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Case Report Open Access

The Use of Dexmedetomidine for The Prevention of Sevoflurane Related Emergence Agitation in a Patient with Angelman Syndrome Who Underwent General Anesthesia for Magnetic Resonance Imaging. "Case Report".

Carlos Ramírez-Paesano*, Camila Carrasco Chacón, Claudia Rodiera Clarens, Josep Rodiera Olive.

Servei Central d'Anestesia (Anestalia), Centro Médico Teknon-Quironsalud, Barcelona.Spain

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***Correspondence:**
*Dr. Carlos Ramírez-Paesano, Servei Central d'Anestesia (Anestalia), Centro Médico Teknon-Quironsalud, Barcelona. Spain; Email: cramirez@anestalia.com.

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ABSTRACT

Angelman syndrome is the consequence of a genetic alteration in the chromosome 15 where the expression of the β3-subunits of GABA-A receptors is encoded. So, unpredictable responses to intravenous GABA-anesthetics may be the result.

We present a 19-year-old male patient with AS who required anesthesia to undergo an MRI and CT-scan. All his previous anesthetic procedures were complicated by severe emergence agitation with physical self-injury. His parents also mentioned that the patient reacted with paradoxical agitation due to benzodiazepines (midazolam) administration in previous anesthesia.

Dexmedetomidine (an α-2- adrenergic agonist) has been used in pediatric anesthesia as an adjuvant to attenuate agitation events after inhalation anesthesia. However, there are few publications on its use in patients with AS.

We describe the use of a single intravenous dose of dexmedetomidine (0.2μg/Kg) to prevent sevoflurane-related emergence agitation with good results.In addition, the potential benefits and precautions in using this non-GABA drug in patients with AS are discussed.

Introduction

The genetic expression of the β3 subunits of GABA-A receptors is encoded on chromosome 15. It is recognized that Angelman syndrome (AS) is the result of a genetic alteration in that chromosome. The expression of the Gamma-Aminobutyric Acid-Type A Receptor Subunit-Beta3 (GABRB3) gene is particularly affected by deletions or mutations that modify the genetic code of the β3-subunit of GABA-A receptors[1].

GABA receptor abnormalities may cause unpredictable responses to intravenous GABA agonists in patients with AS, making them a challenge for the anesthesiologist[2].

Significant intellectual deficit, severe developmental delay and muscular deconditioning are common features. Frequently, they are too restless to undergo studies like MRI and CT-Scan without anesthesia[3].

The aim of this report is to discuss the use of dexmedetomidine to prevent agitation upon anesthetic emergence in a patient with AS which all his previous anesthetic procedures were complicated by severe agitation and uncontrollable aggressive behavior on emergence resulting in physical self-injury[4].

The parents were informed about the use of dexmedetomidine and the informed consent was signed. Also, written and informed consent was obtained from the parents of the patient for publication of this case report.

Case Report

We present a 19-year-old male patient with AS who required anesthesia because of uncooperative behaviors during MRI and CT-Scan. The patient had no history of allergy, weighed 38 kg and was 160cm tall. The patient had severe intellectual impairment and suffered muscle atrophy and marked physical deconditioning. He presented with ataxia, epilepsy, gait disturbance, and chronic intestinal dysfunction. Microcephaly, with a large mouth and tongue protrusion, was also observed.

He came in for an abdominal MRI and a lumbar CT scan on June 30th, 2022 to study the recent onset of urinary incontinence.

His medications included sulfonamide, zonisamide, gabapentin, mirabegron, clobazam, linaclotide, baclofen and terazosin.

His parents also mentioned that the patient reacted with paradoxical agitation due to benzodiazepines (midazolam) administration in previous anesthesia.

