NALOXONE-ASSOCIATED PATIENT VIOLENCE: AN OVERLOOKED TOXICITY?

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OBJECTIVE: To report two cases of a previously unreported adverse effect, violent patient behavior, after the reversal of sedation by intravenous naloxone.

DESIGN: Case report.

PATIENTS/INTERVENTIONS: Responses of two individuals who had reversal of sedation by intravenous naloxone are compared.

RESULTS: Placement of patient restraints before the administration of intravenous naloxone to obtunded or unconscious patients can make an important contribution to the safety of patients, healthcare personnel, and public safety personnel, as illustrated by the violent reaction of one unrestrained patient after naloxone administration.

CONCLUSIONS: Patient restraint should be considered before naloxone administration to protect the patient and healthcare workers. In the prehospital setting, limiting the use of naloxone to patients with decreased mental status and respiratory depression would decrease the likelihood of naloxone-induced violent behavior.

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NALOXONE has generally been associated with very few adverse effects.[1-5] Yealy et al. evaluated the adverse gastrointestinal, cardiovascular, and neurologic effects of naloxone after prehospital administration in 813 patients with decreased consciousness. The adverse effects noted were decreased systolic blood pressure (BP) (2 patients), increased systolic BP (1), vomiting (2), and tonic-clonic seizure (1). Most of these effects occurred in patients with concomitant confounding factors, such as recent ipecac ingestion or a prior history of seizures.[6]

Violent or aggressive patient behavior after naloxone reversal of sedation secondary to opioids has not previously been reported.[2,3,5,6] When healthcare providers are unprepared, such violent behavior can be a hazard both to providers and patients. Two cases at our institution illustrate contrasting outcomes following naloxone administration with subsequent violent patient behavior. These cases suggest that planning for physical control or restraint of patients prior to naloxone administration can prevent injury to both patients and personnel.

CASE REPORTS

CASE 1

Paramedics were called to the residence of a 35-year-old man after he was observed by his family to have a decreased level of consciousness. Family members suspected a drug overdose and indicated that the patient had no significant past medical, neurologic, or psychiatric history. The patient was initially cooperative and admitted smoking marijuana laced with phencyclidine (PCP). He complained of dizziness and numbness. He was assisted, but walked without incident from the front porch of his home to the ambulance. At that time his heart rate was 100 beats/min, respiratory rate was 18 breaths/min, and BP was 180/110 mm Hg. Paramedics obtained intravenous access and performed a Dextrostick, measuring a blood glucose concentration of 4.4–6.7 mmol/L. The patient was breathing spontaneously and had a gag reflex. Before contacting the base station physician, the paramedic administered naloxone 2.0 mg iv bolus, later citing as his rationale standing orders permitting the administration of naloxone for altered mental status, as well as a curiosity regarding whether the patient's altered mental status was narcotic-related. The patient abruptly became extremely violent and disconnected his intravenous line. Paramedics, fearing for their safety, called their dispatcher for assistance. Because of his continued and escalating violent behavior, more than ten police and fire personnel were called to the scene to physically subdue the patient with limited success. A base station order by a resident physician for diazepam 5 mg im had little effect. Butorphanol tartrate 2 mg im ordered by the staff attending physician sedated the patient over a period of approximately five minutes. Four-point restraints were placed on the patient in the ambulance, and he was transported to the emergency department (ED) without further incident.

Upon arrival at the ED, the patient was placed prone in four-point leather restraints. Heart rate was 100 beats/min, respirations were 24 breaths/min, BP was 172/98 mm Hg, and electronically recorded oral temperature was 100.3 °F. General physical examination revealed a muscular, well-developed male with no signs of trauma. Needle track marks were noted in the antecubital fossae. The patient was alert; oriented to person, place, and time; and moved all four extremities well. He had no gross sensory deficits. Facies was symmetric and his speech was clear. No nystagmus was noted. The cardiac monitor showed a regular sinus rhythm between 90 and 105 beats/min. Accucheck blood glucose concentration was 11.1 mmol/L. Urine was negative for blood by dipstick. Urine toxicologic screening was not obtained at this time. However, on a return visit for diffuse body aches three days later, the patient's urine was positive for PCP and benzodiazepines, and negative for opiates.

