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Case Report

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Remimazolam for Sedation During Magnetic Resonance Imaging in a Toddler With an Acute COVID-19 Infection

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has led to a global surge in hospitalizations due to pneumonia and respiratory distress. As with other infectious medical conditions, the perioperative care of a patient with an active or recent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection must address concerns regarding both the healthcare providers and the patient. SARS-CoV-2-positive patients face a higher risk of pulmonary complications and significantly higher rates of mortality, especially in those with preoperative respiratory symptoms. We present the use of the novel benzodiazepine, remimazolam, to provide sedation in a 9-month-old child with a fever of 106 °F who required sedation and anesthetic care during magnetic resonance imaging following a seizure. The basic pharmacology of remimazolam is discussed, previous reports of its use for procedure sedation are reviewed, and dosing regimens are presented.

Keywords: SARS-CoV-2; COVID-19; Pandemic; Remimazolam; Procedural sedation

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has led to a global surge in hospitalizations due to pneumonia and respiratory distress. This unprecedented outbreak was the result of a novel viral strain within the coronavirus family, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the pandemic [1]. Close contact with infected individuals and the inhalation of respiratory droplets are the main transmission pathways of SARS-CoV-2. Symptoms range from asymptomatic to severe end-organ involvement. As the COVID-19 pandemic continues to evolve, with emergent virus variants such as the delta and omicron strains, it is important to recognize the medical and surgical implications of this virus [2].

As the pandemic increased the number of hospitalizations, there was also an increase in the need for patients with SARS-CoV-2 infections to receive anesthetic care. Given the potential for increased perioperative morbidity in patients with SARS-CoV-2 infections, novel approaches to sedation and anesthesia are needed. We present the use of the novel, ultrashort-acting benzodiazepine, remimazolam, to provide sedation in a 9-month-old child with a fever of 106 °F who required sedation and anesthetic care during magnetic resonance imaging (MRI) following a seizure. As a rapidly acting and metabolized benzodiazepine, remimazolam offers the potential option of providing procedural sedation with spontaneous ventilation and a native airway thereby avoiding the need for airway instrumentation. The basic pharmacology of remimazolam is discussed, previous reports of its use for procedural sedation are reviewed, and dosing regimens are presented.

Case Report

The patient was a 9-month-old, 8.72 kg male without any relevant medical or family history, who initially presented in the emergency department (ED) after SARS-CoV-2 exposure with fever, body-wide shaking for approximately 1 min, and decreased oral fluid intake. Initial evaluation revealed a positive nasal polymerase chain reaction (PCR) swab for SARS-CoV-2 in addition to acute suppurative otitis media of the right ear. The remainder of the physical examination was negative, showing no clinically significant illness at that time, therefore he was discharged home. The patient returned to the ED the same day via emergency medical services (EMS) after a seizure at home with decreased movement on the left side of the body. He was admitted to the hospital for further evaluation and observation. The next day, he had a recurrent fever of 106 °F along with seizure activity, accompanied by reduced motion on the left side of the body and right eye deviation. The seizure activity spontaneously resolved without treatment. The patient was lethargic but responded to stimulation, and his neurologic examination was non-focal. The initial chest radiograph did not show evidence of pneumonia. During transport to comput-

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ed tomography (CT) imaging, the patient had another seizure which resolved with the administration of intravenous lorazepam. Radiological imaging suggested leukomalacia versus focal malformation of the right temporal and parietal lobes along the Sylvian fissure, likely related to a prior insult. As a result, MRI was recommended. Anesthesia was consulted for sedation for MRI. Perioperative vital signs included blood pressure 122/57 mm Hg, pulse 146 beats/min, respirations 41 breaths/min, oxygen saturation 100%, and a temperature of 98.7 °F. Physical examination was unremarkable as was the preoperative laboratory evaluation. He was transported to the operating room and routine American Society of Anesthesiologist monitors were placed. General anesthesia was initiated by administering remimazolam at a rate of 15 µg/kg/min, accompanied by two doses of intravenous dexmedetomidine (4 µg each, separated by 5 - 6 min). Following the administration of the first dose of dexmedetomidine, the remimazolam infusion rate was increased to 20 µg/kg/min and following the second dose of dexmedetomidine, sedation was adequate to start MR imaging. Spontaneous ventilation was maintained via a non-invasive nasal cannula with oxygen supplementation and positive end-tidal carbon dioxide ($ETCO_2$) monitoring. After 37 min of maintenance, the remimazolam infusion rate was reduced to 15 µg/kg/min and discontinued 15 min later. A total volume of 100 mL of lactated Ringer's solution was administered during the 72 min of anesthesia care. During the procedure, oxygen saturation was maintained at 97-99% with oxygen at 2 L/min and the $ETCO_2$ varied from 36 to 43 mm Hg. No episodes of apnea were observed. Even though the patient's postoperative course was unremarkable, the MRI was concerning for a distant prior mild hypoxic-ischemic event with changes in the right temporal and parietal lobes. Further follow-up was scheduled and he was discharged home on postoperative day 2.

Discussion

As with other acute medical conditions, concerns regarding both the healthcare providers and the patient must be considered when anesthetizing a patient with an active or recent SARS-CoV-2 infection. Healthcare workers may be at risk when providing patient care near an aerosol-generating procedure [3, 4]. Additionally, SARS-CoV-2-positive patients face a higher risk of pulmonary complications and significantly higher rates of mortality, especially in those with preoperative respiratory symptoms [2, 4, 5].

