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Dexmedetomidine-induced diabetes insipidus during coronary artery bypass graft surgery

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Dear Editor,

Dexmedetomidine is a sedative commonly used in intensive care units and intraoperatively that works by acting pharmacologically as a selective α-2 agonist [2]. It has been found in several studies to attenuate undesirable effects in cardiothoracic surgery; for example, it has been shown to improve postoperative microcirculation compared to propofol, reduce myocardial damage, reduce narcotic consumption, reduce the incidence of delirium, and reduce the incidence of postoperative tachyarrhythmias [3–6].

However, the potential negative effects of dexmedetomidine such as those on the kidneys have not been fully elucidated in the literature. A randomized placebo-controlled study found that in patients with normal renal function undergoing CABG, patients who received dexmedetomidine during surgery had a mean increase of 74% in urinary output compared with those who had received a placebo. Other cases found in a literature review in conjunction with the case described below indicate that dexmedetomidine may be associated with postoperative diabetes insipidus and specifically so in cardiac surgery patients [7].

Diabetes insipidus (DI) is a condition where the body produces an excess amount of overly dilute urine due to either a failure of production of antidiuretic hormone (ADH) or the ineffectiveness of ADH to function in the kidney's nephrons [8]. The diagnosis of DI begins with a diagnosis of polyuria followed by an examination of the patient's electrolytes and volume status. This is then followed by the determination of the patient's urine osmolarity; a high urine osmolarity in a patient with polyuria and hypernatremia would indicate solute diuresis while a low urine osmolarity in such a patient would be diagnostic of DI [8].

We present our case below demonstrating the development of DI secondary to dexmedetomidine usage during cardiac surgery. Written patient consent was obtained for the publication of this case report.

A 55-year-old male patient presented for a CABG two days after coronary angiography with an intra-aortic balloon pump (IABP) placement following the diagnosis of an ST-elevation myocardial infarction (STEMI) at an outside hospital. The coronary angiography confirmed a diagnosis of multi-vessel obstructive coronary artery disease – 90% stenosis distal left main artery, 80-90% stenosis of the proximal left anterior descending (LAD) artery, 70% stenosis of proximal LAD and total occlusion of his right coronary artery (RCA). His past medical history is significant for type II diabetes mellitus (HbA_{1c} of 6.3%) and hyperlipidemia. He had no prior surgical history. Upon diagnosis of a STEMI, the patient was loaded with aspirin, atorvastatin, and heparin. Following the angiography and IABP placement, the patient was transferred to the cardiac critical care unit where he remained for two days until his surgery.

The patient was scheduled for a three-vessel CABG including a free

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left internal mammary artery (LIMA) graft to LAD and a single vessel bypass graft (SVG) to the LAD and the obtuse marginal (OM) artery. Preoperative laboratory tests indicated overall electrolytes within normal limits (sodium 143 mmol L^{-1}, potassium 3.8 mmol L^{-1}, ionized calcium 1.18 mmol L^{-1}, magnesium 2.3 mg dL^{-1}) with an elevated creatinine (1.2 mg dL^{-1}) relative to patient's baseline (0.8 mg dL^{-1}) suggesting a mild acute kidney injury without evidence of chronic kidney disease. Complete blood count showed appropriate starting haemoglobin (13.5 g dL^{-1}) and slight thrombocytopenia (130,000/L) that did not necessitate transfusions. His IABP was set to a ratio of 1 : 1, which the patient tolerated well.

After the placement of standard ASA monitors and a pre-induction arterial line, the patient was induced without complications with fentanyl, lidocaine, etomidate, and rocuronium. Per protocol, he was started on aminocaproic acid infusion after an initial loading dose and a dexmedetomidine drip at 0.5 µg kg^{-1} h^{-1} was started at the incision. Antibiotics included vancomycin and cefazolin. Titration of norepinephrine and epinephrine was used to maintain MAP via an arterial line of > 65 mmHg. 24,000 units of heparin (400 units kg^{-1}) were used prior to initiation of CBP with sufficient activated coagulation time (ACT). Post-CPB heparin reversal was completed with 400 mg of protamine and the repletion of electrolytes included 2 g magnesium sulfate, 20 mEq potassium chloride and 2 g calcium chloride. The patient also required 6.4 units total of IV insulin for glycemic control.

