

# Critical anesthetic induction of a premature neonate with Spina Bifida.



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## Observation

A 35 weeks 3/7 premature male baby was scheduled to undergo spina bifida correction and Chiari malformation surgery the day after Cesarean delivery. The pregnancy was characterized by intrauterine growth retardation and microcephaly that were not diagnosed early. Indeed, the 1st, 2nd and 3rd trimester obstetric ultrasounds were normal. The endocrine triple test prenatal screening wasn't realized. After 32 weeks 1/7, the parturient was hospitalized at the mother intensive care unit with a diagnosis of migraine. Pulmonary maturation of the fetus was induced at 33 weeks and she was hospitalized again at 35 weeks 2/7 for a micro-oscillating fetal monitoring. The day after, fetal monitoring showed fetal distress, and led to an emergency cesarean section under spinal anesthesia. The presentation was cephalic, and the Apgar score was reassuring (7/9/x). Immediately after birth, a spina bifida, closed by a thin membrane and partially open, was discovered. Once in the neonatal care unit, clinical examination revealed a few signs of dimorphism, including microcephaly, micrognathia, large tip of the nose, and folded ears. Cardiac and pulmonary auscultations were normal. Neurological examination revealed good motility of the inferior limbs, and normal left rotulean reflex. The right rotulean reflex couldn't be tested, due to the lateral decubitus position of the baby. Recorded parameters upon admission to the neonatal unit included heart rate (HR) at 131/min, respiratory rate (RR) at 24/min, temperature at 36,5°C, arterial blood pressure at 53/27/36 mmHg, peripheral saturation in oxygen (SpO<sub>2</sub>) at 100% in room air, weight of 2045g (P25), height of 44 cm (P15), and head circumference of 28.5cm (-3SD).

The mother's medical history was characterized by the occurrence of a stroke a few years earlier (2008). This stroke had been caused by hyperhomocysteinemia. The mother also had aortic and mitral insufficiency. Gravidity was 2, and parity was 0. Surgical past medical history encompassed curettage for a miscarriage in 2011. Her serology for HIV, HBV, and HCV was negative. She was immunized against toxoplasmosis and rubella.

The preoperative blood test of the baby was fairly normal. His blood type was A-. The transfontanellar ultrasound confirmed a type II Chiari malformation, and a subependymal hemorrhage. The neonate entered the operating room wrapped into a sterile bag. A nasogastric tube and umbilical venous catheter had already been placed in the neonatal unit. He was installed on the table, heated by a lamp. Monitoring included SpO<sub>2</sub>, and a 3 derivation ECG. After a 2 minute pre-oxygenation, sevoflurane induction of anesthesia was initiated, starting at an inhaled concentration of 6.5 %. Many boluses of propofol were administered intravenously up to 40mg, 2 minutes after a 0.1mg bolus of rapifen. Marked peripheral desaturation occurred at that time, with an SpO<sub>2</sub> falling to 70%, and a relative bradycardia at 100/min, despite the ease of facial mask ventilation. One orotracheal intubation was successfully performed, using a size 3 cuff-free endotracheal tube (ETT). The patient was evaluated Cormack Lehane grade I. Even though the auscultation, the symmetrical movements of the thoracic wall and a capnogram confirmed adequate position of the ETT, the oxygen saturation kept on decreasing. At that time, rate and pressure of manual ventilation were majored, and sevoflurane delivery diminished to 1%. No improvement was noticed. The peripheral saturation remained below 75%. A first attempt to increase the heart rate was done, using 10 µg of atropine

that were repeated 2 minutes later. This maneuver was not efficient, and HR did not pass over 100/min. Artifactitious SpO<sub>2</sub> measurement was excluded several times by changing the sensor position on the fingers. Three minutes later, isoprenaline was titrated by few boluses (0.4, 0.2, 0.4, 0.4, 0.4, and 0.4 µg within 20 minutes), until HR reached 120/min and stayed so. This resulted in a partial increase in oxygen saturation for a few seconds. Insofar as saturation kept on oscillating despite ongoing treatment, a crystalloid (Plasmalyte®) fluid challenge of 10 mL was attempted, followed by naso-tracheal intubation. Auscultation, thoracic movement, capnogram, and radioscapy again confirmed the good position of the endotracheal tube. Finally, a continuous infusion of isoprenaline (2.5 µg/mL) at a rate ranging from 1 mL/h at the end of induction, to 13 mL/h at the end of surgery was initiated. The vital parameters remained stable during the procedure. The arterial saturation was maintained above 95%, and HR between 110 and 140/min, during the continuous isoprenaline infusion, and NIBP ranged between 50 and 40/10 and 20 mmHg. Blood pressure was also optimized by Plasmalyte® fluid challenges of 10, 10, 10, 10, 20, 10, and 10 mL in one hour. Neurosurgery lasted 3 hours, and plastic surgery for closure of skin lasted one hour. The intubated and ventilated newborn was transferred with the isoprenaline infusion at a rate of 13mL/h to the neonatal unit once surgery was over.