Upon arrival in the MRI area, the patient was in a state of distress and moved about restlessly. The presence of his parents was required to proceed with the procedure. Psychomotor agitation was present from the beginning of the procedure. Routine monitors before anesthesia were used: Non-invasive blood pressure, heart rate, electrocardiogram and pulse oximeter saturation(SpO2). Inhalation induction with sevoflurane (4 vol.%) and O_2/Air (FiO_2 0.5) was performed. Then, a venous line was accessed, and atropine 0.01 mg/Kg was administered. The patient was quickly put under anesthesia. A Laryngeal Mask Airway (LMA) #3 was inserted and EtCO2 was monitored. Rocuronium bromide, 20mg intravenously (iv.), was administered to achieve adequate coupling to mechanical ventilation. Dexmedetomidine 0.2 µg/Kg, iv. over 15 minutes was also administered. Anesthesia was maintained with sevoflurane 0.5 MAC. The procedures lasted 150 minutes. Systolic blood pressure was maintained between 100-110 mmHg, diastolic blood pressure between 50-55 mmHg, heart rate 90-110 beats per minute, and SpO2 98-100%. Neither BIS™ nor neuromuscular blockade monitoring could be performed due to incompatibility with the MRI area. After the imaging studies were completed, the patient was awakened in a room outside the magnetic field. The patient presented a very calm awakening, without any agitation. The response to muscle stimulation was evaluated by the use of the "Toff-Cuff Method NMT-Monitor-RGB". The initial dose of sugammadex (2.0 mg/Kg) was insufficient to achieve 100% neuromuscular blockade reversal. Therefore, an additional 1.0 mg/Kg of sugammadex was administered. Once a TOF ratio of 100% was achieved the patient regained muscle tone, the LMA was removed and the patient was transferred to the post-anesthetic recovery room for observation. Throughout his stay in the post-anesthetic recovery room until hospital discharge, the patient remained calm and showed no agitation nor aggressive behaviors. No cardiovascular complications were seen.

Discussion

Angelman syndrome is the result of a genetic alteration in chromosome 15, a chromosomal disorder inherited by the disruption of the UBE3A gene on the maternal side. The genetic expression of the β3 subunits of GABA-A receptors is encoded in chromosome 15. In AS, deletions of chromosome 15 (chromosome 15q11.2-q13) are the most frequent abnormalities (75%)[5]. GABA receptor abnormalities in AS may explain the unpredictable response to intravenous GABA agonists and their variability in terms of dose requirements. However, there is no evidence as to which intravenous hypnotic is the most appropriate to use. Balanced anesthesia and total intravenous anesthesia have been used without side effects even though the duration of the drug's effect can be highly variable. The response to anesthetic intravenous drugs can be challenging to predict[2].

Inhalation anesthetics act through the α-subunit GABA-A receptor, and their anesthetic effects may be more consistent[6]. Due to this fact, we think that there was no resistance to the action of sevoflurane in our patient. During inhalation induction and maintenance, the MAC was relatively low.

The possibility of post-anesthetic agitated emergence in the pediatric population is well documented in the literature when sevoflurane or desflurane is used[7]. Dexmedetomidine has been used in pediatric anesthesia as an adjuvant to reduce MAC and to attenuate agitation events after inhalation anesthesia[8-10] . A meta-analysis shows that dexmedetomidine might be the best choice to prevent sevoflurane-related emergence agitation in children[11].

As background, the patient's mother reported that all the patient's post-anesthetic awakenings had been characterized by excessive agitation, combativeness and aggressive behaviors. Also parents mentioned the patient's history of increased agitation with the use of benzodiazepines. For these reasons, and aligned with the evidence found in the studies mentioned above [8,10,11] ,we decided to use dexmedetomidine as it would be a reasonable option to prevent or attenuate a post-anesthetic agitation and aggressiveness in this patient. We considered that the use of benzodiazepines (midazolam) was not an option for this case. The use of an opioid such as fentanyl was also not justified since the imaging studies were not painful.

There are few case reports of patients with AS in which dexmedetomidine for sedation was used for neuromonitoring with good results [4]. We only found one case report, not formally published, regarding the use of dexmedetomidine for prevention of post-operative agitation in a 14 year-old male with AS underwent heel surgery. The patient had an awakening without agitation or pain. However, this report has important biases to attribute the post-operative results to dexmedetomidine. In that case report, midazolam was administered preoperatively and the authors did not mention what type of general anesthesia was given or the use of another type of analgesic administered. Finally, the dose of dexmedetomidine was 0.2 µg/kg (iv.) over 10 minutes before finishing the surgery[Cheon & Tkachencko. University of Chicago, IL. USA. http://www2.pedsanesthesia.org]. On the contrary, our patient received only dexmedetomidine as coadjuvant, and sevoflurane was given as sole anesthetic.

Dexmedetomidine is an α-2- agonist adrenergic and its pharmacological effects are not directly related to GABA-A receptors. Therefore, its pharmacological effect might be more predictable in AS patients compared to midazolam which action is related to GABA receptors. Based on this reasoning, we think that dexmedetomidine was a good option in this particular patient .As a result, a post-anesthetic awakening without agitation was obtained.

