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CASE REPORT

Sedation Weaning in a Patient with a Substance Abuse and Psychiatric History

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Abstract

Background Achieving therapeutic doses of sedation and analgesia are necessary for the safety and comfort of mechanically ventilated patients. Patients with complicated psychiatric histories, are neurocritical, and have acute respiratory distress syndrome usually require maximum sedation, making sedation weaning an arduous task.

Case Presentation A 42-year-old female presented with a chief complaint of headache, hypertensive crisis, confusion, and nausea. Her past medical history is notable for hypertension, attention deficit hyperactivity disorder, bipolar II disorder, manic depression, agoraphobia, anxiety, and prior suicide attempts. Noncompliance with anti-hypertensive and psychiatric medications and prior substance abuse history was reported. A head computerized tomography scan revealed multifocal intraparenchymal hemorrhages and multifocal subarachnoid hemorrhages throughout the cerebrum. Within two hours, the patient became obtunded and required intubation. The patient's severe agitation, likely due to metabolic encephalopathy, was difficult to control. Despite being on maximum dexmedetomidine, fentanyl, and quetiapine doses, the patient's agitation remained. Due to her substance abuse and psychiatric history, a methadone and clonidine taper was initiated to attempt sedation weaning.

Conclusion Sedation and analgesia weaning protocols for patients with psychiatric or substance abuse histories may aid in decreasing time on mechanical ventilation and/or in the ICU. The successful clonidine and methadone taper utilized in this patient has potential to be utilized in patients with similar histories. Future trials and approved sedation and analgesia weaning protocols for patients with a profound psychiatric and substance abuse history are urgently needed.

Keywords Hypoxic brain injury · Sedation · Methadone · Clonidine · Encephalopathy

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1 Introduction

In patients who are mechanically ventilated, therapeutic doses of sedation and analgesia are necessary for patient safety and well-being. Achieving these doses of sedation and analgesia often leads to a complex task: balancing patient comfort with the consequences of extensive and prolonged sedation [1]. Overcoming this obstacle is especially difficult in patients with a perplexing psychiatric history, in a neurocritical state, and experiencing acute respiratory distress syndrome.

With increased requirements of sedation, weaning patients can be quite challenging. In 70% of mechanically ventilated patients, weaning from sedation is uncomplicated. For the remaining 30% of patients, the weaning process can be long and complex, taking up to 40–50% of the total mechanical ventilation time [2, 3].

This is a case of a middle-aged female with uncontrolled psychiatric conditions who was subsequently intubated secondary to respiratory compromise after becoming obtunded. Throughout the intensive care unit (ICU) stay, she developed severe agitation that was difficult to manage despite maximum dose parenteral sedatives and analgesics along with high dose antipsychotics. Due to the patient's prior history of substance abuse and outpatient use of psychiatric medications, our interdisciplinary team explored the option of using a methadone and clonidine taper.

2 Case Presentation

A 42-year-old female presented in acute distress with a chief complaint of headache, confusion, and nausea. The headache was described as acute, diffuse, and severe. Her medical history is notable for hypertension, attention deficit hyperactivity disorder (ADHD), bipolar II disorder, manic depression, agoraphobia, anxiety, and prior suicide attempts. The patient reported that she was unsure of adherence with daily antihypertensive medication administration as her initial systolic blood pressure was 188 mmHg. She exclaimed "I'm going to die" while rocking in bed. Her family reported that the patient had a prior history of opioid and benzodiazepine abuse and nonadherence with her lithium and brexpiprazole.

The patient's confirmed home medications are atorvastatin 40 mg daily, clonazepam 1 mg three times daily, dextroamphetamine 10 mg three times daily, lithium carbonate 300 mg ER three times daily, omeprazole 40 mg daily, brexpiprazole 3 mg daily, valsartan 80 mg daily, and a short course of methocarbamol 500 mg (prescribed 12 days prior to admission). Other medications found within the electronic medical record, but not confirmed, included lacosamide 100 mg twice daily, melatonin 6 mg at bedtime, quetiapine 150 mg at bedtime, valproic acid (unknown dose and frequency), and acetaminophen 650 mg every 6 h as needed. The patient was a poor historian, and no family or caregivers were able to participate in medication reconciliation.