The postoperative period was marked by important cardiovascular events. The isoprenaline at a maximum rate of 13 ml/h or 0.25 µg/Kg/min maintained the blood pressure around 45/16/26 mmHg. It was finally replaced by a continuous infusion of dopamine at a rate of 20 µg/Kg/min, according to the preferences of the neonatal pediatricians. The patient faced major oscillating phases of hypotension, associated with sinus bradycardias and desaturations. The increase of dopamine infusion rate led to hypertension that needed a rapid decrease in sympathomimetic medication rate of infusion. No arguments for intracranial hypertension, or convulsive incidents were noted. The electroencephalogram was normal. There also wasn't any unwanted dopamine boluses during changes of syringe, for example. A Transthoracic echocardiography excluded a cardiogenic origin. Cardiac anatomy was normal, but the foramen ovale was patent, and a ductus arteriosus was present. The ventricular function was good. Pulmonary artery hypertension was noticed at day 2. The cerebral ultrasounds performed at day 0, 1, and 2 showed a normal morphology of the cerebral structures, and the stability of the Chiari malformation. Given the continuous fentanyl sedation (2 µg/Kg/h), a neurological examination couldn't be performed during the first day after surgery. The neuropediatrician hypothesized a neurologic origin of the cardiovascular instability. Despite the absence of intracranial hypertension, the neurosurgeon pleaded for compression by the Chiari malformation. After lowering the sedation at day 2, a neurological examination revealed a guarded prognosis, the patient being at high risk of sphincter disorders, lower limb paralysis, and cognitive deficit. Parents and medical team made a joint decision of treatment withdrawal. A progressive weaning of ventilation support and an increase in fentanyl infusion rate led to the death of the patient on the third day. The karyotype was normal, and it's molecular analysis revealed a possible benign duplication of approximately 140kb of the region 13q12.3. The retained diagnosis was the one of an hemodynamic instability caused by a possible compression of the cerebral trunk by the Arnold Chiari malformation.

## **Discussion**

Neonate myelomeningocele patients are at high risk of central nervous system infection due to the direct exposure of the nervous tissue. Myelomeningocele repair is a surgical emergency that should occur within the first 24 hours of life. Preoperative screening doesn't require a cardiac evaluation, insofar as the incidence of heart disease is not increased in patients with central nervous system lesions(1, 2). We identified 2 causes that could explain the desaturation episode after the induction of anesthesia. Low systemic and high pulmonary vascular resistance defines fetal circulation. Most of the cardiac output flows through the ascending aorta while the blood from superior vena cava is directed towards the pulmonary artery and the ductus arteriosus. Clamping of the umbilical cord and expansion of the lungs after delivery produce major changes, such as an increase in blood return from the lungs to the left atrium, causing the closure of the foramen ovale. Several factors can be responsible for a return in fetal circulation, including any cause of hypoxia, hypercarbia, and anesthesia-induced changes in peripheral vascular tone (3, 4). Hypoxemia can occur when the right atrial pressure exceeds the left atrial pressure, or when preferential flow from the vena cava towards the patent foramen ovale persists, just as in the prenatal circulation (5). In our patient, we believe that the overdose of propofol used during induction of anesthesia (40mg), which equals to 19.5 mg/Kg, and associated with sevoflurane, was responsible for a major cardiovascular depression (HR decreased from 140 to 100/min). Isoprenaline, through its  $\beta_1$  effect (positive chronotropic, and dromotropic), partially helped compensating myocardial depression.

The second putative mechanism could involve the Chiari malformation. A downward herniation of the cerebellar tonsils below the foramen magnum, with elongation and compression of the brain stem, and obliteration of the cisterna magna can have occurred (6). This event may be responsible for bradycardia through a compression of the dorsal nucleus of the vagus (7).

## **Conclusion**

This case report underlines the dangers of propofol induction of anesthesia in neonates, as well as the dangers of anesthesia induction in neonates with patent foramen ovale. The use of propofol in neonates, particularly when a patent foramen ovale is present, is not well documented in the literature. Extreme precautions should prevail, keeping in mind that the return to fetal circulation is possible during the neonatal period. Two trials (NEOPROP (8) and NEOPROP2 (9)) are currently running to assess the induction dose of propofol in neonates. As advised by the authors of the first mentioned study, it is worth remembering to follow a “start low – go slow” model, using a 1 mg/Kg bolus dose.

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