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Case Reports

Use of dexmedetomidine to treat delirium primarily caused by cannabis☆

Abstract

Dexmedetomidine is increasingly used to treat major withdrawal symptoms and hyperadrenergic crisis. We present 3 young adult cases of cannabis/drug-induced delirium unresponsive to traditional tranquilizer treatment but were responsive to dexmedetomidine as adjunct therapy. All cannabis metabolite urine concentrations were greater than 264 ng/mL upon presentation. Appropriate sedation was achieved within 5 hours in all 3 cases. Thus, dexmedetomidine, along with other tranquilizers, was effective in treating delirium due to cannabis/drug ingestion.

Dexmedetomidine is increasingly used to treat major withdrawal symptoms and hyperadrenergic/crisis [1-4]. To our knowledge, this is the first description of drug/cannabis associated hyperadrenergic delirium (with associated cannabis levels) in young adults treated with dexmedetomidine.

A 21-year-old man, with a history of attention deficit hyperactivity disorder, (treated with amphetamine-dextroamphetamine 30 mg daily, noncompliant for 2 weeks), smoked hashish up to 9 times daily for several months. Last use was 6 days before admission. He had been extremely agitated, combative, had incoherent speech with word salad speech pattern, and was unable to sleep 1 week before admission. His blood pressure was 147/76 mm Hg, with heart rate of 116 to 159 (sinus). Agitation, paranoid ideation, and hallucinations increased more than 13 hours despite receiving chlorpromazine 25 mg intramuscular (IM), benztropine 1 mg IM, olanzapine 20 mg IM, haloperidol 30 mg IM, and lorazepam 6 mg IM. He was placed in locked restraints. His temperature was 102°F and rhabdomyolysis (peak serum creatinine kinase, 13 745 IU/L) subsequently developed. Upon intensive care unit transfer, lorazepam (totaling an additional 11 mg IV more than 5 hours) and dexmedetomidine mean dose 0.4 μg/kg per h were administered. After 3 hours, the fever resolved, he slept, and locked restraints were removed. Tachycardia resolved in 5 hours. Dexmedetomidine was continued a total of 19 hours. Serum tetrahydrocannabinol (THC) and carboxy-THC concentrations were 14.7 ng/mL and greater than 100 ng/mL, respectively, 7 days after last use. The urine carboxy-THC was greater than 500 ng/mL, 7 days after the last reported use; other drugs (including amphetamines and phencyclidine) were negative.

A 20-year-old woman was admitted after a 40-mg alprazolam and 100-mg olanzapine ingestion. She also admitted to smoking hash multiple times daily for 5 weeks. The patient became delirious 3 hours after ingestion. Her blood pressure was 140/53 mm Hg with a pulse of 174. Her pupil size was small with incomprehensible speech. Urine drug analysis was positive for carboxy-THC at 444 ng/mL and α-OH alprazolam at 8013 ng/mL. Dexmedetomidine at a mean intravenous (IV) dose of 0.25 μg/kg per h was started. After 1 hour on dexmedetomidine, the patient was described as "less aggressive at this time, seems to be calming down" and was sleeping at 2 hours. The patient was sedated with tachycardia resolution at 9 hours and dexmedetomidine was discontinued at 13 hours with normal mental status. A total of 5 mg of diazepam was also given.

A 19-year-old man was admitted to the emergency department; he had ingested twenty 300 mg tablets of gabapentin 24 hours before presentation. He was also a daily cannabis user (at least 3 times daily). He was admitted with "racing thoughts," paranoid ideation, agitation, and hallucinations for 2 weeks (escalating). He was afebrile but hyperadnergic with a maximum pulse of 170 (sinus) and a maximum blood pressure of 159/88 mm Hg. Laboratories were unremarkable except the urine carboxy-THC concentration was 264 ng/mL. Eventually, he was placed in 4-point restraints and was initially given olanzapine (10 mg, oral), haloperidol (2.5 mg, IM) and lorazepam (8 mg, IV) with little effect. Patient was requiring a 4-point restraint despite above agents, and discussions about intubation for propofol sedation took place with anesthesia at bedside, but dexmedetomidine was initiated at 0.7μg/kg per min and subsequently administered for a total of 25.5 hours. Richmond Agitation Sedation Score decreased from +4 (combative) to −3 within 1.5 hour of initiating dexmedetomidine infusion and for 11 hours dose was maintained at 0.5μg/kg per min and eventually weaned off as patient became calm and cooperative. No further benzodiazepines or any other sedatives were administered in conjunction with dexmedetomidine. All the laboratories (including the rest of the urine drug screen) were unremarkable accept for mild rhabdomyolysis.

Dexmedetomidine, a highly selective, potent parenteral presynaptic central α_2-agonist similar to clonidine, has been increasingly used to manage drug or alcohol withdrawal along with delirium [1-4]. Its anxiolytic and analgesic properties have even been recently demonstrated to be useful for procedural sedation for pediatric patients in the emergency department [5]. It has sedating properties (due to G-protein activation in the brainstem), without profound sedation or respiratory depression through inhibition of norepinephrine release in the locus cerulus and increased vagal tone on the heart [2-4]. With its relatively short distribution and elimination half life (6 minutes and 2 hours, respectively), it is easily titratable and thus is an ideal IV agent to treated delirium in the intensive care unit [3]. Dexmedetomidine has even been used as an intranasal preparation at a dose of, up to, 4 μg/kg in children 1 to 5 years of age [5]. The most frequently seen adverse effects are hypotension, bradycardia, and nausea and appear to be due to a rapid infusion rate; these are all usually transient and do require any intervention.

