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Anaesthetic Considerations for a Seven-Month-Old Infant with Suspected Malignant Hyperthermia: A Case Report

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Abstract

Introduction: Malignant hyperthermia (MH) is a life-threatening pharmacogenetic skeletal muscle disorder resulting in increased myoplasmic calcium concentrations leading to sustained muscle contraction. In cases susceptible to MH, a total intravenous intravenous anaesthesia (TIVA) approach is employed to avoid the use of MH triggering agents namely volatile anaesthetics and suxamethonium.

Case presentation: In this case report, we present a seven-month-old male infant with MH susceptibility that was scheduled for a rectal biopsy under general anaesthesia. The patient was managed according to MH guidelines and paediatrics dosing schemes for TIVA; using propofol and remifentanil as an adjuvant. The case was management successfully and uneventfully.

Conclusion: MH is a potentially life-threatening disorder, hence following the evidence-based precautions and management of patients with suspected MH is key. Moreover, managing a paediatric patient with MH suspicion often impose additional challenges. In this case report, the perioperative considerations for infants with MH suspicion is discussed.

Keywords: Malignant Hyperthermia, Total Intravenous Anaesthesia, Steur propofol infusion scheme.

Introduction

Malignant hyperthermia (MH) is an uncommon pharmacogenetic skeletal muscular characterized by a potentially fatal, progressive hyperthermic reaction occurring in response to exposure to volatile anaesthetic agents and succinylcholine [1, 2]. Clinical manifestations are a result of increased intracellular calcium in skeletal muscles leading to muscle rigidity, hypermetabolism and rhabdomyolysis. Signs include increased end-tidal CO_2, most sensitive and earliest sign, tachypnea, tachycardia, blood pressure fluctuation and hyperthermia [1].

In patients with susceptibility to MH, total intravenous anaesthesia (TIVA) is sought to avoid the use of the contraindicated volatile agents. When opting for TIVA, an infusion of propofol along with some adjunctive drugs such as opioids, are used to reach adequate depth of anaesthesia. The objective of this case report is to present a case of an infant with suspected malignant hyperthermia undergoing TIVA.

Case Presentation

A seven-month-old male infant with chronic constipation under evaluation was scheduled for examination under anaesthesia with rectal biopsy. On preoperative anaesthesia assessment, baby was medically free, physical status ASA I, active, feeding well, and gaining weight appropriately. No prior history of anaesthesia exposure, however, there was family history of malignant hyperthermia from his paternal side. The family experienced a loss of a distant relative, who was in his 40s, ten years ago after exposure to anaesthetic agents and was diagnosed with malignant hyperthermia intraoperatively, differential diagnoses such were ruled out. The family were thus advised to alert their anaesthetist if there is anaesthesia to be given to any family member. The patient's older sister underwent tonsillectomy under general anaesthesia with precautions and her surgery was uneventful.

On examination, baby was vitally stable; heart rate of 132 beats per minute, blood pressure of 110/74, oxygen saturation of 100% in room air. The patient weighed 7.9 kg, height was 67 cm, giving a body mass index of 18.26 kg/m^2. On examination, cardiovascular and respiratory systems were normal and unremarkable. Moreover, a neurological examination revealed a fully alert and active baby with normal muscle tone, power and reflexes. Examination of the gastrointestinal system shows a distended, soft abdomen with palpable faecalomas. Laboratory investigations were within normal range.

Necessary anaesthesia precautions were taken according to the established guidelines for malignant hyperthermia. Regarding the anaesthetic machine, vaporizers were removed, a new soda lime (CO_2 absorbent) was installed. O_2 at a flow rate of 10 l/min was blown through the machine for two hours, following the recommendations for the GE healthcare Aisys machine that suggested an average washout time for sevoflurane of 55 minutes [3]. New breathing circuits and laryngeal mask airway (LMA) were used. Dantrolene was made available in the operating theatre in case required.

The patient was taken to the operating theatre, oximetry,

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electrocardiogram, non-invasive blood pressure monitors were attached, and vitals were noted. The patient was preoxygenated with 100% FiO_2 at a flow rate of 10 l/min for three minutes. A 24-gauge intravenous cannula was secured on the right dorsum hand. On induction, Lidocaine 1 mg/kg and 2.5 mg/kg propofol were administered. Size 1.5 LMA was inserted. Total intravenous anaesthesia (TIVA) was used for maintenance of anaesthesia. Propofol infusion, using an infusion pump, was started at a rate of 15 mg/kg/hr for the first ten minutes, which was reduced to 10 mg/kg/hr for the second ten minutes, and a rate of 5 mg/kg/hr was maintained for the remaining duration of the procedure. Meanwhile, remifentanil infusion was started and titrated at a rate of 0.1-0.3 mcg/kg/min. Patient was kept on pressure support ventilation mode (PSV-Pro).

Throughout the procedure, vitals including heart rate, electrocardiography, blood pressure and end-tidal CO_2 were monitored closely to detect early signs of MH. The surgery lasted for 30 minutes only, infusions were stopped, patient started taking spontaneous regular breaths and was extubated uneventfully. Patient was shifted to the recovery room for close observation and was then shifted to the ward and inpatient monitoring was resumed.