A head computed tomography scan was obtained in the emergency department and revealed multifocal intraparenchymal hemorrhages in left frontal and left posterior parietal vertex; multifocal subarachnoid hemorrhages in the left frontal, parafalcine frontal and right frontal parietal vertex were present. Initial laboratory results were remarkable for white blood cell count: 18,000 cells/mcL, calcium: 14.7 mg/dL, and serum creatinine: 4.03 mg/dL. Her urine drug screen was positive for amphetamines due to the dextroamphetamine that she takes for ADHD.

Within two hours of presentation, the patient's condition rapidly deteriorated; she became obtunded and required intubation. She remained in the Trauma/Surgery Intensive Care Unit (TSICU) for 47 days, 36 of which required ventilatory support using assist control ventilation. The patient's long, complicated hospital course included acute kidney injury, multi-drug resistant *Pseudomonas aeruginosa* ventilator-associated pneumonia, hypoxic brain injury, and acute metabolic encephalopathy.

The patient's neurological and psychological function was a tedious challenge throughout her admission. She had severe agitation throughout her ICU stay, likely due to the metabolic encephalopathy. The patient continuously fought to remove her gastrostomy tube and ventilator equipment, resulting in restraint placement.

During admission, the patient required heavy doses of sedating medications. The patient required maximum doses of dexmedetomidine and fentanyl infusions and maximum daily doses of quetiapine to control her agitation. Despite being otherwise clinically stable for extubation, the requirement for high doses of these medications were a barrier to successful ventilation cessation. Multiple adjustments were made to wean sedation, but the patient continued to remain distressed. The care team tried several nonpharmacologic and pharmacologic measures to control her episodes as sedative weaning was attempted but they were not found to be effective. The pharmacologic measures are seen in Fig. 1.

Alternative sedatives were considered for this patient. Ketamine was not utilized due to the medication's risk of causing hallucinations and increasing intracranial pressure, both of which would have been detrimental to our patient given her baseline and acute conditions. The patient had received propofol within the sedation regimen earlier in her hospitalization and remained agitated despite titration to maximum doses. The medication was discontinued due to her lack of responsiveness and to proactively prevent propofol infusion syndrome. Nonpharmacologic measures included frequent patient reorientation, maintaining sleep/wake cycles, and ensuring patients had necessary medical devices such as her eyeglasses. As her hospital stay continued, her hemorrhages and neurological function improved, although she had severe agitation. On day 10 of admission, spontaneous breathing trials were attempted. However, the patient failed each attempt due to severe agitation, highlighting that her agitation was not solely due to her cerebral hemorrhages. As a result, sedating and analgesic medications continued to be required along with intubation.

On day thirty-seven of admission, a novel methadone and clonidine taper was initiated simultaneously to wean the patient off sedation and to facilitate extubating. The fentanyl infusion was titrated down by 25 mcg/kg every 30 min to an hour. Within the same day, the fentanyl infusion was turned off and the methadone taper was initiated. The dosing of the taper consisted of 10 mg by mouth every 8 h (q8h) for 48 h, 7.5 mg by mouth q8h for 48 h and 5 mg by mouth q8h for 48 h. The methadone and clonidine tapered approaches are seen in Figs. 2 and 3 respectively. Additional sedative

Fig. 1 Relevant Pharmacologic and Nonpharmacologic Interventions Throughout Hospital Stay