Prior to CBP, the patient produced 200 mL of urine output (UOP) over 3 hours equating to 1.0 mL kg^{-1} h^{-1} with the patient only receiving input of 500 mL lactated ringers (LR) and 500 mL of 5% albumin. Over the next 1.5 hours on CBP and until the end of the procedure, the patient produced 5300 mL more of urine, equating to 15.5 mL kg^{-1} h^{-1}. His rapid drop of intravascular volume as reflected by NIBP prompted succinct resuscitation off CBP with an additional 1500 mL of crystalloids and 1000 mL of 5% albumin. One unit of fresh frozen plasma (FFP) and one jumbo packet of platelets were administered intraoperatively due to operative oozing noted. Dexmedetomidine-induced DI was suspected and the dexmedetomidine infusion was immediately discontinued. Overall, the patient produced 6000 mL of urine with an estimated blood loss of 1000 mL. Following the procedure, the patient was transferred to the surgical intensive care unit (SICU) in stable condition.

In the SICU, the patient was diagnosed with dexmedetomidine-induced DI based on his elevated postoperative urine output (additional 3.9 L produced in 24 hours), postoperative hypernatremia (sodium 149 mmol L^{-1}), and a low urine osmolarity (252 mOsml kg^{-1}). On post-op days 1 and 2, the patient's urine output decreased, and his electrolytes normalized. On post-op day 5, the patient's urine output normalized, and his DI was presumed to have resolved. On post-op day 9, the patient was discharged.

Our patient was diagnosed with diabetes insipidus secondary to dexmedetomidine use intraoperatively. Generally, the vast majority of patients with DI present with preliminary symptoms of excess urination of dilute urine and excessive thirst. After the exclusion of more common causes of excessive urination, a 24-hour urine volume should be collected. If this exceeds 3 L, the patient is diagnosed with polyuria. In the case described within this report, the patient produced 9.4 L in 24 hours (5.5 L intraoperative and 3.9 L postoperative). This volume output, coupled with hypernatremia and low urine osmolarity, suggests DI over solute diuresis. Dexmedetomidine use can result in both central and nephrogenic DI [9].

Central DI can be differentiated from nephrogenic DI by administering desmopressin, a synthetic analogue of ADH, and following urine osmolarity after administration to determine the ability of the nephron to concentrate urine. Testing with desmopressin was not conducted for our patient, likely due to his condition improving on post-op day 2 and resolving completely by post-op day 5.

While the diagnosis of DI was established, the cause originally remained unclear. Several studies have noted anecdotally that surgeries involving the central nervous system are more likely to result in dexmedetomidine-induced polyuria, likely due to the fact that AVP is released by the posterior pituitary gland [10–12]. However, polyuria has also been observed in a wide variety of patients receiving dexmedetomidine including, patients in their sixties undergoing orthopaedic surgery, otolaryngologic surgery, and a 32-year-old male in the ICU for burns [12–14]. A literature review found that the renal effects of dexmedetomidine on patients undergoing CABG surgery have been examined with an experimental trial. While the original purpose of the trial was to determine how intraoperative use of dexmedetomidine affected the creatinine clearance of patients undergoing CABG, the authors found that the biggest disparity between the two groups was urinary output. In the first four hours after the insertion of a urinary catheter, there was a 74% increase in urinary output in CABG patients who received dexmedetomidine compared to those who had not [7]. With respect to the underlying mechanism of action for how dexmedetomidine affects the functioning of ADH and thus causes DI, animal studies have proven the most fruitful in determining a potential answer. One study of rats showed that dexmedetomidine inhibited hypothalamic paraventricular nucleus (PVN) magnocellular neurons (which are involved in ADH release) by activation of a G protein-coupled inwardly rectifying K^+ current and inhibited PVN parvocellular neurons by suppression of Ih, which are hyperpolarization-activated currents that control PVN neurons [15]. Other studies in rats have shown α-2 agonists like dexmedetomidine bind to α-2 receptors in both the medullary and cortical collecting ducts of the nephron which inhibits ADH-

stimulated osmotic water permeability [16]. Therefore, dexmedetomidine may precipitate both central and nephrogenic DI.

The findings presented in this case study are significant for multiple reasons. First, the presence of dexmedetomidine-induced DI in a cardiothoracic surgery patient is indicative of the fact that this complication of dexmedetomidine should be considered by anesthesiologists during cardiac surgery. In addition, polyuria can cause devastating intravascular volume depletion if patients' intakes and outputs are not observed closely. This is particularly relevant in patients with potentially poor cardiovascular function because acute hypovolemia has been shown to worsen cardiovascular health outcomes. Acute hypovolemia episodes have been shown to increase inflammation in blood vessels leading to greater development of atherosclerotic lesions, decreased endothelial function, and increased aortic stiffness [17]. In patients undergoing CABG surgery and/or other cardiothoracic surgeries, the risk of precipitating such an episode should be weighed against the benefits of dexmedetomidine before proceeding with its use.