Discussion

MH is defined as hypermetabolic crisis occurring when a susceptible individual is exposed to a volatile anaesthetic, such as sevoflurane, isoflurane, desflurane or halothane, or the depolarizing neuromuscular blocking agent, succinylcholine [2]. Incidence ranges from 1:5,000 to 1:100,000 reported cases, occurring more commonly in the paediatric population and amongst males [2, 4]. This may be a suboptimal estimation considering variable penetrance of the disease, as well as the various gene mutations that can result in MH susceptibility [5]. MH is an autosomal dominant inherited disorder; pathogenic variant of Ryanodine receptor 1 (RYR1) gene is the most common cause of MH-susceptibility [6]. This pathologic variant is associated with other disorders, including heat- or exercise-induced exertional rhabdomyolysis, central core disease, atypical periodic paralysis and congenital myopathies associated with weakness and hypotonia [7]. Other gene mutations found to cause MH include Calcium Voltage-Gated Channel Subunit Alpha1 S (CACNA1S), skeletal muscle sodium channel (SNC4A) and SH3 And Cysteine Rich Domain 3 (STAC3) pathogenic variants [8, 9].

In MH, a defect in a skeletal muscle receptor causes excessive concentrations of calcium ions to accumulate in the myoplasm caused by increased leak of calcium from the sarcoplasmic reticulum intracellularly, following exposure to the aforementioned triggers [10]. This consequently leads to sustained muscular contraction, cellular hypermetabolism and consequent anaerobic metabolism and acidosis, rhabdomyolysis, and hyperkalemia [2]. The onset of symptoms after exposure to the triggering agent varies among individuals. Symptoms can start becoming apparent right after exposure, during maintenance of anaesthesia or even during the recovery period and hence monitoring is mandated throughout these stages for patients with susceptibility to MH [11]. Initial signs include an increase in end-tidal CO_2, tachypnoea or spontaneous breathing against the ventilator. Other early signs involve tachycardia, muscle rigidity with resistance to muscle relaxation, rigidity commonly affects the masseter muscles resulting in biting of endotracheal tubes, in addition to electrocardiography changes. With hypermetabolism, heat is generated leading to hyperthermia [2]. The three diagnostic features of MH, and most common signs in the paediatric population, are hypercarbia, tachycardia and hyperthermia [2, 12]. Rhabdomyolysis and resulting hyperkalaemia with its consequent electrocardiogram changes are late signs of malignant hyperthermia which may be seen in the postoperative period even in patients with no other clinical signs suggesting the diagnosis [13, 14]. Therefore, in our case, we focused on monitoring the patient closely intra- and post-operatively for any signs suggestive of malignant hyperthermia.

In cases of suspected MH, TIVA is sought to prevent exposure to volatile agents. This employs a sedative, with propofol being the most frequently used, and an adjunct analgesic drug, such as an opioid for maintenance of anaesthesia. A size 1.5 LMA was inserted, and no neuromuscular blockade was indicated. Patient was breathing spontaneously, was kept on a pressure support ventilation mode (PSV-Pro) throughout the procedure.

Distribution of propofol follows a three-compartment model, in which the initial dose of propofol, given on induction, acts on the central compartment yielding the anaesthetic effect. In this case, 2.5 mg/kg of propofol bolus was used. The anaesthetic effects of propofol starts to wear off as it gets distributed to the other compartments, and hence it is essential to replace the redistributed drug and thus maintain the anaesthetic effect by starting an infusion [15]. The Steur propofol infusion scheme for children less than or equal to three years of age was used in this case [16]. This scheme considers the varying pharmacokinetics in different age groups which is of great significance in the paediatric population [17].

To limit propofol requirements and to provide adequate analgesia, an adjunct drug is usually coupled with propofol infusion. In this case, remifentanil infusion was started. 0.1-0.3 mcg/kg/min of remifentanil was used as per the TIVA guidelines for children [18].

Unlike volatile agents, consciousness level cannot be predicted using minimal alveolar concentration (MAC) and thus monitoring using a bispectral index (BIS) is utilized to ensure adequate depth of anaesthesia in adults. However, since BIS measures the consciousness level using electroencephalogram (EEG), that renders the tool inaccurate in the paediatric population, especially infants, due to the rapid changes in EEG signals associated with growth and development of this population [19]. Therefore, in our case, we were content with close monitoring of vitals.

Upon reviewing the literature, only one case was reported, by Lee et al. [20], on the prevention of MH in an infant. In that case, an 8-month-old diagnosed with osteogenesis imperfecta was scheduled for liver transplant. Due to the risk of MH associated with osteogenesis imperfecta, MH precautionary measures were taken. Similarly, in our case report, the chosen mode of anaesthesia was TIVA with propofol and remifentanil infusions following the paediatrics dosing scheme.

Other modes of anaesthesia, such as neuroaxial and caudal anaesthesia are chosen can serve as an alternative to general anaesthesia in such patients. Patel A, et al. reported two cases where spinal anaesthesia was successfully achieved in two infants with family history of MH [21]. However, in this age group, patients tend to be

less cooperative and thus sedation could be mandated at any time, therefore it was decided to opt for general anaesthesia.

Conclusion

MH is a life-threatening hypermetabolic disorder resulting in sustained muscle contraction and a sequela of consequent manifestations. The cardinal features for MH are increased end-tidal CO_2, tachycardia, and hyperthermia. In cases susceptible to MH, TIVA approach is sought to avoid the use of MH triggering agents. After reviewing the literature, few cases reports were found where MH was avoided through strict application of these guidelines. However, only one case was reported, of an infant with suspected MH. In this case report, the anaesthetic considerations for a seven-month-old male infant are discussed, including the use of total intravenous anaesthesia (TIVA) following the paediatrics dosing schemes. The use of TIVA in paediatrics is uncommon as the monitoring of anaesthesia depth with TIVA can be inaccurate in the paediatric, hence, following the recommended perioperative precautions is key for successful case management.

Clinical Message

In this case report seven-month-old male infant with MH susceptibility received general anaesthesia for a rectal biopsy. Patient was managed according to MH guidelines and paediatrics dosing schemes for TIVA and the case was done uneventfully.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.
Conflict of interest: Nil **Source of support:** None

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