General Anesthetic Management Of A Pediatric Patient With Angelman Syndrome For Dental Rehabilitation

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INTRODUCTION

Angelman Syndrome is a genetic disorder characterized by a partial deletion of chromosome 15, which contains subunits of the γ-aminobutyric acid (GABA) receptor. This syndrome often manifests with delayed development, intellectual disability, seizures, and speech impairment. It has previously been demonstrated that patients with this disorder have relative deficiencies of β3 and α5 subunits of GABA-A receptors. (1,2) As a majority of commonly used anesthetic agents exert their effect on the CNS via GABA-A receptors, this pathology carries profound implications on anesthetic management. We report successful inpatient-based general anesthesia for an Angelman Syndrome patient undergoing dental rehabilitation.

METHODS

A 15-year-old male with Angelman Syndrome with global developmental delay and epilepsy underwent dental rehabilitation requiring general anesthesia. As the patient was hyperactive and uncooperative upon entering the operating room, the patient was successfully sedated with 70mg ketamine intravenous (IV) with co-administration of 0.1mg glycopyrrolate IV. At this point, secondary IV access was able to be obtained. Induction was accomplished successfully via a combined intravenous and inhalation approach with vecuronium for paralysis.

Patient was induced with an additional 30mg ketamine IV, 6mg vecuronium, nitrous oxide at 7.5 L per minute, and isoflurane at 0.6%. During intubation, video laryngoscopy via a Cmac with D-blade was used to obtain a Cormack-Lehane grade I view of the glottis. A nasal RAE endotracheal tube was successfully placed via the right nare with the help of a size 30 Fr nasopharyngeal airway. Anesthesia was maintained with nitrous oxide and isoflurane, and no further paralysis was required. Patient received a total of 100mg ketamine, 6mg vecuronium, 0.2mg glycopyrrolate, 1000mg Ofirmev, 1185 L of nitrous oxide over 300 minutes (at an average rate of 3.95 L/min), isoflurane at an average of 0.84% over 300 minutes, and 1 L of Plasma-lyte. Intraoperative hypotension required up-titration of fluids and a minimal dosage of 30mcg phenylephrine.

Additionally, patient was also given 10mg metoclopramide, 8mg decadron, and 4mg Zofran for anti-emesis. Emergence was complicated by an episode of laryngospasm post-extubation, which we successfully broke by utilizing the Larson Maneuver and continuous positive airway pressure. The patient tolerated the procedure well, and post-operatively the patient's mother reported that he had returned to his baseline mental status and patient was lying comfortably with no apparent distress. He had no episodes of nausea, emesis, or respiratory compromise. Patient was subsequently discharged from the post-anesthesia care unit after two hours of monitoring with no other complications.

DISCUSSION

There are four known genetic mechanisms that result in Angelman syndrome, including molecular deletions involving the meiotically unstable 15q11.2-q13 critical region, paternal uniparental disomy (UPD), imprinting defects (IDs), and mutations in the ubiquitin-protein ligase E3A gene (mUBE3A).1 These genetic mechanisms are thought to result in a functional absence of UBE3A, which accounts for approximately 90% of cases, while the other 10% of Angelman syndrome patients have no identified genetic abnormality. (3) Additionally, genes for the subunits that make up the γ-aminobutyric acid (GABA)-A receptor are also found at the 15q11-13 locus, and it is thought that deletions at this locus result in disorders of GABA-A receptors, as well as changes in GABA synthesis and release, causing either hyperfunction or hypofunction of the GABA system. (3, 4) Because the majority of currently used anesthetics affect the CNS through the GABA system, the implications on anesthetic management can be profound.

Patients with Angelman syndrome appear to have a relative deficiency of β3 and α5 subunits of GABA-A receptors. Because the majority of currently used anesthetics affect the CNS through the GABA system, it has been suggested that patients with Angelman syndrome are at increased risk for complications both during and following the administration of anesthesia due to modified receptor kinetics and pharmacodynamic unpredictability. (5) In this case, we utilized ketamine, which primarily acts via NMDA-antagonism, and nitrous oxide, which is suspected to have some action on the NMDA system in addition to its effect on the GABA system, as the primary anesthetic agents. (6)

CONCLUSIONS

As patients with Angelman syndrome typically present with developmental delay, intellectual disability, and speech impairment, they impose numerous challenges in the peri-operative setting. Furthermore, the pathophysiology involves various changes in GABA-A receptors, which is the primary target for many anesthetic agents. Highlighted in this case is an approach that employs agents such as ketamine, which depends primarily on NMDA-antagonism, to achieve successful general anesthesia with minimal hemodynamic instability or other complications.

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