ANESTHESIA MANAGEMENT IN AN INFANT WITH GLYCOGEN STORAGE DISEASE TYPE II (POMPE DISEASE)

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Abstract

Pompe or Glycogen Storage Disease type II (GSD-II) is a genetic disorder affecting both cardiac and skeletal muscle. Historically, patients with the infantile form usually die within the first year of life due to cardiac and respiratory failure. Recently a promising enzyme replacement therapy has resulted in improved clinical outcomes and a resurgence of elective anesthesia for these patients. Understanding the unique cardiac physiology in patients with GSD-II is essential to providing safe general anesthesia. Additional care in maximizing coronary perfusion pressure and minimizing arrhythmia risk must be given. For these reasons, it is recommended that anesthesia for infantile Pompe patients should specifically avoid propofol or high concentrations of sevoflurane and, instead, use an agent such as ketamine as the cornerstone for induction in order to better support coronary perfusion pressure and to avoid decreasing diastolic blood pressure (DBP) with vasodilatory agents. We present the anesthetic technique in a case of infantile type Pompe disease.

Keywords: metabolic disorders, Pompe disease, anesthesia.

Introduction

Pompe disease, also known as glycogen storage disease type II or acid maltase deficiency, is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid a-glucosidase[1,2]. For the infantile-onset subtype specifically, the birth prevalence is reported to range between 1: 40 000 and 1: 138 000 among different nations[3]. The early-onset, infantile subtype is typically fatal because of rapid intracellular accumulation of glycogen, which causes infiltrative pathology of the myocardium and skeletal muscle. Common presenting signs include cardiomegaly, hypotonia, macroglossia, failure to thrive and hepatomegaly. Without treatment, sequelae include rapidly progressive hypertrophic cardiomyopathy, arrhythmias, systolic and diastolic heart failure and chronic respiratory failure, followed by death usually within the first year of life[1,2]. During the last decade a promising enzyme replacement therapy, with recombinant human acid aglucosidase (rhGAA), has resulted in improved clinical outcomes in the treatment of infantile-onset Pompe

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disease[4]. For this reason after early diagnosis, it is imperative for the infant to start as soon as possible enzyme replacement therapy (ERT) using rhGAA. We present the anesthetic management of an infant with Pompe disease.

Case Description

This is the case of a 2-month-old male (4.7 kg), with uncomplicated pregnancy and full term normal vaginal delivery. After birth the infant presented hypotonic and cyanotic. He was admitted to the NICU and remained 4 days under supplemental oxygen support and investigation. Electrocardiogram showed normal sinus rhythm, biventricular hypertrophy, ST depression and inverted T wave in inferior leads. Echocardiography demonstrated non obstructive hypertrophic cardiomyopathy with severe biventricular hypertrophy. The estimated left ventricular mass index (LVMI) on echocardiography was 169.6 g/m^2 (normal 48.8 ± 8). LVMI was calculated by Devereux′s formula[5] considering the diastolic measurements of left ventricular internal diameter (LVID), interventricular septal thickness (IVST) and posterior wall thickness (PWT): LVMI (g/m^2) = (1.04 [(IVST+LVID+PWT)3-LVID3]-14 g)/ Body surface area. The above findings led to an eventual diagnosis of infantile-onset Pompe disease. Diagnosis was confirmed in specialized laboratory centre in Germany, using whole blood and lymphocyte samples[5,6]. The infant was then scheduled to undergo general anesthesia for the placement of a central venous catheter prior to starting rhGAA therapy.

Standard monitoring was applied. Baseline heart rate ranged from 140 to 160 b/min) and blood pressure was 85/49 mmHg. The patient had a history of hypotonia, small mouth opening, macroglossia, and gastroesophageal reflux disease with adequate weight gain. Intravenous induction with ketamine (1 mg/kg) and fentanyl (2.0 mcq/kg) was performed. The patient was successfully intubated at the second attempt (Cormack and Lehane grade 3) without muscle relaxant. Following induction and after the fentanyl administration the heart rate transiently decreased to 110 b/min (>20% from baseline) and resolved spontaneously. Anesthesia was maintained with sevoflurane 1-2% and 50% nitrous oxide in oxygen. Maintenance intravenous fluids D5% LR were infusing at a rate on 100 ml/hr. About 10 minutes after induction, blood pressure decreased to 55⁄20 (>30% from baseline systolic and diastolic pressures, respectively) and restored with a fluids bolus of 5ml/kg. Postoperatively, the patient was transferred to the intensive care unit and discharged home 2 days later without incident.

Discussion

Pompe or Glycogen Storage Disease type II (GSD-II) is a genetic disorder affecting both cardiac and skeletal muscle. The intracardiac buildup of glycogen in infantile onset Pompe disease leads to a progressive hypertrophic cardiomyopathy characterized by abnormal diastolic function. Therefore, the hypertrophic cardiomyopathy in infantile-onset Pompe disease requires a delicate hemodynamic balance during induction and early maintenance of anesthesia. A noncompliant left ventricle predisposes these infants to diastolic heart failure with elevated left ventricular end-diastolic pressure (LVEDP), at lower ventricular volumes and an increased potential for subendocardial ischemia, necessitating adequate hydration and preload to maintain cardiac output. At the same time, diastolic blood pressure (DBP) must remain sufficiently higher than LVEDP to maintain adequate coronary perfusion pressure[7].

Glycogen accumulation can also be present in the cardiac conduction system, as evidenced by the glycogen infiltration of the sinoatrial and atrioventricular nodes[8]. Coupled with a hypertrophied heart and an already labile coronary perfusion pressure, infantile Pompe patients become especially sensitive to the development of ventricular and supraventricular arrhythmias[9]. As such, patients suspected of having Pompe disease should routinely undergo extensive preoperative evaluation, conservative intraoperative management and have appropriate postoperative disposition. Preoperatively, it is essential to obtain, in addition to an ECG, echocardiography to assess ventricular cavity volume. In particular, measurement of LV mass index (LVMI) is imperative to help stratify risk. There is strong evidence for an association between LVMI and mortality risk[9]. Deaths resulting

from arrhythmias appeared to correlate with LVMI >350 g/m^2 [9].

Propofol, should be avoided specifically for infantile Pompe patients, given its known rapid reduction in systemic vascular resistance and DBP. The use of propofol during induction or maintenance of anesthesia, has resulted in severe and even fatal arrhythmias and has been associated with negative outcomes[9]. Although sevoflurane is an acceptable anesthetic in these infants, the concentrations must be kept low to avoid hypotension, and therefore should only be used if other agents allow the sevoflurane to have an additive effect in an infant where immobility is difficult to obtain with a single agent. Sevoflurane does not appear to be a safe option as the sole anesthetic for this purpose.

In our case ketamine, known for its stable cardiovascular profile, was used for induction in combination with fentanyl and low concentration of sevoflurane. According to the current literature ketamine is suggested as the first choice in this group of patients[9]. Additionally, regional anesthetic techniques have been used successfully as alternative to general anesthesia for infants with Pompe disease[10].

Conclusion

With the availability of enzyme replacement therapy (ERT) using rhGAA, increased survival is anticipated and more infantile Pompe patients will likely present for surgical procedures. Additional care in maximizing coronary perfusion pressure and minimizing arrhythmia risk must be given.

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