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Hyperadrenergic (or hyperactive) delirium is characterized by psychomotor overactivity, agitation, and autonomic instability along with clouding of consciousness. Visual hallucinations are commonly seen as well as distortion of time and space. The 3 patients described in this case series demonstrated the core manifestations of delirium (disorientation, memory deficits, thought disturbance, impaired visual spatial abilities, and sleep/wake cycle disturbances) [6,7]. Cannabis intoxication/overdose can present as a hyperadrenergic delirium (as noted in these 3 cases) [8-11]. We believe that cannabis intoxication was the primary cause of delirium in these patients (especially in patients 2 and 3 because the coingestants, alprazolam, gabapentin, and olanzapine do not usually produce hyperadrenergic delirium in overdose). Furthermore, all 3 patients had used cannabis multiple times daily and had significantly elevated urine and/or blood cannabis metabolite concentration relative to the last exposure of this drug. Delirium has been especially associated with cannabis use in adolescents taking tricyclic antidepressants [9-11]. Dexmedetomidine infusion (up to 0.7 μg/kg per h) has been previously reported to have been successfully used as an adjunct with midazolam (1 mg) in treating a 9-month-old male infant with hyperadrenergic (heart rate, 160 bpm) agitation due to accidental cannabinoid ingestion [12]. It should also be noted that dexmedetomidine has been used to counteract the sympathomimetic actions of cocaine, amphetamines, and even serotonin syndrome [13,14]. It has even been used to treat grade IV scorpion envenomation in a 9-month old [15]. A more recent review of 22 poisoned adult patients receiving dexmedetomidine noted a median time to target Richmond Agitation Sedation Score and duration of therapy was 6.5 and 44.5 hours, respectively [16]. By comparison, the 3 patients described in this report achieved sedation and the duration of infusion therapy was within a lower period (approximately an average of 5 hours and 14 hours, respectively).

Dexmedetomidine was effective in stabilizing and treating our patients with hyperadrenergic delirium from cannabis/drug intoxication that was refractory to various psychotropic and tranquilizing agents. Also, dexmedetomidine prevented administration of escalating doses of tranquilizers. It should be further noted that intubation was avoided in all 3 patients [17]. We believe that dexmedetomidine is a useful and safe adjunct medication for use in controlling drug and/or cannabis induced delirium.

Dexmedetomidine with tranquilizer use was effective in treating hyperadrenergic delirium due to cannabis/drug related delirium in our case series of 3 young adult patients.

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References

[1] Darrouj J, Puri N, Prince E, et al. Dexmedetomidine infusion as adjunctive therapy to benzodiazepines for acute alcohol withdrawal. Ann Pharmacother 2008;42:1703–5.
[2] Rayer SG, Weinert CR, Peng H, et al. Dexmedetomidine as adjunct treatment for severe alcohol withdrawal in the ICU. Ann Intensive Care 2012;2(12):1–6.
[3] Gerlach AT, Dasta JF. Dexmedetomidine: an updated review. Ann Pharmacother 2007;41:245–54.
[4] Jiang YK, Wang S, Lam TS, et al. Prevalence of delirium and coma in mechanically ventilated patients sedated with dexmedetomidine or propofol. Pharm Ther 2016; 41(7):442–5.
[5] Neville DNW, Hayes KR, Ivan Y, et al. Double-blind randomized controlled trial of intranasal dexmedetomidine versus intranasal midazolam as anxiolysis prior to pediatric laceration repair in the emergency department. Acad Emerg Med 2016;23(8): 910–7.
[6] Lipowski ZJ. Delirium (acute confusional states). JAMA 1987;258(13):1789–92.
[7] Cerejeira J, Mukaetova-Ladinska EB. A clinical update on delirium: from early recognition to effective management. Nurs Res Pract 2011;2011, 875196. http://dx.doi.org/10.1155/2011/875196 [12 pages].
[8] Andre C, Jaber-Filho JA, Bento RM, et al. Delirium following ingestion of marijuana present in chocolate cookies. CNS Spectr 2006;11(04):262–4.
[9] Mannion V. Case report: adverse effects of taking tricyclic antidepressants and smoking marijuana. Can Fam Phys 1999;45:2683–4.
[10] Wilens TE, Biederman J, Spencer TJ. Case study: adverse effects of smoking marijuana while receiving tricyclic antidepressants. J Am Acad Child Adolesc Psychiatry 1997;36(1):45–8.
[11] Bechtold J, Hipwell A, Lewis DA, et al. Concurrent and sustained cumulative effects of adolescent marijuana use on subclinical psychiatric symptoms. Am J Psychiatry 2016;173(8):781–9.
[12] Cipriani F, Mancino A, Pulitano SM, et al. A cannabinoid-intoxicated child treated with dexmedetomidine: a case report. J Med Case Reports 2015;9(1):1.
[13] Menon DV, Wang Z, Fadel PJ, et al. Central sympathology as a novel counter measure for cocaine-induced sympathetic activation and vasoconstriction in humans. J Am Coll Cardiol 2007;50(7):626–33.
[14] Akingloola OA, Singh D. Dexmedetomidine to treat lisdexamfetamine overdose and serotonin toxicidrome in a 6-year-old girl. Am J Crit Care 2012;21(6):456–9.
[15] Levine M, Zorn L, O'Connor AD, Truitt C. Use of dexmedetomidine in the treatment of scorpion envenomation. Clin Toxicol 2009;47(7):763.
[16] Mohorn J, Vakkalanka JP, Rushton W, et al. Evaluation of dexmedetomidine therapy for sedation in patients with toxicological events at an academic medical center. Clin Toxicol 2014;52(5):525–30.
[17] Amusina O, Zell-Kanter M, Clouse A, Leikin JB. Dexmedetomidine as an adjunct in patients undergoing treatment for ethanol withdrawal in the critical care setting. Clin Toxicol 2015;50(7):579–80.

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