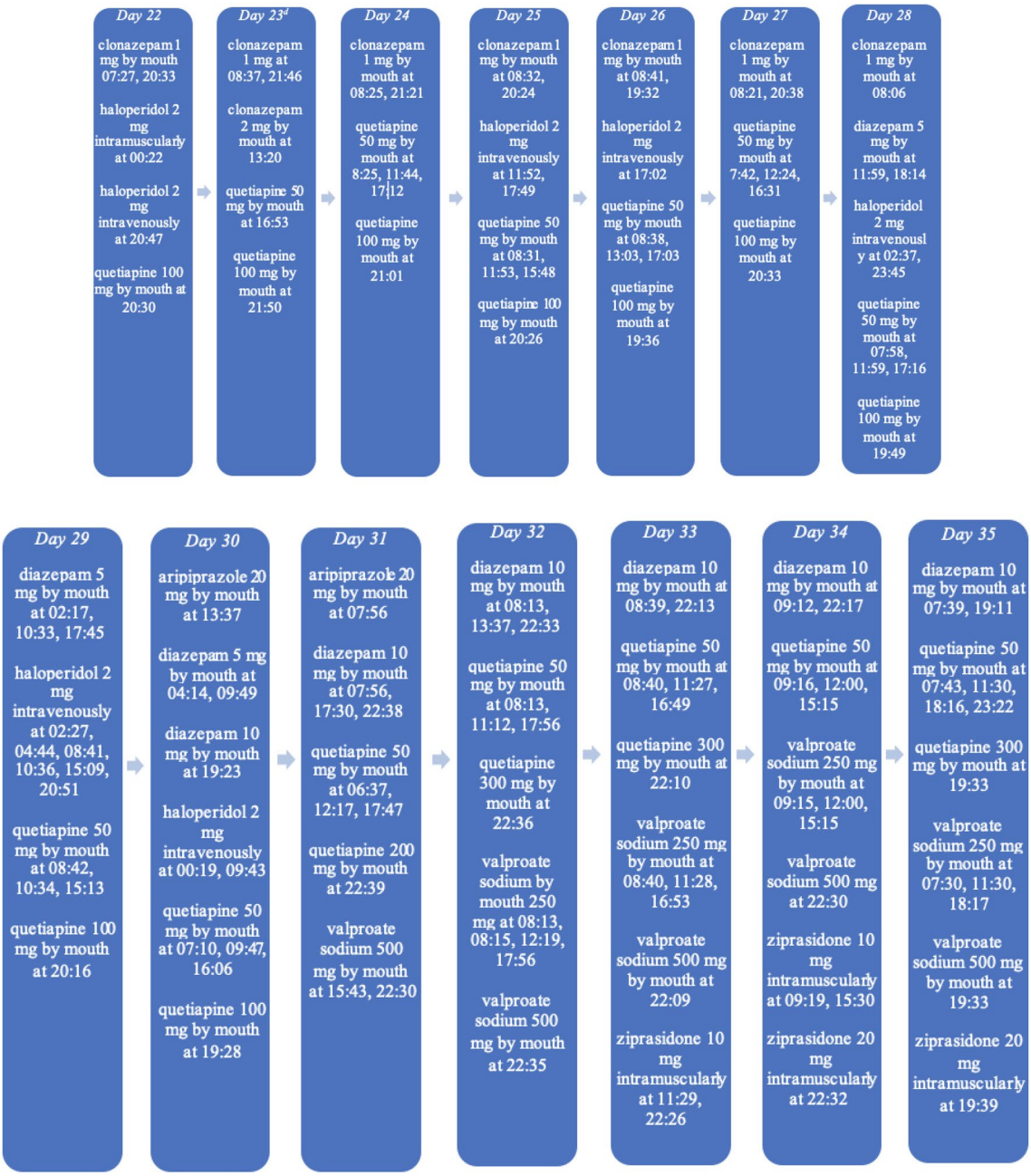
medications were given throughout the tapering process due to her extensive pre-existing psychiatric history. Seven days after initiating these tapering approaches (day 44), intravenous sedation and ventilatory support were successfully and permanently discontinued. The patient was discharged to an acute rehabilitation facility.

3 Discussion

This case report highlights the need for sedation and analgesia weaning tapers for patients with a profound psychiatric and substance abuse history.

Clonidine is an anti-hypertensive medication that acts centrally on alpha-2 adrenergic receptors as an agonist. Besides hypertension, clonidine has multiple off-label uses, including managing symptoms from opioids, benzodiazepines, and alcohol. It also has an off-label use for ICU sedation during the dexmedetomidine weaning primarily to manage potential rebound hypertension related to withdrawal symptoms [4]. However, in this patient, clonidine was required because the rate of dexmedetomidine could not be reduced without her agitation increasing; oral clonidine provided a similar pharmacologic effect to dexmedetomidine for her agitation which allowed us to ultimately and successfully discontinue the infusion.