In addition to other routine perioperative concerns, patients with COVID-19 and other respiratory infections mandate the use of specific techniques to prevent exposure and infection of healthcare providers and prevent postoperative respiratory failure or perioperative respiratory adverse events (PRAEs) [6-8]. Aerosols can transmit SARS-CoV-2 from patients to healthcare providers, making anesthesiologists and perioperative healthcare workers particularly vulnerable to infection. Procedures that involve the airway and respiratory system such as endotracheal intubation, positive pressure ventilation, high-flow nasal cannula (HFNC), bronchoscopy, and nebulizer treatments provide the greatest risk due to the aerosolization of infectious particles. Aerosolized viral shedding can extend beyond the operating room, contaminating the hallways and areas near the operating rooms. To avoid these concerns, anesthetic care of SARS-CoV-2 patients should focus on specialized techniques during airway management, appropriate choice of anesthetic techniques according to the surgical procedure, use of personal protective equipment, optimization of operating room configurations, careful patient transportation protocols, and meticulous scheduling [1-4].

PRAEs and pulmonary complications occur more frequently in adult patients with perioperative SARS-CoV-2 and a similar pattern of adverse events has been reported among pediatric patients, including those who are asymptomatic [8-12]. Park et al retrospectively evaluated the perioperative outcomes of 446 children with SARS-CoV-2 infections compared to 446 case-matched controls [8]. The overall incidence of PRAEs was significantly higher in children with SARS-CoV-2 (odds ratio (OR) 1.92); however, no difference was noted in mortality. The most pronounced differences were observed in instances of high peak inspiratory pressure $\geq$ 25 cm H_2O during the intraoperative period (OR 11.0). The risk of PRAEs was highest in those diagnosed within 2 weeks of anesthesia or symptomatic on the day of care. Similarly, in a single-center, retrospective, case-control study of 35 pediatric patients with confirmed SARS-CoV-2 infection and 70 non-SARS-CoV-2 control patients, matched 1:2 by age and type of procedure, 26% of SARS-CoV-2-positive patients had post-anesthesia complications compared to 1% of controls (OR 18.0) [12].

Children with significant respiratory symptoms during SARS-CoV-2 infection experience a higher risk of transient blood oxygen desaturation in the post-anesthesia care unit (PACU). The aerosolization of the SARS-CoV-2 virus and the increased risk of PRAEs are both dependent on the airway management of these patients, with the highest risks being during endotracheal intubation. As the choice of airway management may impact the risk of aerosolization of the virus as well as the perioperative outcomes, we chose procedural sedation with remimazolam rather than general anesthesia.

Given these concerns, we chose to provide procedural sedation and maintain spontaneous ventilation with a native airway in our patient to avoid the potential of aerosolization of the SARS-CoV-2 virus during airway instrumentation and tracheal extubation. There are numerous acceptable options for procedural sedation during MRI, including benzodiazepines, propofol, ketamine and/or dexmedetomidine [13]. Remimazolam, the ultrashort-acting and rapidly metabolized benzodiazepine, may be a novel option for procedural sedation. Remimazolam is an ester-metabolized intravenous benzodiazepine with sedative, anxiolytic, and amnestic properties similar to midazolam [14-16]. Remimazolam undergoes hydrolysis by tissue-esterases with a reported half-life of 5 - 10 min and a limited context-sensitive half-life. These properties allow for its administration by bolus and/or continuous infusion, with the attainment of a deep level of sedation while allowing for rapid awakening. Following approval by the US Food and Drug Administration (FDA) for use in adults in 2020, initial clinical trials demonstrated its efficacy for sedation of adults during invasive procedures such as gas-

trointestinal endoscopy and bronchoscopy [17-20]. These trials have demonstrated efficacy with limited adverse effects on respiratory and hemodynamic function, a lack of pain with intravenous administration, reduction of post-procedure nausea and vomiting (PONV), and a rapid return to baseline neurologic function.

In our patient, the sedative effects of remimazolam were effective with no significant impact on respiratory or hemodynamic function. These results align with previous reports on the efficacy and safety profile. Preliminary experience has demonstrated its potential utility in pediatric-aged patients for a variety of procedures including radiologic imaging [15, 16]. Our current findings provide additional anecdotal experience regarding the efficacy of remimazolam for procedural sedation during radiologic imaging and extend this to include a SARS-CoV-2-positive patient.

Learning points

Infectious respiratory conditions such as SARS-CoV-2 may significantly increase the risk of PRAEs following anesthetic care. Additionally, airway manipulation during such procedures may place healthcare providers at risk due to aerosolization of the virus. Healthcare providers close to aerosols-generating procedures are at high risk of infection; therefore, avoidance of unnecessary airway manipulation should be carefully considered to prevent further contamination of the providers and surrounding areas. The decision to meet these criteria should be made on a case-by-case basis. Procedural sedation with remimazolam has previously been demonstrated to be a safe and effective option in the adult population. The preliminary experience in pediatric-aged patients suggests that it may be a valuable alternative or adjunct to propofol, dexmedetomidine, and ketamine for procedural sedation.

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None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

The guidelines of the IRB of Nationwide Children's Hospital (Columbus, Ohio) were followed. Informed consent was obtained for anesthetic care and the use of de-identified information for publication.

Author Contributions

EV: preparation of initial, subsequent, and final draft; JDT: concept, writing, and review of all drafts; AD: perioperative care of the patient, and review of final draft.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

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