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CASE REPORT

Apnea with ketamine sedation in a patient with severe anorexia nervosa: A case report

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Abstract

Background There is a paucity of literature around sedation and anesthesia in patients with severe anorexia nervosa. Chronically malnourished patients are known to have myopathy, neuropathy, and altered neurotransmitter signaling. Ketamine is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist that is an established general anesthetic and short-acting dissociative analgesic agent. It generally has a reassuring adverse event profile and rarely has been reported to result in apnea. We aim to raise awareness of this untoward adverse event in patients with severe anorexia nervosa among sedation providers and those referring patients for hospitalization or sedation.

Case presentation We describe an episode of apnea, a rare adverse event of ketamine, which was given for procedural sedation to a severely malnourished 13-year-old female with anorexia nervosa, generalized anxiety disorder, and high-functioning autism spectrum disorder. She had no history of apnea nor of ketamine sedation. She was given a standard dose of ketamine and had no other central nervous system depressants within 24 h. Within 1 min after slow medication administration, she had a 9-min period of apnea without laryngospasm. She was supported with bag-valve-mask ventilation throughout this period and did not require intubation. She returned to baseline shortly after procedural sedation.

Conclusions This case describes apnea after ketamine sedation in a patient with severe anorexia nervosa. It supports the importance of a thorough pre-procedure review of a patient's underlying medical problems and the consideration of how sedatives may interact with these conditions. We aim to alert those who care for this complex population of the possible altered neurotransmitters, myopathy, and adverse response to sedation, anesthetics, and analgesics.

Keywords Anorexia · Apnea · Ketamine · Sedation · Anesthesia · Adverse event · NMDA

Abbreviations

AN	Anorexia nervosa
RS	Refeeding syndrome
NMDA	N-methyl-D-aspartate
GAD	Generalized anxiety disorder
ASD	Autism spectrum disorder
NG	Nasogastric

Introduction

Anorexia nervosa (AN) is the third most common chronic disease among female adolescents and holds the highest overall mortality rate of any mental illness. It is characterized by an overwhelming fear of gaining weight coupled with strict measures to reduce net calorie intake and a distorted perception of body image. There is a 10% reported mortality rate that increases to 15% in the period around sedation and anesthesia as severe malnutrition may impact nearly every organ system [1, 2]. These nutritionally deprived patients may also have an altered typical response to many sedatives as a result.

Patients with severe malnutrition are at risk of refeeding syndrome, the metabolic alterations that develop with nutrition repletion of severely malnourished patients. Refeeding syndrome is characterized by electrolyte disturbances that can result in fatal arrhythmias, heart failure and coma among many others [3]. Prevention of and monitoring for refeeding are of the utmost importance [3].

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There are many imbalances that can occur with severe malnutrition and refeeding system including abnormal neurobiological factors. Zinc is crucial in regulating one pathway of glutamate-induced excitotoxicity via negative feedback [1[. This may be compromised in AN by chronic zinc deficiency which could then lead to N-methyl-D-aspartate (NMDA) receptor upregulation [1]. Ketamine hydrochloride is a non-competitive NMDA receptor antagonist that is an established general anesthetic and short-acting dissociative analgesic agent that has been widely used for more than 50 years [1, 4].

Young adult female patients with severe AN have impaired muscle function on strength testing and myopathy on histology and electromyography. As a result, they may have prolonged recovery from neuromuscular blockade and a decreased dose of sedatives is often recommended [3]. It is plausible that this myopathy and chronic zinc deficiency may affect a patient with AN's NMDA receptors and ketamine responsiveness as well. Ketamine is also highly lipophilic and distributes rapidly from systemic circulation so patients with depleted fat stores (as in severe anorexia nervosa) conceivably have different pharmacokinetics and pharmacodynamics resulting in altered ketamine sensitivity as well [5]

Ketamine can be administered via the intravenous or intramuscular route, resulting in analgesia, amnesia, and sedation while generally maintaining spontaneous breathing, protective airway reflexes, and adequate hemodynamics [4]. It overall has a reassuring adverse event profile; laryngospasm and respiratory depression are rare [4]. Apnea is one of the most common adverse events experienced during procedural sedation but is infrequently reported with ketamine. It is most often reported if the drug is delivered rapidly intravenously, with a large weight-based dose, and with concurrent intravenous sedative medications [4, 6].