A previously reported clinical trial has found that patients receiving clonidine were able to wean from dexmedetomidine more rapidly, compared with patients weaned from dexmedetomidine alone [5]. Patients receiving clonidine were able to transition off dexmedetomidine in a median of 19 h, which led to a considerable cost savings ($1,553.47 per patient) and with no difference in adverse effects. There was no difference in the incidence of two or more dexmedetomidine withdrawal symptoms ((1) agitation as per a RASS score greater than + 1, (2) delirium as per a positive Confusion Assessment Method for the ICU assessment, (3) withdrawal as per a Withdrawal Assessment Tool Version 1 (WAT-1) score greater than 2, (4) tachycardia defined as heart rate greater than 90 beats per minute, and (5) hypertension defined as systolic blood pressure greater than 140 mmHg or mean arterial pressure greater than 90 mmHg) in patients being weaned off of prolonged dexmedetomidine infusions either alone or with a clonidine taper. This study concluded that clonidine may be a safe and effective medication for more rapid weaning of dexmedetomidine in patients



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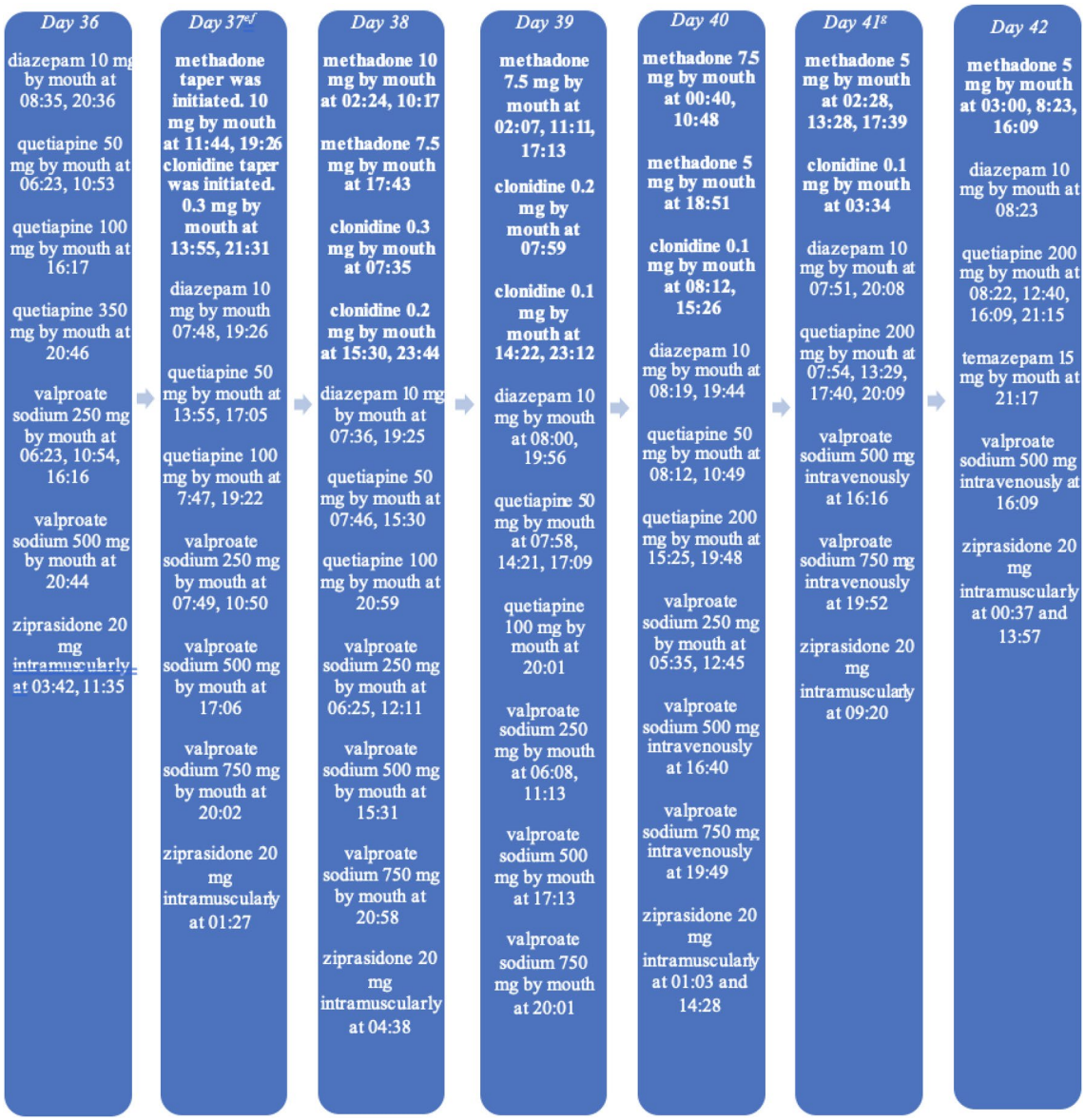
on prolonged infusions. Larger randomized controlled trials may be beneficial to confirm these results [5]. Unlike patients in this study, this patient had a more significant uncontrolled psychiatric history, required doses of dexmedetomidine that was 33% higher, and experienced metabolic encephalopathy due to an anoxic brain injury. Despite these variables, the patient was able to achieve a similar response as the less complicated patients evaluated in the study.

