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Acute pulmonary edema associated with ketamine use in a patient with coronary artery disease

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To the editor,

I read with a great interest the case report from Burmon et al. [1] relating the occurrence of an acute pulmonary edema in an obese 58-year-old patient with a past history of coronary artery disease (CAD), given 50 mg of intravenous ketamine for procedural sedation.

Even if the described extreme pain exerted a potential role, it is unquestionable that ketamine was responsible for an acute hypertensive and tachycardic event (with a heart rate as elevated as 180 bpm), which was obviously a precipitating condition in this patient with CAD. Initial atropine dose was possibly an aggravating process in this setting, because it is known that it takes a while before reducing secretions and because atropine itself has been reported to be responsible for acute events in CAD [2].

Burmon et al. are right when they call our attention to the dangers of the increasing use of ketamine in the ED without a strict protocol; but I believe there is no need for a change in the safety profile of ketamine, because caution is clearly warranted when using ketamine in such patients. CAD has always been a relative contra-indication to the use of ketamine and it has been recognized since the first reports by Domino et al. (in the sixties) that ketamine induced tachycardia and hypertension through sympathetic activation. The fact that this patient with type 2 diabetes and hypertension had benefited from a CABG 10 years before was obviously not a guarantee against the deterioration of her ischemic heart disease.

Having used ketamine in hundreds of patients over more than 25 years, I observed that even very small boluses (10 mg) are seldom responsible for an unexpected tachycardia. The 50-mg intravenous dose over 2 min was clearly not a small bolus, but a definitely dangerous dosage in this context, and, although rare, this kind of clinical response is not completely surprising.

Ketamine sedation must always be carefully titrated, especially in patients with relative contra-indications like patients with a history of ischemic heart disease or hypertension or both. As a professor of anesthesia, I always recommend to begin procedural sedation with little or even very little boluses. Because I seldom observed unexpected unwanted psychological effects with ketamine boluses as small as 5 mg, I personally begin with 2 or 2.5 mg. In most cases, but not always, this very low dosage results in nearly no effect, thus rapidly authorizing (within 1 or 2 min) the administration of a second bolus of 5 mg and then repeated 10 mg boluses if necessary. A very low infusion and the addition of small boluses of propofol (10 mg) are also an option.

Otherwise, the dissociative and antihyperalgesic effects of ketamine mostly arise from the blockade of NMDA channels. Its action on central μ receptors is minor and its analgesic effects are not reversed by naloxone [3]. Other mechanisms imply the blockade of hyperpolarization-activated cyclic nucleotide-gated channels 1 (HCN1 channels), interactions involving noradrenergic and serotoninergic neurons, anti-proinflammatory effects and local anesthetic properties. Its sympathomimetic effects are due to inhibition of catecholamines uptake [4] and also to inhibition of the parasympathetic tone [5].

To conclude, it is important to warn clinicians against the danger of using ketamine without a careful titration. Tachycardia is always of concern in the context of ischemic heart disease. Unlike morphine, ketamine reaches its receptors within no more than 1 min, thus authorizing a rapidly progressing titration. Beginning with very small boluses is not a difficulty because efficient doses may be attained in a few minutes.

Conflicts of interest

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