Two hours after arrival for his initial visit, the patient was calm and the restraints were removed. He was alert, fully oriented, appropriate, and requested to be discharged. He denied homicidal or suicidal ideation or any knowledge of narcotic ingestion. The patient was discharged two and a half hours after arrival, after being warned about the risks of PCP use. At this time he was polite and thanked us for his care.

CASE 2

A 31-year-old woman was brought by a friend to the ED because "she looked blue" and had nearly stopped breathing. The friend was unaware of any recent narcotic use by the patient, but stated that the patient had a prior history of narcotic abuse. There was no history of neurologic or psychiatric abnormalities.

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The patient's initial respiratory rate was 4–6 breaths/min, and a gag reflex could not be elicited. She received ventilatory support via bag-valve-mask and had an intravenous line placed. A brief physical survey was significant for 1.5-mm reactive pupils, perioral and acral cyanosis, poor responsiveness to pain, and antecubital needle tracks. In anticipation of narcotic reversal by naloxone, the patient was placed in four-point restraints.

Naloxone 2.0 mg iv bolus was administered. Within 60 seconds the patient was fully awake and combative with slurred speech. Her pupils widened to 3.5 mm. Piloerection of the skin was noted, and the patient yawned repeatedly while complaining that she felt cold. A brisk gag reflex returned. Pulse oximetry documented 97% oxygen saturation.

Because she had been restrained before naloxone was administered, the patient posed no safety threat to herself, other patients, or personnel in the ED After about five minutes she was no longer combative and subsequently volunteered that she had "shot heroin" to relieve toothache pain unalleviated by acetaminophen. She was observed for a five-hour period after receiving activated charcoal 50 g. No repeat doses of naloxone were required. The piloerection and yawning ceased approximately two hours after the naloxone was administered. The patient's urine drug screen was positive for acetaminophen, ethanol, and opiates. Her serum acetaminophen concentration was 0 and her blood alcohol concentration was 59 mmol/L. She was discharged to a dental clinic for treatment, and went home from there without incident.

Sudden reversal of central nervous system (CNS) depression by naloxone may unmask or precipitate unexpected violent patient behavior. The mechanisms involved may be related to the physical discomfort of withdrawal, the confusion of awakening in an unexpected setting, anger at losing the altered mental status "high," the effects of other concomitantly ingested medications no longer opposed by narcotics, underlying personality disorder(s), or other causes. The precipitation of violent behavior can place both the patient and medical personnel at risk for avoidable injury. This risk can be minimized by preemptive placement of restraints when feasible, as illustrated by case 2. Because of our experience with the patient described in case 1, we have begun to more actively discourage the routine prehospital administration of naloxone to patients with diminished levels of consciousness *unless* respiratory depression is also present. The general medical prehospital standing paramedic orders have since been revised to reflect this change.

It is unclear whether case 1 represents a reversal of opiate toxicity or PCP toxicity by naloxone. Studies in humans suggest that naloxone can decrease the anesthetic effects of ketamine, a PCP analog.[7] The patient in case 1 became combative with purposeful activity after intravenous naloxone administration, and was resedated after intramuscular butorphanol administration. Because a drug screen was not performed at the initial hospital visit, a definitive determination of whether opiates were involved could not be made.

The 2-mg dose of naloxone administered to the two patients we have described is the most commonly recommended dose. Although 2 mg was greater than the mean dose used by Yealy et al. it was not greater than the highest dose administered by these investigators (2.4 mg).[6] It remains unclear whether the magnitude of the dose administered to our patients correlates with the development of combative or violent behavior. The proper dosing of naloxone remains controversial.[2,5-7]

The choice of sedative used and its route of administration for the first patient, after he became violent and discontinued his intravenous access line, was limited by the availability of only two injectable agents with CNS depressant effects (diazepam and butorphanol) in the paramedics' drug boxes and by the lack of any intravenous access. It has long been known that diazepam absorption after intramuscular injection is slow and quite variable, hence, the lack of efficacy of this medication is readily explained.