We identified one prospective study of ketamine used in AN by Mills et al. [7]. They utilized ketamine for treatment of AN in a severe and older adult population. Analgesic doses of ketamine were used with prolonged infusions over 10 h and patients were also administered an oral opioid antagonist. They did administer "small" boluses prior to infusion start but the doses were not specifically stated. Hirose et al. investigated proposed perioperative criteria to manage severe AN that focuses on a thorough evaluation and nutrition plan but does not indicate recommended pharmacologic therapy [3]. Primarily, their recommendations were around perioperative nutrition; in our patient's case, she needed sedation to facilitate optimization of nutrition.

To our knowledge, there are no reports of ketamine utilized as a primary sedative in patients with anorexia nervosa, or of the associated adverse effects. We describe a case in which a patient with severe anorexia nervosa, generalized anxiety disorder (GAD), and autism spectrum disorder (ASD) who was given a standard dose of ketamine for procedural sedation and had an episode of prolonged apnea. This case report may facilitate further research into the safety of sedation of this chronically ill population and raise awareness of this possible adverse event.

Case history

This case involves a 13-year-old Caucasian female adolescent with generalized anxiety disorder (GAD) and a recent diagnosis of high-functioning autism spectrum disorder (ASD) who presented with a six month history of disordered and restrictive eating behaviors consistent with AN. She is a straight A student in honors classes. At the time of admission and diagnosis, she met American Society for Parenteral and Enteral Nutrition criteria for severe malnutrition as evidenced by 24% weight loss over 4-month period (36.9 kg on admission), BMI-for-age Z-score (1.92), and 50% estimated energy intake. She had previously been managed on escitalopram for her anxiety which was increased to 20 mg about 6 weeks prior to admission with minimal change in mood or anxiety. Her only other home medications are ranitidine and senna.

She was admitted directly from clinic due to hypotension, symptomatic orthostasis, neutropenia, and hypophosphatemia. On admission to the hospital, she was verbally abusive and irritable. We initiated thiamine, phosphorous, sodium, and potassium supplementation and olanzapine in the morning to aid in her mood in addition to her home escitalopram.

On hospital day two, she was noted to have refused nearly all of her food and supplements since admission. She continued to have behavioral outbursts. She had increasing bradycardia to 40 beats per minute and blood pressures down to 64/40 the following night. A peripheral IV was placed after multiple attempts, requiring 4-point restraints. Nasogastric (NG) tube placement was indicated given her refusal to eat but the team was concerned that she would require sedation due to combativeness and given her low blood pressure this was unsafe to do without monitoring in a higher level of care. She was, thus, transferred to the pediatric intermediate care unit for procedural sedation for NG placement and a more secure PIV placement to assist in frequent refeeding lab draws.

The day of sedation she refused all supplements and anxiolytics (last given 24 h prior to procedural sedation). Her morning electrolyte panel was normal with a phosphorous of 4.8 mg/dl and bicarbonate of 22 mmol/L. She was conversant and had easy work of breathing in room air with clear lung fields on auscultation and saturations of 100% in room air. After following pre-sedation checklists and a time-out, ketamine (50 mg which is 1.3 mg/kg) was given over 1 min. Typical ketamine induction dosing is usually 1–3 mg/kg. This drug was chosen as the sedative due to its favorable adverse event profile and ability to raise blood pressure thru catecholamine

release. Around one minute after the medication administration, she abruptly became apneic as evidenced by loss of end tidal CO_2 ($ETCO_2$) monitoring and lack of respiratory effort. She desaturated from 100 to 94% prior to bag-valve-mask (BVM) ventilation initiation which was started around 45–60 s after onset of apnea. She was easily bagged and there was no evidence of obstruction or laryngospasm. Her heart rate and blood pressure were unchanged. Every 2 min, BVM was paused for 20 s to assess for spontaneous respiratory effort, which returned at 9 min following ketamine administration. Her $ETCO_2$ monitor demonstrated 39 mmHg when spontaneous respirations resumed. Her NG tube secured via bridle was then placed as well as a large bore IV to assist in lab draws without further incident. She was awake and back to her baseline within 45 min of sedation initiation. Fortunately, she suffered no other complications from this short-lived event. We verified ketamine concentration and dose were as intended.

