

Malignant Hyperthermia

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Introduction

Malignant hyperthermia (MH) is an inherited myopathy characterized by a hypermetabolic state which is triggered when the patient is exposed to some anesthetic agents. Classic MH most often manifests in the operating room, but it can also occur within the first few hours of recovery from anesthesia.

The syndrome is thought to be due to a reduction in the reuptake of calcium by the sarcoplasmic reticulum necessary for termination of muscle contraction. Consequently, muscle contraction is sustained, resulting in signs of hypermetabolism, including acidosis, tachycardia, hypercarbia, glycolysis, hypoxemia, and heat production (hyperthermia).

Some susceptible patients may develop MH despite multiple prior uneventful exposures to triggering drugs. Typically MH is triggered by succinylcholine (Sch) or volatile anesthetics. Some other drugs have been found safe in patients susceptible to MH. See Table 1

Table 1 Unsafe drugs

Depolarizing muscle relaxants (Sch)

Potent inhalational agents (halothane, isoflurane, enflurane, desflurane, sevoflurane)

Insufficient data / controversial

d-Tubocurarine

Phenothiazines

Safe drugs

Antibiotics

Antihistamines

Antipyretics

Barbiturates (thiopental, methoexital)

Benzodiazepines (midazolam, diazepam, lorazepam)

Droperidol

Ketamine (inherent circulatory effects may mimic MH)

Local anesthetics (lidocaine, bupivacaine)

Nitrous oxide

Nondepolarizing muscle relaxants (pancuronium, rocuronium, vecuronium)

Opioids (morphine, meperidine)

Propofol

Propranolol

Vasoactive drugs

Incidence and Epidemiology

MH is estimated to occur in 1 in every 15000 pediatric anesthetics and 1 in every 50000 adults anesthetics, with a mortality rate of about 10%.

Etiology

Inheritance of MH is autosomal dominant with variable penetrance, such that 50% of children of MH susceptible parents are potentially at risk.

A mutation in the ryanodine receptor (a calcium release channel) has been shown to cause MH in about 20% of affected human families.

Other two mutations have been isolated and mapped - fc20 and fc34 - and seem to cause MH-like responses to volatile anesthetics, without involving the ryanodine receptor.

Clinical features and Intraoperative diagnosis

The initial signs of MH are increase in end-tidal carbon dioxide and decrease in arterial oxygen saturation, tachycardia and dysrhythmias, rigidity (despite the use of muscle relaxant), and tachypnea (in spontaneously breathing patients). An unexplained tachycardia, however, is usually the first sign. Other findings are hyperthermia and cyanosis. See Table 2. When clinical signs are suggestive of MH, several laboratory tests may lead to a presumptive diagnosis. A blood gas analysis may be obtained to determine whether metabolic acidosis is present (venous blood is better than arterial to observe the immense production of carbon dioxide). Other possible metabolic abnormalities include hyperkalemia, hypercalcemia, hyperphosphatemia, creatine kinase levels >1000 IU, and myoglobinuria. All these tests are suggestive of the diagnosis of MH, but not definitive.

Table 2 Clinical manifestations of MH

Hypercarbia (the most sensitive indicator of potential MH in the OR)

Tachycardia

Tachypnea

Temperature elevation (usually a late sign of MH)

Hypertension

Cardiac dysrhythmias

Acidosis

Hypoxemia

Hyperkalemia (it should be considered first in case of cardiac arrest)

Skeletal muscle rigidity (the most specific sign)

Myoglobinuria

Diagnostic tests for MH

A suspicion that testing is needed is based on patient's history, positive family history, or use of an anesthetic remarkable for clinical diagnosis of MH. Key features in the patient's history include strabismus, myalgias on exercise, tendency to fever, myoglobinuria, muscular disease, and intolerance of caffeine. Patients requiring a more definitive diagnosis are referred for muscle biopsy.

Although several tests have been described, the halothane-caffeine contracture test remains the gold standard. It is performed on muscle obtained by biopsy (usually the vastus lateralis), which is bathed on a solution containing 1-3% halothane and caffeine - they decrease the threshold for muscle contraction and therefore facilitate diagnosis. This test is 85% specific and 100% sensitive. Creatine phosphokinase is elevated 70% of susceptible patients. A genetic test of the ryanodine receptor may eventually be developed.

Treatment of MH

When MH is diagnosed early and treated promptly, the mortality rate should be near zero. Whenever anesthesia is administered, dantrolene should be readily available as well as a protocol for management of MH. Dantrolene is, at the

moment, the only known drug that treats MH. It impairs calcium-dependent muscle contraction and controls hypermetabolism manifestations. See on Table 3 treatment of MH step by step.

Table 3 Treatment of MH

1. Call for help; management is involved and difficult for one person.
2. Stop triggering agents.
3. Hyperventilate patient with 100% oxygen.
4. Finish or abort procedure.
5. Administer dantrolene (2.5mg/kg bolus; may repeat 2mg/kg every 5 minutes, then 1-2mg/kg/h).
6. Cool patient (cold IV normal saline, cold body cavity lavage, ice bags to body, cold nasogastric lavage, cooling blanket).
7. Change to a clean circuit not exposed to volatile agents.
8. Monitor and treat acidosis (follow serial arterial blood gases and administer sodium bicarbonate).
9. Promote urine output (maintain >2ml/kg/h urine output with conscientious fluid management; furosemide, mannitol).
10. Treat hyperkalemia.
11. Treat dysrhythmias with procainamide and calcium chloride.
12. Monitor creatinine kinase, urine myoglobin, and coagulation for 24-48 hours.

Management of MH-susceptible patients

There have been no deaths from MH in previously diagnosed MH susceptible patients when the anesthesiologist was prospectively aware of the problem. This information is useful to allay patient's preoperative anxiety. In a MH-susceptible parturient, it should be considered first an epidural anesthesia without dantrolene pretreatment, and close monitoring of vital signs. If general anesthesia is necessary for delivery, follow the same steps of management of MH-susceptible patients on Table 4. No adverse fetal effects of dantrolene have been observed .

Table 4 Management of MH-susceptible patients

1. Clean machine; remove vaporizers; replace CO2 canisters, bellows, and gas hose.
2. Flush machine for 20 minutes with oxygen 10L/min.
3. Bring the MH cart in the OR (this cart contains all the supplies to resuscitate a patient with MH).
4. Schedule the patient as the first case of the day, and notify the postanesthesia care unit to be prepared to provide the necessary manpower.
5. Consider dantrolene and sedation as premedication.
6. Check creatinine kinase and complete blood count preoperatively.
7. Consider anesthetic alternatives; monitored anesthetic care with sedation and local anesthesia, regional anesthesia, or a general anesthetic using nontriggering agents.
8. After surgery check laboratory values and monitor patient in an appropriate setting.

Differential diagnosis

After an intubating dose of Sch with loss of twitches on neuromuscular stimulation, difficulty in opening the mouth represents Masseter Muscle Rigidity (MMR). Such patients may be susceptible to MH. The incidence of MMR is 1% in children induced with halothane and Sch, and 2.8% in children having strabismus surgery. Such patients are prone to an increase in creatinin kinase, myoglobinuria, tachycardia, and dysrhythmias independent of MH. It is controversial whether to proceed with an anesthetic if the patient develops MMR. Some anesthesiologists elect to cancel the schedule procedure, whereas others continue the case using non - triggering agents of MH.

Syndromes associated with MH

There is a strong correlation between Central Core Disease (a sarcoplasmic myopathy characterized by proximal muscle weakness) and MH. Case reports have also linked MH to Muscular Dystrophy and forms of Myotonia.

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