Violent patient behavior is a clinically relevant adverse effect readily anticipatable, but previously not reported following naloxone administration. Combative behavior should be added to the list of previously documented adverse effects of naloxone administration. These include hypertension,[8] pulmonary edema,[9] emesis,[10] seizures,[11] cardiac dysrhythmias,[12] and cardiac arrest.[13] To prevent violent patient behavior and potential physical injury, we suggest that patient restraints be used before the administration of naloxone in the ED or prehospital setting. We also suggest that paramedics' standing orders be revised, if necessary, to encourage prehospital naloxone administration only for cases involving respiratory depression of sufficient severity to cause the paramedic to consider endotracheal intubation of the patient. ≏

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EXTRACTO

Comportamiento violento o agresivo con el uso de naloxona intravenosa para revertir sedación no ha sido informado aún. Informamos dos casos de comportamiento violento después de la administración de naloxona y se contrasta el manejo clínico y el resultado de estos casos. Se sugiere restringir al paciente de sus movimientos antes de administrar naloxona para proteger al paciente y al personal de la salud. En el marco prehospitalario, limitar el uso de naloxona a pacientes con condición mental disminuida y depresión respiratoria disminuye la probabilidad de un comportamiento violento inducido por naloxona.

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RESUME

Aucun comportement agressif n'a été rapporté après avoir renversé la sédation chez 813 patients à l'aide du naloxone administré par voie intraveineuse lors d'une récente revision d'une série de cas sur ces effets secondaires. Nous rapportons ici deux cas de comportement agressif après l'administration de naloxone. L'approche clinique et les résultats de ces cas sont mis en contraste. Dans les deux cas on suggère de restraindre les mouvements du patient avant de lui administrer le naloxone afin de le protèger lui ainsi que les intervenants de la santé. Dans un contexte préhospitalier, limiter l'usage du naloxone chez les patients ayant un statut mental altèré et une détresse respiratoire diminuerait la possibilité d'induire des comportements agressifs avec le naloxone.

CHANTAL GUEVREMONT

SHORT REPORTS

TOPICAL TREATMENT WITH MINOXIDIL 2% AND SMOKING INTOLERANCE

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OBJECTIVE: To report smoking intolerance that occurred in two patients while they were treated with minoxidil.

DATA SYNTHESIS: Minoxidil is a potent vasodilator useful in treating severe hypertension. Topical minoxidil was approved as a treatment for androgenital alopecia. Only few side effects have been reported during treatment with topical minoxidil, most of them localized skin reactions. Two of our patients developed smoking intolerance during treatment with topical minoxidil for androgenital alopecia. The relation between treatment with minoxidil and smoking intolerance was emphasized by stopping treatment and the disappearance of the smoking intolerance, and then by rechallenge in both patients.

CONCLUSIONS: Topical minoxidil may cause smoking intolerance; further studies are needed to evaluation this side effect.

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MINOXIDIL IS A POTENT VASODILATOR used in the treatment of severe hypertension. Hypertrichosis (excessive hair growth) occurs in nearly all patients treated with oral minoxidil for more than four weeks. This side effect has been evaluated in some controlled studies and minoxidil has been proven to be effective in the treatment of male pattern baldness. This drug (in the form of a topical 2% solution) was approved by the Food and Drug Administration in August 1988 for the treatment of men with androgenetic alopecia at the vertex region of the scalp.[1] Only a few adverse effects have been reported with the use of topical minoxidil. These include localized skin reactions (e.g., irritation, pruritus, burning, allergic contact dermatitis)[2-5] and systemic reactions such as headaches,[3] noncardiac substernal chest pain,[2,3] dizziness and weakness, taste alteration,[2] impotence,[2,4] minor electrocardiographic changes,[6] and a mild increase in blood pressure after discontinuation of therapy.[7]

We report on two patients who developed smoking intolerance during topical treatment with minoxidil. We conducted a search of the literature (Medline) and consulted with the manufacturer of the product (Rogaine, Upjohn). To our knowledge, this is the first report dealing with this side effect.

CASE REPORTS

CASE 1

A 42-year-old man with male pattern alopecia of ten years' duration, but otherwise healthy, had a 25-year history of smoking 40 cigarettes/day. He was on no medication. He began treatment with topical minoxidil 2% 1 mL bid. Laboratory studies (hemogram, automated chemistry panel [SMA-12], urinalysis, and electrocardiogram) were within normal limits. Three weeks after the initiation of treatment, the patient reported an intolerance to smoking. He experienced an unpleasant taste sensation when smoking, but reported no other taste alterations or change in appetite. He stopped the treatment after only three weeks. Three days later the smoking intolerance disappeared and he began to smoke again. A week later he resumed the topical minoxidil applications and the phenomenon of smoking intolerance reappeared within 48 hours. The patient continued minoxidil treatment for five months and completely stopped smoking. He is continuing the treatment on a long-term basis and is pleased

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