also believe lipophilic beta adrenergic antagonists such as metoprolol and combined alpha/beta adrenergic antagonists such as labetalol represent further treatment options, with mitigation of central and peripheral nervous system hyperadrenergic effects [7]. We recognize the use of this class of medication for the treatment of sympathomimetic toxicity is also subject to dogma, as previously highlighted by two of the co-authors of this review in their correspondence regarding the safety of beta-blockers in the acute management of cocaine-associated chest pain, our correspondence, and a dedicated review article [8-10]. We have routinely utilized metoprolol and labetalol in our treatment of agitated, hypertensive, and tachycardic patients with sympathomimetic toxicity over the past several decades with efficacious and safe results.

In addition to dogmatists who forbid the use of antipsychotics for this patient subgroup, we have also encountered a cabal of clinicians who believe inflexibly in benzodiazepine monotherapy. When asked what should be done for the agitated patient who has received multiple and increasing doses of benzodiazepines, their response is simply "Give them more" rather than consider the synergy between the aforementioned medications to achieve sedation with less risk of respiratory depression from excessive

benzodiazepines [11]. We agree with the authors' conclusion: "We encourage clinicians to adapt treatment based on specific circumstances and characteristics of their individual patients." Emergency physicians on the front line caring for agitated patients should choose the most effective, rapid, and safe combination of medication based on their education, experience, objective evidence, and not the outdated opinions of a few.

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References

[1] Connors NJ, Alsakha A, Larocque A, Hoffman RS, Landry T, Gosselin S. Antipsychotics for the treatment of sympathomimetic toxicity: a systematic review. Am J Emerg Med 2019;37:1880–90.
[2] Richards JR, Derlet RW, Duncan DR. Chemical restraint for the agitated patient in the emergency department: lorazepam versus droperidol. J Emerg Med 1998;16(4):567–73.
[3] Richards JR, Derlet RW, Duncan DR. Methamphetamine toxicity: treatment with a benzodiazepine versus a butyrophenone. Eur J Emerg Med 1997;4(3):130–5.
[4] Derlet RW, Rice P, Horowitz BZ, Lord RV. Amphetamine toxicity: experience with 127 cases. J Emerg Med 1989;7(2):157–61.
[5] Richards JR, Albertson TE, Derlet RW, Lange RA, Olson KR, Horowitz BZ. Treatment of toxicity from amphetamines, related derivatives, and analogues: a systematic clinical review. Drug Alcohol Depend 2015;150:1–13.
[6] Richards JR, Garber D, Laurin EG, Albertson TE, Derlet RW, Amsterdam EA, et al. Treatment of cocaine cardiovascular toxicity: a systematic review. Clin Toxicol (Phila) 2016;54(5):345–64.
[7] Luauté J, Plantier D, Wiart L. Tell L; SOFMER group. Care management of the agitation or aggressiveness crisis in patients with TBI. Systematic review of the literature and practice recommendations. Ann Phys Rehabil Med 2016;59(1):58–67.
[8] Connors NJ, Bajaj T, D'Angelo M, Howland M, Hoffman RS. In response to "Safety of beta-blockers in the acute management of cocaine-associated chest pain". Am J Emerg Med 2013;31(6):986–7.
[9] Derlet RW, Horowitz BZ. Cocaine-associated myocardial ischemia. N Engl J Med 1996;334(8):535–6.
[10] Richards JR, Hollander JE, Ramoska EA, Fareed FN, Sand IC, Izquierdo Gómez MM, et al. β-Blockers, cocaine, and the unopposed α-stimulation phenomenon. J Cardiovasc Pharmacol Ther 2017;22(3):239–49.
[11] Yap CYL, Taylor DM, Knott JC, Taylor SE, Phillips GA, Karro J, et al. Intravenous midazolam-droperidol combination, droperidol or olanzapine monotherapy for methamphetamine-related acute agitation: subgroup analysis of a randomized controlled trial. Addiction 2017;112(7):1262–9.

Evidence over dogma and anecdotes

Keywords:
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Sympathomimetic toxicity

To the Editor:

We thank the authors for their interest in our work and their complimentary assessment of our systematic review. We agree that dogma without some foundation in evidence can be counterproductive. Unfortunately the authors also introduced their opinions about issues not within the scope of our review. As such, the propagation of anecdotal care without scientific basis is equally counterproductive. Specifically, their assertions about the utility of antihistamines, lipophilic beta-adrenergic antagonists, and multiple combined therapies are offered without providing the level of supporting evidence that we provided for the therapies within the chosen scope of work. Likewise their unsupported personal communications with unspecified clinicians have no place in evidence based medicine. Finally, they misinterpret our inability to find a signal of harm as evidence of safety. These two statements are quite distinct and rarely, if ever, to be used interchangeably.

While we agree that better evidence is needed, the answers we seek are likely only to be found in controlled trials that are well designed, rigorously implemented, and thoroughly analyzed. We strongly reject the notion that the appearance of safety in anecdotal and uncontrolled interventions should take precedence over the need to prove efficacy. While it is challenging to make rapid decisions in uncertain and life-threatening circumstances we must shift the focus of knowledge translation away from statements that begin with "we routinely…" toward ones that sound like "the evidence shows that..." or "the evidence suggests that…." We hope that our systematic review helps shift that focus.

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