

Pharmacological Arguments Against the Use of Ketamine in Nonmedical Settings

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On behalf of the **ACCP Public Policy Committee**

The American College of Clinical Pharmacology strongly opposes the nonmedical use of ketamine for law enforcement purposes in individuals who do not have a justifiable medical reason to warrant its administration.

Ketamine is a dissociative anesthetic agent that is approved by the US Food and Drug Administration (FDA) for the following indications: (1) as the sole anesthetic for diagnostic and surgical procedures that do not require skeletal muscle relaxation; (2) for the induction of anesthesia prior to the administration of other general anesthetic agents; and (3) as a supplement to other anesthetic agents.¹ The FDA-approved dosage and administration specifications on the drug label state that ketamine should be administered “by or under the direction of physicians experienced in the administration of general anesthetics, maintenance of a patent airway, and oxygenation and ventilation.” Providers are instructed to “continuously monitor vital signs in patients receiving ketamine” and that “emergency airway equipment must be immediately available.”

Recently, increased attention has been called to the use of ketamine as a means for chemically incapacitating individuals in law enforcement scenarios in the United States. Two separate incidents occurring in Colorado in 2019 were reported in the lay press, garnering national awareness.² These incidents involved the use of ketamine in the field to subdue 2 male individuals involved in a law enforcement interaction; one encounter resulted in the individual requiring life support, and the other ended in fatality. In 1 case, the total administered ketamine dose was markedly higher than the labeled dosing for an individual of such body weight.

These incidents and others prompted several professional and medical organizations to issue statements opposing the practice of nonmedical use of ketamine for law enforcement purposes. The American Medical Association, the largest national professional association of physicians and medical students, announced

its opposition to the use of sedative/hypnotic and dissociative drugs, including ketamine, in a law enforcement setting without a legitimate medical reason in June 2021. While one of the publicized cases of ketamine use by law enforcement revealed paramedic logs documenting that the individual suffered from “excited delirium,” the American Medical Association also announced in this statement that current evidence does not support “excited delirium” as an official diagnosis and denounces “excited delirium” as a sole justification for use of excessive force by law enforcement.³ Similarly, in 2020, the American College of Emergency Physicians and the American Society of Anesthesiologists issued a collaborative statement to “firmly oppose the use of ketamine or any other sedative/hypnotic agent to chemically incapacitate someone solely for a law enforcement purpose and not for a legitimate medical reason.”⁴ Various other state and national professional organizations of emergency responders and health care providers have issued similar statements clearly opposing the use of ketamine for such nonmedical purposes.⁵ Several jurisdictions, cities, and states across the country are now reviewing their law enforcement programs and policies regarding ketamine.^{6,7}

Ketamine is a noncompetitive N-methyl-D-aspartate receptor antagonist, and it also blocks HCN1 receptors. It is administered intravenously or intramuscularly, and dosing is individualized on the basis of body weight and titrated to the desired effect. Ketamine is a lipid-soluble agent with a large volume of distribution and readily penetrates the central nervous system. It has a rapid onset of action

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and a half-life of ≈ 10 to 15 minutes, and undergoes hepatic metabolism and is excreted in the urine. In addition to producing a dissociative anesthetic state characterized by profound analgesia, ketamine also has pharmacodynamic effects impacting the respiratory and cardiovascular systems. Specifically, ketamine is a potent bronchodilator. Mediated through central and peripheral catecholamine reuptake, ketamine also increases heart rate and cardiac output and elevates blood pressure (typically peaking at a 10%-50% increase in systolic blood pressure and diastolic blood pressure). As such, ketamine is contraindicated for use in patients for whom significant elevations in blood pressure would constitute a serious hazard and carries a warning in its product labeling regarding the risk of respiratory depression that may occur with overdose or too rapid infusion, sometimes requiring supportive ventilation. Other warnings in labeling include the potential for hemodynamic instability, which requires monitoring vital signs and cardiac function during ketamine administration, and the potential for emergence reactions or confusional states that may occur during the recovery period following ketamine administration. The pharmacokinetic and pharmacodynamic properties support the FDA-approved recommendation in the prescribing information that ketamine be administered by experienced providers with supportive measures immediately available. For these same reasons, there are major safety concerns over the growing off-label use of this agent.⁸

In the setting of a law enforcement interaction in the field, an individual's medical history, including any underlying health conditions or concomitant medication usage, is very rarely known. Specifically, an individual's body weight will most likely be unknown in a law enforcement encounter, and would therefore require a rapid, unaided estimate in the field to determine an appropriate ketamine dose for administration—a practice that could and has resulted in under- or overdosing individuals with potentially fatal consequences.

Administration of ketamine to individuals receiving certain concomitant medications can potentially lead to drug-drug interactions with serious implications. For example, administration of ketamine in patients taking theophylline or aminophylline, bronchodilator agents used to treat asthma, emphysema, and other lung problems, may lower the seizure threshold, while concomitant use of ketamine with opioid analgesics, benzodiazepines, or other central nervous system depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Again, knowledge regarding concomitant medication usage is typically lacking during law enforcement encounters but is critical to the safe administration of ketamine and

appropriate monitoring and support during and after administration.

In conclusion, the American College of Clinical Pharmacology joins other professional and medical organizations in strongly opposing the nonmedical use of ketamine for law enforcement purposes in individuals who do not have a justifiable medical reason to warrant its administration. The pharmacological properties of ketamine, including its complex dosing, powerful pharmacodynamic effects, and potential for serious harm or even fatality when used incorrectly, support the argument against its use in this context.

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Conflicts of Interest

J.C.M. is an employee and shareholder of Pfizer Inc. D.J.G. declares no conflicts of interest.

Disclaimer

The opinions expressed in this article are those of the authors on behalf of the American College of Clinical Pharmacology and should not be interpreted as the position of the entities or institutions at which the authors are employed.

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