In conclusion, this case report shows the potential complication of DI when using dexmedetomidine intraoperatively. The primary limitation of the case is the lack of differentiation in this individual between central and nephrogenic DI. However, as noted in the literature review, the mechanisms by which dexmedetomidine can cause DI and affect ADH production, release, and function are not entirely clear. In the future, anesthesiologists should be aware that this is a potential complication in any case where dexmedetomidine is used and that this complication could have a negative effect on patient care.

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REFERENCES

1. Peng K, Shen YP, Ying YY, et al. Perioperative dexmedetomidine and 5-year survival in patients undergoing cardiac surgery. Br J Anaesth 2021; 127: 215-223. doi: https://doi.org/10.1016/j.bja.2021.03.040.
2. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000; 59: 263-268. doi: https://doi.org/10.2165/00003495-200059020-00012.
3. Liu X, Zhang K, Wang W, et al. Dexmedetomidine versus propofol sedation improves sublingual microcirculation after cardiac surgery: a randomized controlled trial. J Cardiothorac Vasc Anesth 2016; 30: 1509-1515. doi: https://doi.org/10.1053/j.jvca.2016.05.038.
4. Chi X, Liao M, Chen X, et al. Dexmedetomidine attenuates myocardial injury in off-pump coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth 2016; 30: 44-50. doi: https://doi.org/10.1053/j.jvca.2015.06.026.
5. Priye S, Jagannath S, Singh D, et al. Dexmedetomidine as an adjunct in postoperative analgesia following cardiac surgery: a randomized, double-blind study. Saudi J Anaesth 2015; 9: 353-358. doi: https://doi.org/10.4103/1658-354x.154715.
6. Kadam SV, Tailor KB, Kulkarni S, Mohanty SR, Joshi PV, Rao SG. Effect of dexmeditomidine on postoperative junctional ectopic tachycardia after complete surgical repair of tetralogy of Fallot: a prospective randomized controlled study. Ann Card Anaesth 2015; 18: 323-328. doi: https://doi.org/10.4103/0971-9784.159801.
7. Leino K, Hynynen M, Jalonen J, et al. Renal effects of dexmedetomidine during coronary artery bypass surgery: a randomized placebo-controlled study. BMC Anesthesiol 2011; 11: 9. doi: https://doi.org/10.1186/1471-2253-11-9.
8. Mutter CM, Smith T, Menze O, Zakharia M, Nguyen H. Diabetes insipidus: pathogenesis, diagnosis, and clinical management. Cureus 2021; 13: e13523. doi: https://doi.org/10.7759/cureus.13523.
9. Granger S, Ninan D. Intraoperative dexmedetomidine-induced polyuric syndrome. Cureus 2017; 9: e1218. doi: https://doi.org/10.7759/cureus.1218.
10. Fuhai J, Liu H. Intraoperative hypernatremia and polyuric syndrome induced by dexmedetomidine. J Anesth 2013; 27: 599-603. doi: https://doi.org/10.1007/s00540-013-1562-3.
11. Adams PS, Cassara A. Dexmedetomidine-related polyuria in a pediatric patient. J Anesth 2015; 30: 352-355. doi: https://doi.org/10.1007/s00540-015-2101-1.
12. McGuire JA, Niazi SA, Sizemore DC. Transient dexmedetomidine bolus-induced excessive urination intraoperatively in a 68-year-old male. Case Rep Anesthesiol 2020; 2020: 6660611. doi: https://doi.org/10.1155/2020/6660611.
13. Chen Z, Chen T, Ye H, Chen J, Lu B. Intraoperative dexmedetomidine-induced polyuria from a loading dose: a case report. J Int Med Res 2020; 48: 0300060520910643. doi: https://doi.org/10.1177/0300060520910643.
14. Vani S, Stackpole A, Kovacevic MP. Probable dexmedetomidine induced diabetes insipidus: a case review. J Pharm Pract 2023; 36: 685-688. doi: https://doi.org/10.1177/08971900211053261.
15. Shirasaka T, Kannan H, Takasaki M. Activation of a G protein-coupled inwardly rectifying K+ current and suppression of hcontribute to dexmedetomidine-induced inhibition of rat hypothalamic paraventricular nucleus neurons. Anesthesiology 2007; 107: 605-615. doi: https://doi.org/10.1097/01.anes.0000281916.65365.4e.
16. Kudo LH, Hebert CA, Rouch AJ. Inhibition of water permeability in the rat collecting duct: effect of imidazoline and alpha-2 compounds. Proc Soc Exp Biol Med 1999; 221: 136-146. doi: https://doi.org/10.1046/j.1525-1373.1999.d01-67.x.
17. Watso JC, Farquhar WB. Hydration status and cardiovascular function. Nutrients 2019; 11: 1866. doi: https://doi.org/10.3390/nu11081866.