Her vitals improved over the following day with fluids and nutrition and she was transferred back to the medical floor for the remainder of her inpatient treatment.

Discussion

There are no guidelines for procedural sedation or perioperative management of patients with severe AN other than that to recommend nutrition optimization pre-procedure in an effort to decrease morbidity and mortality. Unfortunately, our patient's combination of ASD, GAD, and AN required procedural sedation to place a secured feeding tube and a larger IV to allow for appropriate lab monitoring of refeeding syndrome.

Ketamine is generally devoid of prolonged respiratory depressant effects but there are reports of its occurrence, and it is likely that given our patient's critically ill and malnourished state and possibly some altered NMDA receptor signaling, that this may have predisposed her to this adverse event event even when getting a slow bolus with sub-standard dosing. Unfortunately, we did not have a pre-sedation zinc level. Use of multiple sedatives can also make respiratory depression more likely but given that she had not had any other central nervous system depressants in over 24 h, that is an unlikely contributory factor in this case.

Conclusion

In summary, further studies are warranted in assessing pharmacokinetics of sedatives and analgesics used for procedural sedation for patients with severe AN. This case emphasizes the importance of thorough pre-procedure review of a patient's underlying medical conditions and the consideration of how sedatives may interact with these conditions. We would like to alert those who care for this complex population of the possible altered neurotransmitters, myopathy, and adverse response to sedation, anesthetics, and analgesics specifically the proven occurrence of apnea in relation to ketamine administration.

Authors' contributions WM conceived of the case report and wrote the manuscript. All authors read, edited, reviewed, and approved the final manuscript.

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Availability of data and materials All confirmed and transparent.

Declarations

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication Family consented to publication of this report.

References:

1. Driver BE, Reardon RF (2017) Apnea after low-dose ketamine sedation during attempted delayed sequence intubation. Ann Emerg Med 69(1):34–35
2. Hermens DF, Simcock G, Dutton M, Bouças AP, Can AT, Lilley C et al (2020) Anorexia nervosa, zinc deficiency and the glutamate system: The ketamine option. Prog Neuropsychopharmacol Biol Psychiatry 101:109921
3. Hirose K, Hirose M, Tanaka K, Kawahito S, Tamaki T, Oshita S (2014) Perioperative management of severe anorexia nervosa. Br J Anaesth 112(2):246–254
4. Krauss BS, Andolfatto G, Krauss BA, Mieloszyk RJ, Monuteaux MC (2016) Characteristics of and predictors for apnea and clinical interventions during procedural sedation. Ann Emerg Med 68(5):564–573
5. Vadivelu N, Schermer E, Kodumudi V, Belani K, Urman R, Kaye AD (2016) Role of ketamine for analgesia in adults and children. J Anaesthesiol Clin Pharmacol 32(3):298–306
6. Maynard R, Christensen E, Cady R, Jacob A, Ouellette Y, Podgorski H, et al. Home health care availability and discharge delays in children with medical complexity. Pediatrics. 2019;143(1).
7. Mills IH, Park GR, Manara AR, Merriman RJ (1998) Treatment of compulsive behaviour in eating disorders with intermittent ketamine infusions. QJM 91(7):493–503
8. Strayer RJ, Nelson LS (2008) Adverse events associated with ketamine for procedural sedation in adults. Am J Emerg Med 26(9):985–1028
9. Zenker J, Hagenah U, Rossaint R (2010) Anesthesia in patients with anorexia nervosa and bulimia nervosa. Anaesthesist. 59(3):261–272 (**Quiz 73**)