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Total Intravenous Anesthesia in Joubert Syndrome Patient for Otorhinolaryngology Surgery: A Case Report and Mini Review of the Literature

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Male, 13-year-old
Final Diagnosis: Joubert syndrome
Symptoms: Apnea
Medication: —
Clinical Procedure: Total intravenous anesthesia (TIVA)
Specialty: Anesthesiology

Objective: Congenital defects/diseases

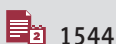
Background: Joubert syndrome is a rare autosomal recessive disorder first described in 1969, with an estimated prevalence of 1 in 100 000. Joubert syndrome is characterized by partial or complete agenesis of the cerebellar vermis – the structure that connects both parts of the cerebellum. This results in the main clinical symptoms, such as muscular hypotonia, ataxia, mental retardation, abnormal eye movements, and a central apnea breathing pattern. Joubert syndrome can combine neurological signs with variable multi-organ involvement, mainly of the retina, kidneys, liver, and musculoskeletal system.

Case Report: A 13-year-old boy presenting with recurrent otitis media, fever, respiratory infections, and tonsillar hyperplasia needed surgery. At the otorhinolaryngology outpatient clinic, the indication for surgical paracentesis, adenoidectomy, and tonsillectomy under general anesthesia (first in his life) was set. We performed a total intravenous anesthesia (TIVA) using propofol (described as safe) and remifentanyl (organ-independent metabolism) without any side-effects. For postoperative pain therapy we used metamizole instead of paracetamol in order to avoid liver injury.

Conclusions: Due to the possible facial dysmorphism we recommend a critical evaluation of the airway to assess a potential difficult airway preoperatively. Our case underlines that TIVA, with the medications used in this case, is safe. We refrained from premedication in order not to trigger central apnea. For safety reasons, all preparatory procedures were carried out in the recovery room under monitor surveillance and with audio-visual distraction for the patient in order to reduce the stress level. For postoperative pain therapy, we recommend the use of metamizole.

MeSH Keywords: Anesthesia, General • Apnea • Cerebellar Diseases • Congenital Abnormalities • Propofol • Rare Diseases

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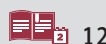
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Background

Joubert syndrome (JS) is a rare autosomal recessive disorder with an estimated prevalence of 1 in 100 000. It was first described in 1969 in 4 siblings with agenesis of the vermis cerebellar presenting intellectual disability, episodic hyperpnoea, and abnormal eye movement [1]. With the further development of the diagnostic possibilities of a pathognomonic mid-brain-hindbrain malformation, the so called “molar tooth sign” (MTS) was described. In 2004, this neuroradiological sign was suggested as a binding criterion for the diagnosis of “Joubert syndrome and related disorders” (JSRD) a new group including all diseases with MTS [2]. The syndrome is genetically heterogeneous, that is why the diagnosis is based on clinical appearance. There are 35 causative, ciliopathy-related genes that have been identified so far. The inheritance is autosomal recessive [3].

This genetic dysfunction results in a partial or complete agenesis of the cerebellar vermis – the structure that connects both parts of the cerebellum.

The clinical presentation is very heterogeneous. The main clinical symptoms are muscular hypotonia, ataxia, mental retardation, abnormal eye movements, and a central apnea breathing pattern. JS can combine neurological signs with variable multiorgan involvement, mainly of the retina, kidneys, liver, and musculoskeletal system.

The JS is characterized by frequent respiratory anomalies. Alternating episodes of apnea and hyperpnea may occur. Often these symptoms appear for the first time shortly after birth and intensify during emotional stress. In most cases the symptoms improve with age and disappear around the sixth month of life. Nevertheless, cases have been reported ranging from short episodes every few days to extremely frequent episodes (several times per day) and long-lasting apnea attacks requiring intensive care treatment and assisted ventilation [1,4].

To the best of our knowledge, there is little information available on performing total intravenous anesthesia (TIVA) in this population with the outlined medication for otorhinolaryngology surgery. Therefore, we want to share and discuss our findings of a patient with JS who was admitted to our hospital for a surgical paracentesis, adenoidectomy, and tonsillectomy undergoing general anesthesia using a TIVA.

Case Report

A 13-year-old male patient of 23 kg bodyweight presented with repeating fever attacks, recurrent otitis media, respiratory infections, and tonsillar hyperplasia at the otorhinolaryngology outpatient clinic. The ENT-colleagues set the indication for



Figure 1. Intubated patient with Joubert syndrome. Inserted Davis-Mayer spatula and mouth gag. Although OrphanAnesthesia [5] reports a frequent difficult airway in Joubert syndrome patients, in our case, with a wide mouth opening and good reclamation, there was no difficulty in securing the airway. Above the ary cartilage (highlighted in green) the tube disappears between the vocal folds.

surgical paracentesis, adenoidectomy, and tonsillectomy and therefore his first general anesthesia.

The patient's mental retardation made communication with the patient impossible. However, the mother reported that her son was suffering from apneic phases, especially at night and under stress. He had been provided with a non-invasive ventilation at home. The aforementioned reasons led to some challenges for the preoperative management. We refrained from premedication in order not to trigger central apnea. For safety reasons, we decided to place an IV access using transdermal anesthesia (EMLA of lidocaine 2.5% and prilocaine 2.5%, Aspen Pharma Trading Limited, Ireland) in the presence of the mother, in the recovery room under monitor surveillance and with audio-visual distraction by his favorite cartoon show. The procedure proved to be recommendable.

We could not evaluate the airway preoperatively, based on an uncooperative patient. We did have a mirror examination performed the day before by the ENT-colleagues of the mouth and upper pharynx at our disposal. Preoperative computed tomography/magnetic resonance imaging was not performed.

