Case Reports

Altered Mental Status and Hyponatremia After 20 Hours of Amiodarone Therapy

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A 66-year-old woman with no relevant medical history presented at the emergency department with new-onset atrial fibrillation. We initiated intravenous amiodarone therapy. At 20 hours, the patient experienced severe neurologic symptoms, hyponatremia, and syndrome of inappropriate antidiuretic hormone. We discontinued amiodarone, infused saline solution, and restricted the patient's fluid intake. She recovered in 3 days. This case illustrates that amiodarone-induced syndrome of inappropriate antidiuretic hormone with hyponatremia can occur far earlier than expected during acute amiodarone therapy. ***(Tex Heart Inst J 2020;47(3):229-32)***

Amiodarone is prescribed to treat various cardiac dysrhythmias. Unlike long-term amiodarone therapy, which is associated with many adverse effects, short-term amiodarone therapy is typically tolerated well, except for occasional pulmonary, hepatic, or cardiac toxicity.[1] We report the case of a patient who was given amiodarone intravenously; within 24 hours, she developed syndrome of inappropriate antidiuretic hormone (SIADH), as evidenced by severe hyponatremia, high urinary osmolality, and disorientation.

Case Report

In March 2017, a 66-year-old woman with no relevant medical history, addictions, or medication use sought emergency medical attention for palpitations. She had atrial fibrillation with a rapid ventricular response at 112 beats/min and a blood pressure of 144/98 mmHg. Physical examination revealed no evidence of thyroid, pulmonary, or cardiac disease. Results of a complete blood count test and metabolic, hepatic, and thyroid panels were within normal ranges. She was admitted to the hospital.

We initiated intravenous heparin and diltiazem therapy, administered a 150-mg bolus of amiodarone, and then infused amiodarone at 1 mg/min for 6 hours. Finally, the amiodarone infusion was reduced to 0.5 mg/min for 18 hours. At 20 hours, the patient became somnolent, confused, and incoherent. Chest radiographs showed nothing of note; a neurologic examination revealed no motor deficit; and a computed tomogram of the head showed no anomaly. The patient's serum sodium level had decreased from 140 mEq/L on admission to 112 mEq/L, and her urine osmolality was 484 mOsm/kg. In the absence of overt malignancy, pulmonary infection, and existing central nervous system disorders, we attributed the patient's hyponatremia and neurologic symptoms to drug-induced SIADH. We discontinued the amiodarone and diltiazem, started β-adrenergic blockade with metoprolol tartrate for control of ventricular response to atrial fibrillation, and administered a 100-mL bolus of 3% hypertonic saline solution. The saline solution was then infused at 30 mL/hr for 24 hours, with the goal of increasing her sodium level by 10 mEq/L over 24 hours.

At 72 hours, the patient's serum sodium level was 133 mEq/L, her urine sodium level was <5 mmol/L, her urine osmolality was 55 mOsm/kg, and she had recovered normal mental status (Table I). Her morning plasma cortisol level was within normal range. At 120 hours, when the electrolyte imbalance was resolved, she began undergoing direct-current cardioversion. She was discharged from the hospital after a 10-day stay, with instructions to take metoprolol. She was lost to follow-up thereafter.

Key words: *Amiodarone/adverse effects/therapeutic use; hyponatremia/chemically induced/etiology; iatrogenic disease; inappropriate ADH syndrome/chemically induced/complications; sodium/blood; treatment outcome*

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TABLE I. Patient's Course

	Time (hr)			
Variable	**Admission**	**20***	**46**	**72**
Sodium (mEq/L)	140	112	127	133
Heart rate (beats/min)	112	129	71	88
Blood pressure (mmHg)	144/98	133/105	107/58	134/86
Urine osmolality (mOsm/kg)	—	484	—	55
Mental status	—	Disoriented	—	Normal
Treatment	Amiodarone started	Amiodarone stopped within 1 hr	—	—
		Metoprolol and 3% hypertonic saline solution started		
		Fluids restricted to 1,200 mL/d		

*Patient was diagnosed with hyponatremia.