In addition to the dexmedetomidine, the patient was also receiving a continuous infusion of IV fentanyl with a titration range of 25–250 mcg/hr, for which she had been on maximum dose (250 mcg/hr) for 10 days. Fentanyl is often preferred for ICU sedation due to its potency and low risk of inducing hemodynamic instability. Because of its short duration of action, fentanyl is often administered as a continuous infusion to achieve consistent sedation goals and effects. As a result, administration has the potential to lead to the development of tolerance, dependence, and opioid withdrawal syndrome that may result in psychomotor agitation [6]. Methadone is a synthetic opioid and full agonist at



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the μ-opioid receptor and induces other opioid receptors. Methadone is FDA approved for moderate to severe pain non-responsive to non-narcotic drugs and detoxification and treatment of opioid use disorder as part of medication-assisted treatment. The opioid withdrawal time-course and symptoms are less severe, due to the longer half-life of methadone (8–60 h) [7]. While there have not been previous trials that studied methadone tapers to wean patients off fentanyl, there have been a few trials that have evaluated enteral methadone to wean patients from fentanyl and mechanical ventilation. A study by Lugo et al. evaluated the impact of enteral methadone on weaning time from mechanical ventilation (MV). Patients included in the trial required MV and continuous fentanyl infusion for at least 5 days or a dose of fentanyl ≥ 5 mcg/kg/hour for at least 12 h. They were then randomized to either the methadone group (10 mg enterally every 6 h) or the control group, which continued to receive IV fentanyl that was being tapered by 20% every 24 h. The study found that the probability of successful weaning by the fifth day was higher in the methadone group (hazard ratio: 2.64 [95% CI 1.22 to 5.69; $P < 0.02$]) and that MV weaning time was lower in the methadone group (hazard ratio: 2.06 [95% CI 1.17 to 3.64; $P < 0.004$]) [8]. This study concluded that introducing enteral methadone when weaning from sedation and analgesia in mechanically ventilated patients resulted in a decrease in weaning time from MV [9]. Our patient differed from the participants in this study as she received methadone as a taper and not as a flat dose.

