



Establishment and Validation of a Predictive Nomogram for Polyuria during General Anesthesia in Thoracic Surgery: A Mini Review

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ABSTRACT

Thoracic general anesthesia surgery advocates restrictive rehydration, and anesthesiologists focus on the problem of intraoperative oliguria, while the problem of intraoperative polyuria is seldom mentioned. However, in our clinical work, we have observed the phenomenon of intraoperative polyuria in some of the patients who underwent thoracic general anesthesia surgery, so we want to explore the factors affecting intraoperative polyuria in thoracic general anesthesia surgery, and we expect to establish a predictive model that can predict the incidence of intraoperative polyuria in thoracic general anesthesia surgery patients. We searched the literature and found only case reports of intraoperative polyuria caused by dexmedetomidine, ketamine, sevoflurane, propofol, opioids, etc., all of which were mentioned to be associated with the release of antidiuretic hormone. The aim of this study was to identify the factors affecting intraoperative polyuria in thoracic general anesthesia surgery and to establish a prediction model, which was validated to help anesthesiologists better manage volume.

Keywords: Polyuria; General anesthesia; Thoracic surgery

INTRODUCTION

Thoracic surgery is mostly advocated for restrictive fluid infusion, while in the actual clinical work, it was found that some patients had intraoperative polyuria resulting in negative volume balance and circulatory instability appeared. Oliguria is often a concern for anesthesiologists, while intraoperative polyuria is rarely mentioned. In adults, intraoperative polyuria is typically defined as urine volume ≥ 2.5 mL/kg/h according to a study or as ≥ 3 L/24 h or ≥ 40 -50 mL/kg/24 h according to several other studies [1-4]. However, as the factors associated with intraoperative polyuria during general anesthesia remain unclear, we wanted to identify the factors influencing intraoperative polyuria, develop a predictive model, and validate it in this retrospective study.

LITERATURE REVIEW

Case reports related to anesthesia drugs causing intraoperative polyuria

The five drugs used in various studies are listed below:

Dexmedetomidine: A reported case of central polyuria triggered

by dexmedetomidine in a 61-year-old male patient in the intensive care unit was reported by Uddin et al., suggesting that clinicians should raise awareness of uncommon side effects of the drug in February, 2021 [5]. A case report published by Vani et al., in October, 2021 suggested that dexmedetomidine may cause polyuria as well as severe electrolyte abnormalities [6]. Villela et al., studied the effects of dexmedetomidine on the renal system and Arginine Vasopressin (AVP) in adult dogs, and concluded that low doses of dexmedetomidine inhibited AVP secretion, leading to increased urinary excretion. These effects may protect the kidney during the occurrence of ischemic events [7]. In year 2011 Greening et al., reported a 40-year-old patient with chondrodysplasia who underwent posterior spinal fusion under general anesthesia. Urine volume increased from 150 ml/h to 950 ml/h in the 4th hour. Polyuria was accompanied by elevated serum sodium, decreased urine specific gravity, and elevated serum osmolality. Urine volume decreased significantly within 2 hours after stopping dexmedetomidine infusion [8]. In year 2013 Pratt et al., reported a 50-year-old man with a history of alcoholism who was admitted to the ICU after emergency tracheal intubation following a seizure and fall down multiple steps, where polyuria

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was triggered by pumped dexmedetomidine [9]. In year 2013 Ji et al., reported a case of hypernatremia and polyuria associated with dexmedetomidine infusion in a 71-year-old female patient undergoing posterior spinal fusion at L3-L5 of the spine [10]. In year 2016 Adams et al., reported a case of polyuria with hypernatremia in a 12-year-old pediatric patient undergoing surgery for idiopathic scoliosis with intraoperative infusion of dexmedetomidine [11]. In year 2017 Granger et al., reported polyuria with intraoperative dexmedetomidine in a 23-year-old male patient with traumatic cervical spine fracture who underwent anterior and posterior discectomy and spinal fusion [12].

Ketamine: In year 2014 Hatab et al., reported central polyuria induced by ketamine infusion after admission to the pediatric intensive care unit for pneumonia in a 2-year-old girl with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency and stable hypertrophic cardiomyopathy [13]. In year 2015 Gaffar et al., reported a case of central polyuria triggered by ketamine infusion during internal and external carotid artery bypass grafting in an 18-year-old woman with smokers' disease [14]. In year 2019 Kataria et al., report a case of polyuria due to ketamine infusion in a 42-year-old Asian man who underwent cesarean section and splenectomy and was admitted to the ICU [15]. In year 2021 Herity et al., reported 2 cases of delayed central polyuria triggered by the use of ketamine (Patient I 32 h, Patient II after 55 h) [16]. All of these case reports suggest that ketamine-induced polyuria is associated with inhibition of AVP release.