Discussion

Amiodarone maintenance therapy is associated with adverse effects,[1] including corneal microdeposits (in >90% of patients), photosensitivity (25%–75%), hepatotoxicity (15%–30%), pulmonary fibrosis (1%–7%), hypothyroidism (6%), bradycardia (≤10%), ataxia (3%–35%), and peripheral neuropathy (0.3%).[2] Adverse effects occur far less frequently during intravenous therapy or oral loading[1]; respiratory and hepatic failure have been reported.[3-5] It is possible, but not established, that amiodarone therapy induces or worsens chronic heart failure and ventricular arrhythmias.[6]

Many reports of amiodarone's acute adverse effects in fact refer to short exposures of a few days to 6 months.[7] Table II summarizes this issue in terms of amiodarone-induced hyponatremia and SIADH. Of 15 previous patients in whom amiodarone-induced SIADH developed,[8-21] only 6 were given amiodarone for less than 2 weeks and none for less than 3 days. In contrast, our patient had a hyperacute response. Except for age, she had no conditions associated with increased antidiuretic hormone (ADH) release, such as small-cell carcinoma of the pancreas, hypothyroidism adrenal insufficiency, or lung abscess from tuberculosis pneumonia.[22] What caused our patient's hyperacute response is unclear. Her kidneys may have been particularly sensitive to ADH, amiodarone may have increased ADH release, or both. Amiodarone was the most likely cause of SIADH in our patient; however, her severe symptoms and the risk of seizures precluded a repeat amiodarone challenge.

Conclusion

Our patient's severe neurologic symptoms and laboratory findings of SIADH developed within 24 hours of intravenous amiodarone therapy. Amiodarone-induced SIADH with hyponatremia is a rare complication, and our report illustrates that it can occur far earlier than typically seen during acute amiodarone therapy. Recognizing SIADH and immediately discontinuing amiodarone therapy—along with saline infusion and fluid management—successfully reversed our patient's symptoms.

Continued

TABLE II. Reported Cases of SIADH and Hyponatremia Induced by Amiodarone

Reference	Age (yr), Sex	Amiodarone Dose	Time to Hyponatremia	Lowest Serum Sodium Level (mEq/L)	Treatment	Time to Normal Serum Sodium (d)
Muñoz Ruiz AI, et al.[8] (1996)	67, F	NA	4 mo	110	Discontinued	NA
Odeh M, et al.[9] (1999)	62, F	300 mg/d	6 mo	120	Discontinued	5
Ikegami H, et al.[10] (2002)	63, M	800 mg/d	7 d	119	Decreased to 100 mg/d; fluid restriction	28
	87, M	200 mg/d × 7 d; 100 mg/d	15 d	121	Continued at 100 mg/d; fluid restriction	14
Patel GP and Kasiar JB[11] (2002)	67, M	200 mg/d	3 mo	117	Discontinued; fluid restriction	3
Aslam MK, et al.[12] (2004)	72, M	2 g/d loading	5 d	117	Decreased to 200 mg/d	14
Yoshikawa S, et al.[13] (2006)	87, M	NA	10 d	114	Fluid restriction	NA
Shavit E and Sherer Y[14] (2007)	85, M	NA	30 d	122	Discontinued	A few days
Paydas S, et al.[15] (2008)	58, M	NA	5 mo	107	Discontinued	14
Afshinnia F, et al.[16] (2011)	66, M	150-mg IV; 900-mg drip for 24 hr; 400 mg 3×/d	7 d	116	Discontinued	16
Singla S, et al.[17] (2013)	58, M	1,600 mg/d	3 d	120	Discontinued; dialysis	NA
Pham L, et al.[18] (2013)	84, M	150-mg IV bolus and drip; 1,200 mg × 7 d; 400 mg/d	11 d	105	Hypertonic saline solution; fluid restriction; oral demeclocycline	10
Dutta P, et al.[19] (2014)	63, M	100 mg/d	9 mo	109	Discontinued; fluid restriction	3
Maloberti A, et al.[20] (2015)	78, M	200 mg/d	5 yr	110	Discontinued; hypertonic saline solution; fluid restriction	1
Nakamura M, et al.[21] (2017)	43, M	200 mg/d	8 mo	108	Discontinued; fludrocortisone	30
Current case	66, F	150-mg bolus; 1 mg/min for 6 hr; 0.5 mg for 18 hr	20 hr	112	Discontinued; 100-mL bolus + 30-mL/hr infusion of 3% hypertonic saline solution; fluid restriction	3

IV = intravenous; NA = not available; SIADH = syndrome of inappropriate antidiuretic hormone

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