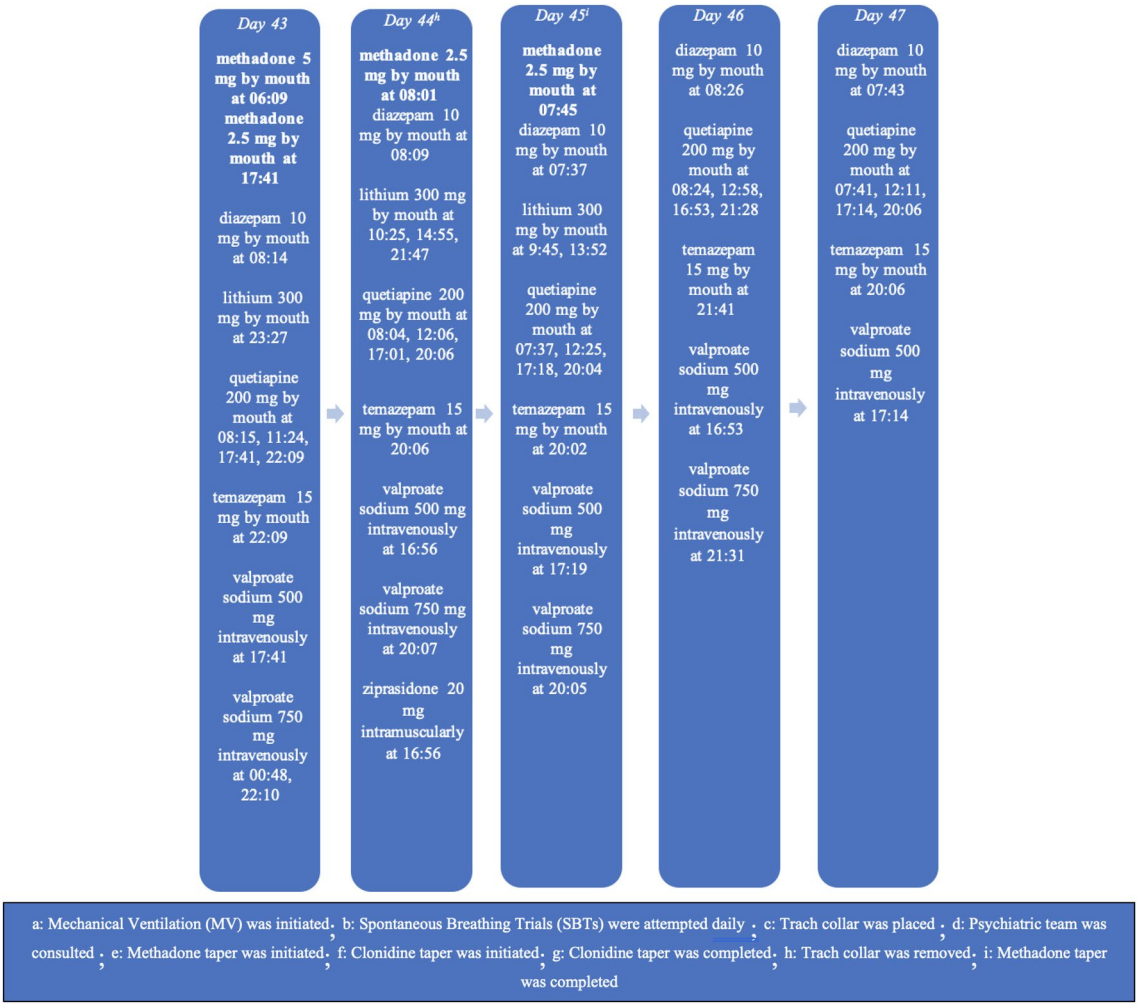

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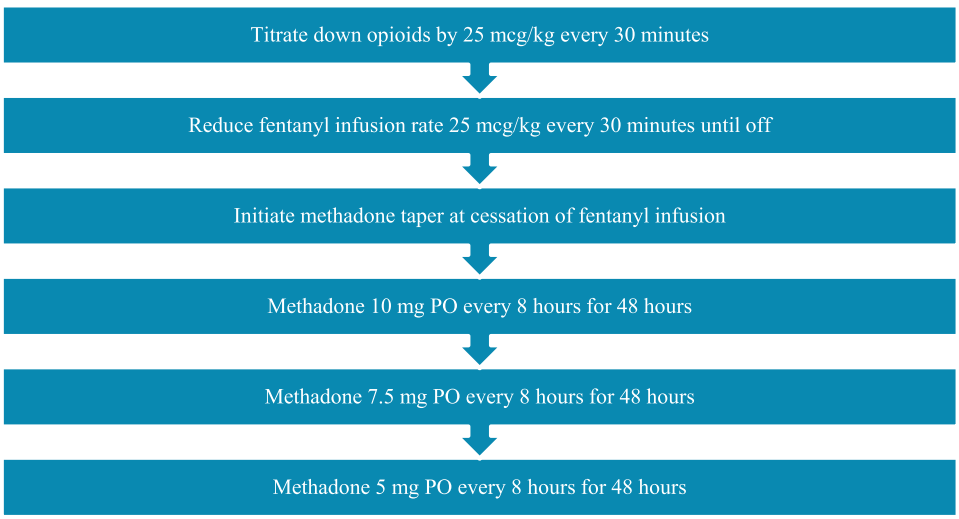
Fig. 2 Methadone Tapered Approach