Propofol: In year 2008 Kassebaum et al., reported polyuria in a 13-year-old boy who underwent parathyroidectomy with propofol infusion, suggesting that it may be able to indicate insidious preoperative cranial injury [17]. In year 2014 Soo et al., reported polyuria in a 66-year-old man undergoing L2-L5 lumbar spine surgery with propofol infusion [18]. In year 2016 Hong et al., reported two cases of intraoperative transient central polyuria in patients with smokers undergoing revascularization surgery, which was considered to be associated with the use of propofol and opioids [19]. As early as 1999 Inoue et al., conducted an animal experimental study on propofol-induced polyuria in rats and concluded that the mechanism was related to inhibition of AVP release [20].

Sevoflurane: Zhou et al., found that sevoflurane anesthesia decreased the pro-social protein Oxytocin (OT) as well as AVP activity in the hippocampus of neonates, impairing social recognition memory formation and social discrimination in young mice, and that the decreased AVP activity may further trigger polyuria [21]. Shimogai et al., concluded that both isoflurane and sevoflurane attenuated AVP-induced vasoconstriction and also inhibited angiotensin II-induced vasoconstriction by inhibiting myofilament calcium ions, resulting in Intraoperative Hypotension (IOH) and polyuria [22]. Volatile anesthetics are able to reduce systemic blood pressure by relaxing blood vessels and inhibiting myocardial contraction, and many anesthetics attenuate vasoconstriction induced by intrinsic neurohumoral factors (e.g., angiotensin II and norepinephrine), resulting in intraoperative hypotension in patients [22].

Opioids: In year 2020 Ohara et al., studied the effect of remifentanyl on fluid balance during anesthesia and found that there was a significant correlation between the rate of urine volume and the rate of remifentanyl infusion, and the authors concluded that a rate of 0.04 ml/kg/min was the threshold for fluids to reach both positive and negative balance [23]. Lehtinen et al., showed that

plasma AVP levels were significantly increased during induction of anesthesia when fentanyl 0.002 mg/kg was given, and that if naloxone was given prior to fentanyl administration it prevented the increase in plasma AVP levels during anesthesia and surgery [24].

A review of case reports causing intraoperative polyuria

A review published in the journal *Anesthesia and analgesia* reviewed case reports of perioperative polyuria due to anesthetic drugs and their possible mechanisms through 2021 [25]. The review reviewed and evaluated cases from 24 cases associated with polyuria due to anesthetic drugs, which involved anesthetic drugs including dexmedetomidine, sevoflurane, ketamine, propofol, and opioids. The review summarized the possible pathophysiological mechanisms of polyuria with hypernatremia and severe intraoperative hypotension associated with commonly used anesthetics, respectively, and suggested that polyuria due to dexmedetomidine, ketamine, propofol, and opioids may be associated with AVP, and polyuria due to sevoflurane may be associated with Aquaporin-2 (AQP-2).

DISCUSSION

In this study, we established and validated a predictive nomogram for polyuria during general anesthesia in thoracic surgery. It shows good discrimination ability and is well calibrated. This will provide useful guidance for subsequent anesthetic management and prevention of intraoperative polyuria and provide additional benefits for perioperative volume management of patients.

Our study revealed fentanyl use, gender, the difference between Mean Arterial Pressure (MAP) at admission and before the operation, operation type, total amount of fluids and blood products transfused, blood loss, vasopressor, and cisatracurium use as the predictors for polyuria in thoracic surgery. This trial revealed fentanyl use as the most important risk factor for intraoperative polyuria. Most previous studies have linked this to AVP release. As a next step, we plan to conduct a multicenter, large-sample study to externally validate the model we derived in order to explore its possible mechanisms.

CONCLUSION

Fentanyl, gender, the difference between MAP at admission and before the operation, operation type, total amount of fluids and blood products transfused, blood loss, vasopressor, and cisatracurium use were identified as predictors of intraoperative polyuria and incorporated into the nomogram. The nomogram shows good discrimination ability on the Receiver Operating Characteristic (ROC) curve and is well calibrated using the Hodgkin Lymphoma (HL) test. Decision curve analysis findings upheld the clinical usefulness of the nomogram. Individualized and precise prediction of intraoperative polyuria allows for better anesthesia management and early prevention optimization.

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