Patients with AS may suffer from an increased vagal tone[12]. A medical history of bradycardia could relatively contraindicate the use of dexmedetomidine. In our case, we decided to administer prophylactic atropine following the recommendations of some authors [6].The decision was also based on not having a cardiac electrophysiological study and us taking the decision to use dexmedetomidine to change the awakening experience. In addition, the performance of general anesthesia in the MRI setting motivated us to be extremely cautious about the possibility of bradyarrhythmia. Therefore, atropine was used.

Another aspect to consider is the muscle atrophy and physical deconditioning that AS patients may present. They make the AS patient more susceptible to the effects of neuromuscular relaxants (NMR). NMR monitoring is advisable, especially during the recovery phase, to avoid residual muscle relaxation. We used rocuronium to achieve coupling to mechanical ventilation during a 150-minute radiological procedure. During the imaging study, there were no NMR monitors compatible with the magnetic field. For this reason, the NMR reversal was performed outside the MRI room using sugammadex. The patient needed a high dose of sugammadex (3 mg/kg) for 100% NMR recovery. This led us to think that the patient had an increased response to rocuronium (dose used : 0.5 mg/Kg) or else the dose administered to this patient was excessive. NMR reversal with anticholinesterase agents should be avoided due to the possibility of extreme bradycardia, even if co-administration with anticholinergics is done. The use of sugammadex may also cause bradycardia but it appears to be a better and safer drug than neostigmine. The use of neuromuscular relaxation monitoring is mandatory to avoid postoperative residual relaxation complications [13,14] .

In general, there is little experience in using dexmedetomidine in patients with Angelman syndrome. We believe, this case might serve as an invitation to consider its use in this type of patients.

Conclusion

We presented a clinical case of a patient with AS under general anesthesia with sevoflurane and dexmedetomidine with good results in terms of MAC reduction and preventing agitation during awakening.

Take note that dexmedetomidine might be considered as an adjuvant to use in balanced anesthesia in patients with AS. Its mechanism of action is not related to GABA-A receptors. That being the case, its effects are more predictable than other hypnotics [4, 6] In addition, it is a drug that can prevent or attenuate agitation on emergence after general anesthesia with sevoflurane or desflurane [8-11]. Dexmedetomidine should be avoided or carefully used if the patient has a diagnosis of an exacerbated vagal tone with risk of extreme bradycardia or asystole[12].

Muscle atrophy and physical deconditioning make patients with AS more susceptible to the effect of RNM, making monitoring mandatory. Reversal with sugammadex seems to be a safer option than anticholinesterase medications [13,14]

Abbreviations

AS: Angelman syndrome; BIS™ : Bispectral Index monitoring system ; CT-Scan :Computerized tomography scan; EtCO2 : End Tidal carbon dioxide; FiO_2 : Fraction of inspired oxygen GABA :gamma-aminobutyric acid; GABRB3: Gamma-aminobutyric acid Type A Receptor Subunit Beta3 ; LMA; laryngeal mask airway ; MAC: minimun alveolar concentration; mg: miligram ; µg: microgram ; MRI: Magnetic resonance imaging NMDA: N-methyl-D-aspartate; NMR: neuro-muscular relaxants; SpO2: pulse oximeter saturation ; TOF: Tren of Four muscular testing, UBE3A: ubiquitin-protein ligase E3A ; vol.%: volume percent.

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Authors Contribution

Carlos Ramírez-Paesano: This author helped in drafting the work and revising it critically for important intellectual content. Substantial contributions to the conception and design of the work. Also the acquisition, analysis and the interpretation of data. Final approval of the version to be published.

Camila Carrasco Chacón: This author helped on the conception and design of the work. Also acquisition, analysis and the interpretation of data.

Claudia Rodiera Clarens: This author helped on the conception and design of the work. Also acquisition, analysis and the interpretation of data.

Josep Rodiera Olive: Substantial contributions to the conception and design of the work. Acquisition, analysis and the interpretation of data. Also, final approval of the version to be published.

Ethics Aprproval And Consent To Participate

The parents of the patient signed the informed consent. The chief of the department of anesthesiology (Anestalia) was consulted about the case and the measure was authorized following our protocols. Likewise, the use of the medication was supported by the Ethics Committee of Centro Médico Teknon under the standards of good clinical practice.

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Conflicts of interest

None.

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