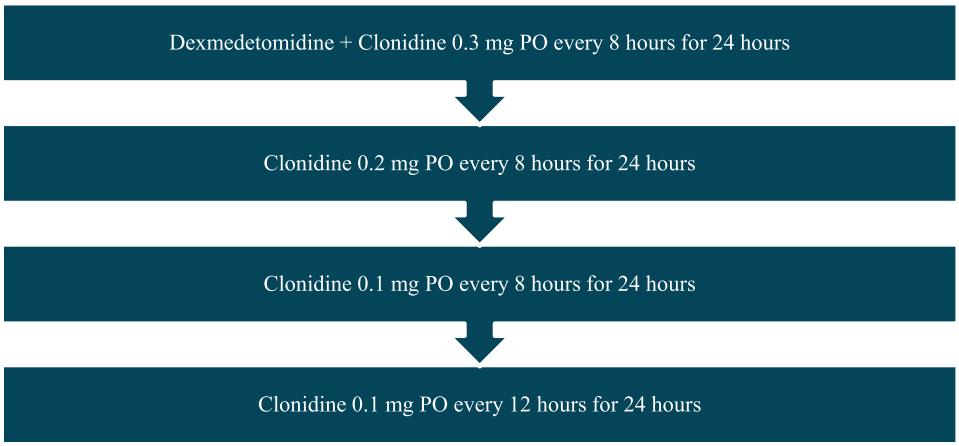


Fig. 3 Clonidine Tapered Approach

It is worth noting the impact of the medications' pharmacology, pharmacokinetics, and pharmacodynamics on the patient's response. Performing the taper with these certain medications allowed the patient's receptors to reset, wean from continuous sedatives, and continue to manage agitation all of which led to successful extubation. As seen in Fig. 1, the patient also received multiple psychiatric medications during her stay. She had been on an antipsychotic and other medications for her pre-existing psychiatric conditions prior to admission; it was felt that continued treatment would facilitate her wean from parenteral sedation. Unfortunately, the medications had suboptimal efficacy despite within class agent switches and escalating doses. After successful sedation weaning and extubation, the patient's psychiatric medications were able to be adjusted to a safe and effective regimen for which she was able to be discharged home on.

4 Conclusion

While sedation and weaning can be challenging for any ICU patient, it can be particularly problematic for patients with substance abuse and profound psychiatric histories such as ours. Sedation and analgesia weaning protocols for patients with a psychiatric and/or substance abuse history may facilitate a more effective and timely weaning process and subsequently decrease unnecessary time on mechanical ventilation and/or in the ICU. This case highlights the need for trials and approved sedation and analgesia weaning protocols for patients with a profound psychiatric and substance abuse history.

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Author contributions AJ collected medical records of the patient and interpreted clinical data to formulate the clinical vignette. AS and AG heavily contributed to the discussion of pharmacodynamics and pharmacokinetics. AJ, AS, and AG all contributed to the writing process of this manuscript. MB and GS both revised this manuscript and offered suggestions; AJ served as the corresponding author. All authors contributed to the article and approved the final submitted manuscript. All authors have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Data Availability All data underlying the results are available as part of the article. No additional source data are required.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethical Approval and Consent for Publication The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance with the tenets of the Helsinki Declaration and has been approved by the authors' institutional review board or equivalent committee.

Consent for Publication Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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