

Case Files of the University of Massachusetts Fellowship in Medical Toxicology: Lethal Dose of Opioids Contained in an Elastomeric Capsule Labeled as Vancomycin

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CASE STUDY

A 67-year-old man presented to the emergency department (ED) with an alteration in mental status. His past medical history included hypertension, hyperlipidemia, vitamin B₁₂ deficiency, and recurrent cellulitis. In addition to aspirin, atorvastatin, cyanocobalamin, and multivitamins, he received vancomycin 1 g IV every 12 hours via a peripherally inserted central catheter for MRSA cellulitis. Approximately 30 minutes after his wife began his most recent infusion of vancomycin, the patient began slurring his speech. When he became difficult to arouse, his wife activated Emergency Medical Services. The ambulance crew found the patient to be somnolent, but arousable, and breathing adequately. During transport to the ED, however, the patient became unresponsive and had depression in respiratory effort to the point that he required assisted ventilation with supplemental oxygen.

On arrival to the ED the patient's vital signs were: pulse 110 per minute, blood pressure 173/83 mmHg, respiratory rate 4 per minute, oxygen saturation 57% while being assisted with 100% oxygen via bag valve mask, and temperature 36.1° C. On physical examination, there were no signs of physical trauma and pupils were 1–2 mm bilaterally. The patient had agonal respirations with rhonchi heard throughout the lung fields. Other than tachycardia, the cardiovascular and abdominal exams were without gross abnormalities. His skin was ashen, cool, and dry, with delayed capillary refill. The neurological examination showed no spontaneous movements and no response to painful stimuli. Because 2.2 mg IV naloxone produced no improvement in respiratory depression, the patient was endotracheally intubated. Although the patient's wife denied access to or the use of narcotics, the patient's qualitative comprehensive urine toxicology

screen (which could identify 1043 drugs and other chemicals) detected morphine, codeine, and naloxone.

What are the appropriate dosages for the opioid antagonists that are used clinically?

Naloxone was introduced to the US market in 1967, and since that time it has become the preferred antidote for opiate overdose. Naloxone is part of the “coma cocktail,” a combination of naloxone, dextrose, and thiamine that is sometimes administered empirically to intoxicated patients with depressed mental status. Since the introduction of naloxone to the pharmaceutical market in the late 1960s, doses of intravenous naloxone between 0.8 mg and 2.0 mg were used to help establish the diagnosis of opioid overdose [1]. A positive response to these doses of naloxone was considered to be an improvement of respiratory effort and an improvement in the level of consciousness. However, the observation that overzealous administration of naloxone could precipitate opioid withdrawal led to the recommendation that serial doses of 0.1–0.2 mg naloxone be used in patients who are suspected of being opioid dependent, to help restore respiratory effort without precipitating acute opioid withdrawal [2].

Naloxone, and its congeners naltrexone and nalmefene, are competitive antagonists at the μ -, κ -, and Δ -opiate receptors [3]. Naloxone and nalmefene are available in parenteral formulations, while naltrexone is available in only an oral formulation [4]. In one study, which used a dual detector system to observe opiate receptor occupancy time, the authors found that nalmefene occupied μ -receptors in the brains of 8 healthy human volunteers longer than did equipotent doses of naloxone [5]. When the receptors were no longer occupied by either naloxone or nalmefene, a radiolabeled opiate was able to occupy the receptors and

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