Perioperative management of a patient with PEHO-Syndrome: Delayed recovery of neuromuscular blockade after rocuronium

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Abstract:

The PEHO syndrome (progressive encephalopathy with brain, facial and peripheral edema, hypsarrhythmia and optic atrophy) is a very rare autosomal recessive disorder with progressive encephalopathy. For diagnosis and therapy, many patients may require deep sedation or even general anesthesia. There are no previous reports on the perioperative management in PEHO-patients. Distinct obstacles have to be obeyed. Lack of pharyngeal control might bear an imminent risk of aspiration. Muscular hypotonia and an immobile state rules out the use of succinylcholine. In the case reported here, a 10-month old boy underwent laparoscopic assisted percutaneous jejunostomy. The anesthetic management consisted of total intravenous anesthesia with propofol and remifentanil, preceded by a rapid sequence induction with 0.6 mg/kg rocuronium. In our patient, recovery from neuromuscular blockade was grossly delayed. Therefore, with all applications of neuromuscular blocking agents in patients with PEHO-syndrome, continuous neuromuscular monitoring is indispensable even on the intensive care unit to determine the end of the neuromuscular block and to exclude residual curarisation.
Introduction:

The PEHO syndrome (progressive encephalopathy with edema, hypsarrhythmia and optic atrophy) is a rare autosomal recessive neurodegenerative disorder with an onset within the first months of life. This infantile progressive encephalopathy was reported first in 1991 by Salonen et al. with an estimated incidence of 1:74000 [9, 11]. Only a few patients have been described in Europe, North America, Australia and Japan. [4, 6, 10]. Diagnosis presupposes the exclusion of other disorders, and is made by clinical criteria and magnetic resonance imaging (MRI). Clinical criteria are an infantile onset of profound muscular hypotonia with concomitant spasms and epilepsy becoming apparent between the second and 52th week of life, showing an interictal encephalographic pattern of hypsarrhythmia. Additionally, arrest of mental development and optic nerve atrophy with the absence or loss of visual fixation with becomes evident by the age of two years. Typical MRI findings are progressive cerebellar and brainstem atrophy. Distinct dysmorphic stigmata as epicantic folds, narrow forehead, short nose, outward turning ear lobes, open mouth and in particular edema of face and limbs with short tapering fingers are reported [4, 6, 11].

Children with PEHO syndrome may require general anesthesia for diagnostic and therapeutic procedures such as MRI, placement of central venous line or endoscopic procedures. Data on sedation, anaesthesia and drugs used during the anesthestic management in patients with PEHO syndrome are lacking.
Case report:

We report the perioperative management of a 10 month old boy (8.3 kg, 62 cm) with PEHO syndrome who was scheduled for laparoscopic assisted percutaneous endoscopic jejunostomy (PEJ).

In our patient, all diagnostic features of PEHO syndrome were present. Therapy-resistant epileptic seizures lead to prolonged episodes of apnoea. Along with aspiration pneumonia caused by gastric regurgitation, the physical status required long time hospitalisation.

For the anesthesiological procedure, premedication with 0.05 mg/kg midazolam intravenously allowed the transfer of the now sleeping infant from the preoperative holding area to the prewarmed operation theater. Routine monitoring including ECG, pulse oximetry (SpO$_2$), and noninvasive blood pressure (Siemens SC 9000 XL, Siemens AG, Erlangen, Germany) as well as neuromuscular transmission monitoring with quantitative acceleromyography at the adductor pollicis muscle using TOF-Watch SX equipment (Organon, Dublin, Ireland) were established. A modified rapid sequence induction technique was applied according to the guidelines of the german scientific workgroup of pediatric anesthesia [10]: With the upper part of the body in a 30° upright position and after 3 mins of preoxygenation, a continuous infusion of 0.5 µg/kg/min remifentanil was started. After additional 2 Minutes, 4 mg/kg propofol were injected. After loss of consciousness and successful pressure controlled mask ventilation (FiO$_2$ 1.0, peak pressure 12 cm H$_2$O, zero PEEP, 20/min), auto calibration of the TOF-Watch SX was performed before starting train-of-four-stimulation every 15 sec. The peak effect of the subsequently applied intravenous 0.6 mg/kg rocuronium was awaited before conducting endotracheal intubation (Micro Cuff ID 3.5, Kimberly-Clark Health Care, Roswell, Georgia, USA).

