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Case Report

A case of central diabetes insipidus after ketamine infusion during an external to internal carotid artery bypass

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Abstract
Study Objective: We report the first teenage case of ketamine-induced transient central diabetes insipidus.
Case Summary: The patient was an 18-year-old woman with moyamoya disease undergoing an external carotid to internal carotid bypass and given a low-dose ketamine infusion. After approximately 2 hours in the supine position, with 0.5 Minimum Alveolar Concentration (MAC) of sevoflurane, a propofol infusion at 50 μg/kg/min, a remifentanil infusion at 0.5 μg/kg/min, and a ketamine infusion at a dose of 10 μg/kg/min, this patient had an excessive urine output. Initially, the Foley catheter contained 50 mL of urine. She was given 1500 mL of crystalloid during the case but produced 2700 mL of urine output. Increasing urine output was noted 1 hour into the procedure around the time that the patient experienced a 2-minute Cushing-like response characterized by bradycardia and hypertension. Several I-Stat samples revealed a worsening hypernatremia. The decision was made to check the urine osmolality and treat the patient with 4 μg of desmopressin (DDAVP). Urine output began to slow down to a normal rate of 2 mg/kg/h, as the patient was transferred from the operating room to the computed tomographic (CT) scanning room for a CT and CT angiogram; both were unremarkable. The neurosurgery team waited until the next day to complete the procedure. The procedure was completed successfully and uneventfully the next day without a ketamine infusion as part of the general anesthetic plan.
Discussion: The Naranjo Adverse Drug Reaction score of 4 suggested a possible relationship between the patient's ketamine infusion and subsequent central diabetes insipidus. The 2 previous cases on this topic have suggested that ketamine, as an *N*-methyl-D-aspartate receptor antagonist, inhibits vasopressin release in the neurohypophysis.
Conclusion: Urine output, urine osmolarity, and serum osmolarity should be monitored in patients given ketamine anesthetic; desmopressin should be present to prevent dangerous long-term sequela.

1. Introduction

Ketamine is a lipid-soluble dissociative anesthetic derived from phencyclidine [3]. It has a rapid onset of action, inhibiting the *N*-methyl-D-aspartate (NMDA) receptor and providing

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a strong analgesic effect without significant respiratory depression [2,5]. It also increases sympathetic response, salivation, cerebral blood flow, and cerebral metabolic oxygen requirement and, therefore, should not be used in patients with increased intracranial pressure or hypertension [2,5]. The increased sympathetic response of ketamine can cause significant hypertension that is usually short lived as well as tachycardia that may conceal the direct myocardial depression effects of this anesthetic [5]. In medical literature, 2 reports exist detailing ketamine-induced transient central diabetes insipidus (DI)—one involves a $2^1/_2$-year-old female toddler [3] and one involves a 28-year-old adult man [8]. We present the first known case of ketamine-induced transient central DI in a teenager—an 18-year-old woman with moyamoya disease.

2. Case

The patient is an 18-year-old woman with a medical history of moyamoya disease, type 2 diabetes mellitus, and the development of a left middle cerebral artery (MCA) stroke approximately 6 months prior. She presented with a 1-week history of headache and left-sided weakness that had since resolved. This episode was diagnosed as a transient ischemic attack, and she underwent a cerebral angiogram. The angiogram showed marked stenosis of her left MCA and evidence of further moyamoya disease progression. She and her family subsequently decided to pursue a left superficial temporal artery to MCA bypass to treat her cerebral ischemia.

The patient was intubated supine. She was maintained on 0.5 MAC sevoflurane and propofol infusion between 100 and 150 μg/kg/min. For induction, the patient was given succinylcholine, propofol, lidocaine, rocuronium, and fentanyl. A remifentanil infusion at 0.5 μg/kg/min and ketamine infusion at 10 μg/kg/min were later used as anesthetic adjuncts. Three hundred micrograms of phenylephrine was used to maintain her systolic blood pressure within the goal of 120 to 150 mm Hg. One hour into the procedure, after scalp incision and during dissection of the superficial temporal artery, the patient acutely developed severe hypertension (270/100) with profound bradycardia (40s beats per minute). This episode lasted approximately 2 minutes. Her urine output increased significantly at the same time, urine osmolality decreased to 117 mOsm/kg, and arterial blood gas indicated a metabolic acidosis of pH 7.27, HCO_3 of 17.9, and serum sodium of 152 mEq/L. Her hypertensive crisis was controlled with atropine, nicardipine, and esmolol, and she was given 4 μg desmopressin (DDAVP). She responded positively to the desmopressin, and her output decreased to 2 mg/kg/h. The procedure was aborted before intracranial entry due to the worry that the patient may develop further crises. The scalp was closed, the patient was extubated and transferred to the intensive care unit, and the procedure was rescheduled for the next day. Throughout the procedure, her total input of crystalloid was 1500 mL, and her total urine output was 2700 mL. Electrocardiogram showed sinus rhythm throughout the procedure, and her temperature also remained stable. Her computed tomography (CT) head, CT angiogram, and magnetic resonance imaging showed no changes from baseline after the aborted procedure.

The following day, the procedure was repeated. The patient was reintubated and placed under general anesthesia without ketamine adjunct. Her systolic blood pressure remained within the goal of 130 to 150 mm Hg during the duration of the procedure. The bypass was completed without complications, and the transfemoral cerebral angiogram showed a patent left MCA recipient vessel and left superficial temporal artery. The patient was then extubated without event and returned to the intensive care unit. She was stable postoperatively and was discharged a few days later.

3. Discussion

This report analyzes an 18-year-old woman with moyamoya disease who underwent a superficial temporal artery to MCA bypass and was diagnosed with transient central DI from a ketamine infusion at 10 μg/kg/min for a total of 60 μg. Her polyuria, decreased urine osmolality, and corresponding hypernatremia 1 hour into the procedure that intersected with her 2-minute Cushing-like response of hypertensive crisis with bradycardia led to the diagnosis of transient central DI. The significant hypertension and CT head and CT angiogram performed after the surgery was aborted were both unremarkable and unchanged from her baseline, ruling out the potential of ischemic or infarcted brain tissue triggering a central DI. The patient's urine output had increased rapidly approximately 1 hour into the procedure, and she was excreting clear, colorless urine with significantly decreased osmolarity. Her abnormal urine output corrected with 4 μg desmopressin, normalizing to 2 mg/kg/h, which further supports her diagnosis of transient central DI.

There are 2 previous reports of ketamine-induced central DI. Hatab et al [3] described a case involving a 2-year-old girl with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency and hypertrophic cardiomyopathy who presented with pneumonia. The pneumonia progressed to acute respiratory failure, and the patient was intubated and given lorazepam and fentanyl for sedation [3]. Because her level of sedation was not ideal, she was then given dexmedetomidine followed by ketamine [3]. She received 1 mg/kg bolus infusion of ketamine with 1 mg/kg/h continuous infusion [3]. She then developed polyuria and transient central DI 7 and 10 hours after the infusion, respectively [3]. Her polyuria and hypernatremia responded positively to 180 mU vasopressin given as a drip over 12 hours [3].

Sakai et al [8] described a case involving a 28-year-old man with a spinal cord injury who had developed increasingly severe pain, without resolution from oral or intravenous analgesics, in his bilateral lower extremities after rehabilitation. He