In the operating room, we started induction of narcosis with 0.3 µg/kg/min remifentanyl (Aspen Germany GmbH, Munich, Germany) and 100 mg of 1% propofol (Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany) followed by a continuous application at 6 mg/kg/h. We decided not to use any muscle relaxants due to reduced muscle tonus. Passage of the glottis (Cormack Lehane Grade I) with the tube was performed

without any problems (see Figure 1). A larynx mask may have been applicable as well. We used the endotracheal tube (according to our clinic's in-house standard), as an endotracheal tube provides a better overview of the surgical situs, prevents aspiration of wound blood during the operation, and blood and secretions can be easily sucked out before extubation. After securing the airway, we reduced the remifentanyl dose to 0.2 µg/kg/min and the initial propofol dose from 6 mg/kg/h to 4 mg/kg/h. In this state, the operation could take place without any problems. As an additional pain medication, the patient received 400 mg of metamizole IV (Ratiopharm GmbH, Ulm, Germany). Ventilation and oxygenation presented without difficulties throughout the whole procedure. Neither the heart rate nor the heart rhythm caused any problems. During induction and over nearly one hour of general anesthesia, the patient was kept warm using an inflatable hot-air blanket (Mistral Air, The Surgical Company, Kleeve, Germany).

Shortly after surgical completion, the patient awoke promptly free from any respiratory or circulatory problems. No additional pain medication was needed in the recovery room. Our patient was sleepy but woke easily when touched. Furthermore, he was respiratory stable in the recovery room, so that we did not have to administer additional oxygen. The waiting mother was immediately taken to the recovery room to calm her son if necessary.

There were no reports of nausea or any other negative side effects after general anesthesia.

Discussion

OrphanAnesthesia (a project of the German Society of Anesthesiology and Intensive Care Medicine) recommendation favors neither a balanced anesthesia nor a TIVA [5]. Since propofol has already been described as safe, we decided to add a short-acting opiate, to reduce the risk of postoperative respiratory depression previously reported [6]. A postoperative stress-triggered apnea would have resulted in a reduced expiration of the volatile anesthetic and could have endangered the patient. Patients with JS require an increased sensitivity of the surgical staff to stress avoidance for the patients in order to prevent apnea phases. We recommend that parents should stay with the patient as long as possible and for clinicians to carry out all measures under monitor control. Furthermore, we recommend not to administer any respiratory depressive premedication and to use audiovisual distraction instead. A topical application of local anesthetics can reduce the stress of IV puncture.

The literature considering general anesthesia in patients with JS is very limited; therefore, we discuss all parts of the TIVA and their influence on the patient.

Opioids

For the TIVA, we used a continuous remifentanyl administration in the dose range from 0.2 µg/kg/min to 0.3 µg/kg/min. We decided to use a short-acting opioid and chose remifentanyl to avoid postoperative respiratory depression. Remifentanyl seemed to be particularly suitable for this purpose. The degradation is organ-independent by non-specific esterases, therefore, a dose adjustment is not necessary in cases of liver or kidney function impairment associated with JS. It is degraded to 98% by hydrolysis of the ester bond and to 2% by N-dealkylation; resulting compounds have practically no opioid effect anymore. The half-life of remifentanyl is stated to be 6 minutes or less [7]. Due to these characteristics, postoperative opioid-induced respiratory depression is not to be expected

Hypnotics

There are reports of the use of volatile anesthesia [8], but since there is no clear recommendation for the use of a volatile anesthesia, we used the drugs aforementioned. It is the potential stress-induced apnea in the discharge phase that would especially hinder the breathing out of the volatile anesthetic. Therefore, we decided to use propofol, which is eliminated independent of respiration.

The propofol concentrations we used (4 mg/kg/h to 6 mg/kg/h) were described as safe and well controllable by a previous case report [9]. We can confirm this conclusion. Bhaskar et al. [10] used dexmedetomidine at a concentration of 0.3 µg/kg/h for postoperative sedation in their published case report. Dexmedetomidine has not attributed a respiratory depressive effect in previous studies [10,11], however, the European Medicines Agency states a possible respiratory depression with an incidence of 1/10 [12]. For this reason, we refrained from postoperative sedation, especially since our patient did not have any indication for sedation in the presence of the mother.

Muscle relaxants

In the described case, we decided to intubate the patient without the administration of a muscle relaxant. Non-depolarizing muscle relaxants should be administered with caution or avoided because of the existing muscle hypotonia. Nevertheless, rocuronium (Inresa Arzneimittel GmbH, Freiburg, Germany) would have been the relaxant of choice for severe airway conditions. Whereas, the antagonizability by suggamadex has the major advantage for prevention of postoperative breathing problems. Intraoperative relaxometry is particularly important for these patients when using a muscle relaxant. As JS patients are often immobile, succinylcholine is contraindicated.

Conclusions

In summary, we present the case of a 13-year-old patient who received a TIVA with propofol, remifentanyl, and without muscle relaxant, which was performed without any incidents. Our case underlines that TIVA with the outlined medication is safe. Propofol has been described in the literature as safe, and we recommend analgesia with a short-acting opioid like remifentanyl. The degradation of remifentanyl is organ-independent by non-specific esterases, therefore, a dose adjustment is not necessary in cases of liver or kidney function impairment associated with JS [7].

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We refrained from premedication in order not to trigger central apnea. For safety reasons, all preparatory procedures were carried out in the recovery room (not on a ward), under monitor surveillance, with audio-visual distraction for the patient, and in presence of the mother in order to reduce the patient's stress level. Throughout the entire procedure, peripheral oxygen saturation was consistently >96%, so no additional oxygen supply was necessary.

Conflict of interests

None.