ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY
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The Maryland Poison Center's Monthly Update: News, Advances, Information

Beyond the Opioid Bubble: Naloxone in Non-Opioid Overdose

Naloxone, a pure μ-opioid receptor antagonist, reverses opioid toxicity by displacing opioids from their receptors. Since its approval in 1971, it has become a cornerstone antidote amid the opioid epidemic. While its efficacy in opioid overdose is well established, emerging evidence suggests potential utility beyond the traditional "opioid bubble."[1]

Clonidine

Management of clonidine toxicity remains largely supportive, including IV fluids, atropine for symptomatic bradycardia, and other targeted interventions. Although the mechanism is unclear, clonidine's central effects may be partially mediated through the endogenous opioid system, providing a rationale for naloxone use.

In a retrospective cohort of 52 pediatric patients with clonidine toxicity, 40 of 51 (78%) somnolent patients awoke after naloxone administration (2-10 mg), though improvement in hypotension and bradycardia was less consistent.[2] A case report also described reversal of prolonged sedation in an adult who received clonidine intraoperatively after a total naloxone dose of 2 mg.[3]

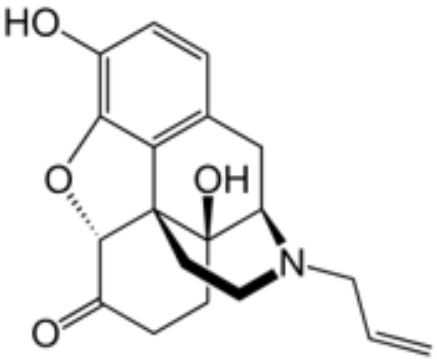
Many toxicologists recommend higher naloxone doses (4-10 mg) for clonidine toxicity, which may help avoid invasive ventilation. Responses to other α_2-agonists are less predictable. Given the complexity of these cases, consultation with a poison center is recommended.

Angiotensin-Converting Enzyme Inhibitors (ACEIs)

ACEI-induced hypotension may also involve the endogenous opioid system, prompting investigation of naloxone for refractory overdose-related hypotension. Successful use has been reported following captopril and lisinopril overdoses.

Trivedi et al. described a patient with combined amlodipine and perindopril overdose who remained profoundly vasoplegic despite several days of standard therapy. Following aliquots totaling 10.6 mg of naloxone and a continuous infusion, vasopressor requirements decreased substantially within an hour.[4] High-dose naloxone may therefore be considered in cases of severe, prolonged ACEI-associated hypotension that is refractory to standard supportive measures.

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Naloxone

Did you know?

Naloxone gets it name from the chemical structure "N-al (n-allyl group), -ox- (derived/modified from oxymorphone), -one (ketone functional group).

References:

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2. Seger DL, Loden JK. Naloxone reversal of clonidine toxicity: dose, dose, dose. *Clin Toxicol (Phila)*. 2018;56(10):873-879. doi:10.1080/15563650.2018.1450986
3. Swift A, Wilson M. Reversal of the effects of clonidine using naloxone. *Anaesth Rep*. 2019;7(1):4-6. doi:10.1002/anr3.12004
4. Trivedi V, Glezerson BA, Chaudhuri D, Davidson M, Douflé G. Naloxone as an antidote for angiotensin converting enzyme inhibitor poisoning: a case report. *Can J Anaesth*. 2020;67(10):1442-1443. doi:10.1007/s12630-020-01680-x

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Conclusion

Evidence from case reports and retrospective studies suggests naloxone may have applications beyond opioid overdose. Although it should not replace standard supportive care, it may be a useful adjunct particularly in clonidine-induced sedation and refractory ACE inhibitor-associated hypotension. For patient-specific recommendations, contact your local poison center at 1-800-222-1222.