Anaesthesia was maintained as total intravenous anesthesia (TIVA) with remifentanil 0.5 – 0.25 µg/kg/min and propofol 6 mg/kg/h, adapted to surgical stimuli and hemodynamic response. Pressure-controlled ventilation (40% oxygen in air) was adjusted to normocapnia (p$_{e}$CO$_2$ 34–38 mmHg, Kion, Siemens AG, Erlangen, Germany). Body temperature was maintained inside a range of 36.0 – 37.0 ºC using a warming blanket system (Bair hugger, Eden Prairie, MN, USA). A venous blood sample showed normal electrolytes, acid-base laboratory, blood glucose and lactate both after induction of anesthesia and at the end of surgery.

Surgery was uneventful. However, recovery from the neuromuscular block was only 5% of the first twitch at the end of surgery (92 min after administration of the intubation dose of
rocuronium). We decided to transfer the sedated, endotracheally intubated and mechanically ventilated infant to the pediatric intensive care unit (PICU) to await the offset of the neuromuscular blockade. Three hours after admission on the PICU, repeated assessments showed a TOF-ratio larger than 0.9 suggesting that the child had full recovery of the neuromuscular transmission. It was breathing spontaneously and could be extubated thereafter. The further course was uneventful.
Discussion:

The perioperative anesthetic management had to face typical main features of the PEHO syndrome. Distinct risks and limitations to the anesthesiological procedure had to be obeyed. First in line, peripheral edema could complicate peripheral venous cannulation, which is a basic prerequisite for intravenous anaesthesia induction (Figure 1). However, choosing volatile induction with sevoflurane alternatively should be applied with great reluctance, as high concentrations of sevoflurane can cause epileptiform enzephalographic acitivity [12] and implies an unsecured airway [13]. In the light of both, the disease specific features of epilepsy and aspiration risk, the authors refrained from volatile induction with sevoflurane and conducted a modified rapid sequence induction with propofol, remifentanil and rocuronium. As the reported patient was affected by episodes of apnoea, short acting substances seemed to be advantageous. TIVA using propofol and remifentanil might minimize residual hypnotic or opioid action and might allow early recovery from anesthesia, awakening free of excitation and prevention of postoperative apnoea [7]. Regarding the impaired pharyngeal control of PEHO patients, the antiemetic properties of propofol could be beneficial [14].

Due to the muscular hypotension and the immobile state of PEHO patients, succinylcholine is apparently contraindicated for neuromuscular block. While the short onset properties made the case for rocuronium [2] and proved to have a normal onset, we found a grossly delayed recovery after administration of 0.6 mg/kg rocuronium in our patient. A reduced dose of rocuronium (0.3 mg/kg), the use of long onset but short acting substance mivacurium or avoidance of all neuromuscular blocking agents might be considered in patients with PEHO syndrome. All of these alternatives are connected to a possibly insufficient neuromuscular block during intubation. Unfortunately, sedation procedures are excluded because of the imminent risk of aspiration in PEHO-patients. The authors would discourage to perform sedations without a secured airway.

Vecuronium is a widespread substance in paediatry and has very similar physicochemical and clinical properties to rocuronium (“Rapid Onset CURONIUM” [1]). Therefore, it is highly likely that vecuronium would show a prolonged action as well in patients with PEHO-syndrome.

A safe but nonetheless costly alternative is reversion of neuromuscular block with the new rocuronium-encapsulator sugammadex [8]. This drug is not approved for children of any age, but there is evidence for the safe use of the substance in children [9]. Sugammadex could also reverse the action of vecuronium [3].
In our case, full neuromuscular recovery has to be awaited on the intensive care unit. In the clinical practice of neuromuscular block, clinical signs of recovery (lifting of the head, adduction of the arm) are insufficient to assess full neuromuscular recovery [5]. Especially residual curarisation of the pharynx and the larynx could not be ruled out clinically and require quantitative neuromuscular monitoring. In our case, full neuromuscular recovery was essential to minimize the risk of aspiration. To assess neuromuscular block, acceleromyography is a well-established quantitative technique, which should be available in each unit where neuromuscular blocking drugs are utilized. It is easy to apply, non-invasive and well evaluated [5]. In such cases, interdisciplinary management as described here might be beneficial.

For the clinical practice, it has to be concluded that with the use of neuromuscular blocking agents in PEHO patients, monitoring of neuromuscular transmission is indispensable. Furthermore, the postoperative availability of intensive care treatment for patients with PEHO syndrome should be strongly recommended. Further reports on the onset and offset of nondepolarizing neuromuscular blocking agents in PEHO patient should be emphasized.
Figure 1: Hand edema in PEHO syndrome
References:


