Malignant Hyperthermia: Is Your Facility Prepared to Treat This Rare Condition?

ABSTRACT

Malignant hyperthermia (MH) is an inherited hypermetabolic disorder of skeletal muscle, triggered by potent inhalational anesthetic agents. It is estimated to occur between 1:10,000 and 1:150,000 adult patients receiving a general anesthetic. While its occurrence is rare, development of MH may be sudden and dramatic with rapid progression of symptoms resulting in death. Manifestations of this disorder can occur without a family history or previous problem with anesthesia. Since June 2004, PA-PSRS has received 15 reports related to MH, including one case that resulted in patient death. Prompt identification and treatment are essential to minimize the possibility of harm or a fatal outcome. Awareness of the broad spectrum of clinical manifestations that present early and/or late during administration of anesthesia is vital for healthcare providers to promptly initiate treatment of malignant hyperthermia. Clinical signs and symptoms may include tachycardia, increased temperature, and sweating. Prompt treatment is necessary to halt the rapid progression of this disorder. The focus for healthcare providers is availability, access, and administrations of dantrolene sodium, the medication of choice in the treatment of malignant hyperthermia.

Since June 2004, PA-PSRS has received 15 reports related to malignant hyperthermia (MH), including one death. Six of the reports were classified as near-miss incidents that identified patients with family histories of MH that were revealed after the initial anesthesia visit and before induction of anesthesia. The information was obtained incidentally while staff prepared the patients for their respective procedures. Four of the procedures were cancelled. Some reports specified that the patient would be referred for genetic testing, and others indicated that the procedure would be rescheduled. Other reports documented patients who manifested clinical symptoms of MH and were appropriately treated during surgery. The following deidentified report indicates that the facility may not have been prepared to treat the patient, and the outcome was fatal.

The patient developed hyperthermia . . . planned treatment involved administration of medication (dantrolene). Medication was not readily available. Another medication was utilized. [Case resulted in patient death.]

In contrast, consider the following deidentified case illustrating prompt recognition and treatment of MH. Staff awareness of additional resources and assistance provided by the Malignant Hyperthermia Association of the United States (MHAUS) resulted in decreased patient harm.

A healthy [adult patient] was admitted to facility for an [operative procedure]. Anesthesia began in the [operating room (OR) on the hour]. The incision [occurred about 25 to 30 minutes later]. The surgery [proceeded] without issue. However, anesthesia noted an increase in [end tidal carbon dioxide (ETCO2)] and heart rate. These vital signs continued to increase, and MH crisis code was called [about 45 minutes after the start of anesthesia] by the medical director. [MHAUS] hotline was contacted [within one minute] and kept on speaker phone in the OR. Dantrolene regime was initiated, [catheter] was inserted, and surgery was aborted. The surgical site was closed, and a dressing was applied. Laryngeal mask airway was removed, and the patient was intubated with endotracheal tube. [Emergency] 911 was called for advanced life support transport to the medical center. Patient responded to treatment with decrease in ETCO2 and heart rate. Patient was stabilized and transferred to [medical center an hour after crisis identified].

Recognition and Education

Healthcare providers may have limited knowledge of MH and subsequent treatment modalities. In 1960, when MH was first recognized as a complication of anesthesia, the case-fatality rate was 70%. Today, with education of healthcare providers about the manifestations of MH and treatment with dantrolene sodium, the mortality rate is less than 5%. While its occurrence is rare, development of MH may be sudden and dramatic with rapid progression of symptoms resulting in death. There is a wide range of occurrence rates in the literature: from 1:10,000 to 1:150,000 in adult patients receiving general anesthesia. Prompt identification and treatment are essential to avoid harm or death. The deidentified events reported through PA-PSRS are presented in the box article “Malignant Hyperthermia Events Reported through PA-PSRS.”

Diagnosis

The gold standard used to determine an individual’s susceptibility to MH is an invasive muscle contracture test performed on freshly biopsied muscle: the caffeine-halothane contracture test (CHCT). The sensitivity of CHCT is 97%, but the specificity is lower with approximately 22% of patients having a false-positive result. However, the test is only available at limited locations in the United States and Canada. Additionally, the test is prohibitive at $6,000 per test, which may not be reimbursed by third-party payers. After years of research involving scientists from many countries, a DNA-based blood test was introduced.
Risk Factors

Risk factors for MH include family history, myopathies, and musculoskeletal disorders such as congenital ptosis and kyphoscoliosis. Individuals with central core disease and/or multiminicore disease, both congenital myopathies, are also susceptible to MH. Additionally, athletic young males are more susceptible to MH. However, manifestations of this disorder are not predictable based on family history or previous exposures to anesthesia. Therefore, early recognition is the key to preventing a fatal outcome. Clinical signs may vary considerably in severity and may appear at various times during administration of anesthesia and the postoperative period. The Table identifies signs and symptoms that may alert providers to the onset of this disorder.

Table. Clinical Signs of Malignant Hyperthermia

<table>
<thead>
<tr>
<th>EARLY SIGNS</th>
<th>LATE SIGNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased end tidal carbon dioxide (ETCO₂)</td>
<td>Cardiac arrest</td>
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<tr>
<td>Skeletal muscle rigidity</td>
<td>Disseminated intravascular coagulation</td>
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<tr>
<td>Muscle spasm</td>
<td>Myoglobinuria</td>
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<tr>
<td>Tachycardia</td>
<td>Elevated creatine phosphokinase</td>
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<tr>
<td>Metabolic and respiratory acidosis</td>
<td>Elevated temperature</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Hypocalcemia or hypercalcemia</td>
</tr>
<tr>
<td>Sweating</td>
<td>Mottled cyanosis</td>
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Treatment

MH is triggered by a variety of anesthetic agents. These include volatile agents such as halothane, suxamethonium, isoflurane, enflurane, desflurane, and sevoflurane. Once MH is identified, begin resuscitative measures immediately. Treatment includes administration of dantrolene sodium, providing 100% oxygen via an endotracheal tube, discontinuing all anesthetic agents, lowering body temperature, and obtaining blood specimens. Potentially abnormal lab values such as hyperkalemia and hypercalcemia may require additional pharmacological treatment.

Dantrolene sodium is the drug of choice for the treatment of MH. It reverses the calcium accumulation within skeletal muscle, resulting in reversal of the condition. For MH crisis, dantrolene sodium 2.5 mg/kg is administered by continuous rapid intravenous (IV) push and may be followed with 1 to 2.5 mg/kg every 10 minutes until symptoms subside or the condition is under control. During the post-crisis period, administer 4 to 8 mg/kg/day orally in four divided doses or administer 1 mg/kg intravenously and titrate as the clinical situation dictates for one to three days after the onset of symptoms to prevent relapse.

After an MH crisis, the patient should be closely monitored in an intensive care unit. Key elements include monitoring creatine kinase (CK) levels to assess kidney function and obtain a coagulation profile to rule out disseminated intravascular coagulation—a known complication of MH crisis. Prior to discharge, counsel the patient and family regarding MH and provide written educational materials and contact information for MHAUS.

Risk Reduction Strategies

Strategies to reduce the potential for harm and provide safe quality care to surgical patients include educating staff, conducting preoperative screening for MH, and implementing processes to ensure that staff are prepared to treat patients who develop MH.

Education

Education efforts include perioperative staff, are ongoing, and focus on describing MH, its clinical manifestations, and treatment. A team approach, similar to the response to a cardiopulmonary arrest, facilitates effective, efficient care in this emergency situation. The following strategies may reinforce perioperative staff preparedness for a MH crisis:

- Provide education sessions for all surgical staff.
- Conduct annual drills that include didactic information and simulation with a patient who develops symptoms of MH.
- Assign specific responsibilities to each operative team member to perform when an MH crisis occurs.
- Provide MH emergency management kits to the anesthesia department. MH kits include airway management supplies and medications.
- Provide all operative staff with pocket-size guides about dantrolene sodium, including indications, dosage and administration, and adverse reactions of dantrolene sodium.
Malignant Hyperthermia Events Reported through PA-PSRS

PA-PSRS has received 15 reports related to malignant hyperthermia since June 2004. These deidentified cases illustrate the types of issues reported.

The six reports below identify a family history of malignant hyperthermia. Of these, four resulted in cancellation of the procedure at that time and place, one resulted in transferral to controlled setting for the procedure to be performed on the same day, and the other patient had surgery without incident. Four of these six events were in ambulatory facilities.

Upon admission, the patient described an allergy to sodium pentothal. Patient had previous surgeries without complication. When anesthesia visited the patient in the preoperative area, nothing else was mentioned. When taken to the [operating room (OR)], the patient elaborated to the certified registered nurse anesthetist that [an older relative] had died during surgery. Patient stated “he burned up.” Malignant hyperthermia testing on patient was never done to rule it out.

After an intravenous (IV) catheter was started in preparation for the [operative procedure], the anesthesiologist discovered while talking to patient that an [older relative] had severe anesthesi allergy and that patient had never been tested for malignant hyperthermia. Anesthesiologist cancelled case until further information is gathered and will perform the procedure in a hospital setting. [Patient did return] preoperative phone call to obtain this information prior to surgery.

Parent reported . . . that procedure had been cancelled for the second time in past [few] months. Procedure was cancelled due to concern about anesthesia/sedation reaction. Patient’s [older relative] has history of malignant hyperthermia, and patient must have sedation/anesthesia administered in controlled setting. Appointment was cancelled due to known history without special precautions taken . . .

When anesthesia consult was conducted, with family being present, [sibling] stated . . . “I have had high fevers with general anesthesia.” Anesthesiologist suspected malignant hyperthermia and wanted patient transferred to hospital so procedure could still be done today.

Patient prepared for surgery, and during anesthesia interview the patient’s [sibling] mentioned that patient’s [sibling] had malignant hyperthermia during surgery. Information was verified and after discussion with surgeon, the case was cancelled for this day. Patient cooperative and will be rescheduled for a later time.

Patient had surgery. Patient had family history of malignant hyperthermia and needed to have urinalysis results prior to being discharged. There was a delay in receiving the results. Investigation revealed that only a urine culture was ordered, not a urinalysis. When this was realized, hematology lab obtained urinalysis results from the existing urine sample. The patient was discharged to home after results were available.

The nine reports below indicate patients who were diagnosed as having malignant hyperthermia: four of the patients were male and five were female. The ages ranged from 6 to 72, with a median of 40. Five of the reports referred to treatment, with four specifically mentioning dantrolene. Eight of the nine cases occurred in hospitals. There was one death as noted in the main text, which specifically mentioned that dantrolene was not readily available.

- Showcase posters describing the signs and symptoms of MH.
- Display posters with the MHAUS hotline number (1-800-644-9737 or 1-800-MH HYPER) in critical areas of the surgical department.

Screening

Screening is a holistic process. Healthcare providers, particularly anesthesia providers, may incorporate an anesthetic history as described below in the standard preoperative screening process.

- Obtain a thorough medical history.2
- Obtain an anesthetic history to identify patients at risk for MH:2
  - Has the patient had general anesthesia before? If yes, what, if anything, happened?
  - If the patient has not had general anesthesia before, does the patient know of a blood relative who had a bad reaction to anesthesia?

If the answer is yes, consider testing for MH susceptibility.

- Perform a physical examination.2
- Assess airway, and identify smoking history and other respiratory illnesses.2
- Obtain and/or review laboratory results for complete blood count, liver function tests, a comprehensive metabolic panel, CK, and a urine analysis.2 Late signs of MH may include abnormal lab values, including hyperkalemia, hypercalcemia, and elevated CK.2
- Obtain baseline 12-lead electrocardiogram.2
- Obtain preoperative baseline vital signs, including height and weight, blood pressure, heart rate, respi rations, and temperature.2

Treatment

Treatment of MH requires rapid interventions to stop disease progression and prevent complications. Call the MHAUS hotline as identified previously. In
Several malignant hyperthermia events were treated with dantrolene.

Patient developed hyperthermia . . . planned treatment involved administration of medication (dantrolene). Medication was not readily available. Another medication was utilized. [Case resulted in patient death.]

A healthy [adult patient] was admitted to facility for an [operative procedure]. Anesthesia began in the [OR on the hour]. The incision [occurred about 25 to 30 minutes later]. The surgery [proceeded] without issue. However, anesthesia noted an increase in end tidal carbon dioxide (ETCO2) and heart rate. These vital signs continued to increase, and MH crisis code was called [about 45 minutes after the start of anesthesia] by the medical director. [MHAUS hotline was contacted [within one minute] and kept on speaker phone in the OR. Dantrolene regime was initiated, foley [catheter] was inserted, and surgery was aborted. The surgical site was closed, and a dressing was applied. Laryngeal mask airway was removed, and the patient was intubated with endotracheal tube. [Emergency] 911 was called for advanced life support transport [to the medical center]. Patient responded to treatment with decrease in ETCO2 and heart rate. Patient was stabilized and transferred to [medical center on hour after crisis identified].

Patient had operative procedure and was discharged home in stable condition. The patient was found unresponsive at home the following day and was readmitted. Lab values were elevated. Anesthesia determined patient may have malignant hyperthermia. Patient was subsequently discharged.

During closure of procedure, patient developed signs of malignant hyperthermia. Patient received initial dose of dantrolene sodium and necessary treatment in OR and was transferred to the [intensive care unit (ICU)].

[Increased] temperature, [increased] heart rate, [decreased] blood pressure immediately post op elective . . . procedure. Identified as probable malignant hyperthermia and treated immediately according to . . . policy. No long-term sequelae.

Patient presented for [procedure]. [During] postoperative period, the patient developed increased heart rate (130s to 140s) [with] temperature of 37°C. Urine is also positive for blood in postanesthesia care unit. There is a strong history of malignant hyperthermia and [patient] was admitted to ICU for observation. In ICU, vital signs were stable with good oxygen saturation, and urinalysis was negative for any red blood cells. Patient was discharged to home later [that day].

Patient received 300 mg of succinylcholine within an eight-hour period. While [this] drug can sometimes be associated with malignant hyperthermia, his temperature maxed out at [101 to 102° F] with no evidence of rigidity and no hemodynamic instability. Patient clearly does have rhabdomyolysis and is most likely related to succinylcholine. The physician monitored and reviewed. . . . Patient had not received [this] drug previously. . . .

Patient to the OR for [operative procedures]. Anesthesia medications [given] were Versed® 2 mg and Fentanyl total of 450. Patient was administered dantrolene 1 mg/kg IV [for probable malignant hyperthermia] with a decrease in temperature temporarily, and then was given] cooled fluids and cooling blanket. No further orders at this time.

Patient received 150 mg succinylcholine (rapid sequence intubation) and subsequently was diagnosed as having malignant hyperthermia.

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Addition, implement the following if patients exhibit clinical signs of MH:

- Withdraw all anesthetic agents.
- Administer nontriggering agents such as sedative-hypnotic agents to maintain unconsciousness.
- Stop surgery as quickly as possible.
- Alert the entire operative department to the situation.
- Assign team members to respond and care for the patient.
- Intubate the patient if not already done, and hyperventilate with 100% oxygen.
- Administer dantrolene sodium as indicated.
- Monitor core body temperature in addition to blood pressure and heart rate and rhythm.
- Lower the temperature in the OR, and cool the patient with cold packs to the groin, axilla, and neck.
- Administer IV fluids to maintain urine output.
- Obtain CK and coagulation profile.
- Obtain arterial blood gas.
- Monitor urine color and amount per hour.
- Assess and correct metabolic acidosis.
- Administer insulin and glucose to correct hyperkalemia.
- Monitor central venous pressure.

Conclusion

Prompt identification of MH and treatment are essential to minimize patient harm. Knowledge of the wide variation of symptoms that may present during administration of anesthesia is vital for healthcare providers to initiate treatment. The focus for healthcare providers is availability and administrations of dantrolene sodium. In addition to knowledge of MH and its treatment modalities, it is essential for perioperative staff to have access to other valuable resources. MHAUS provides information and support to healthcare providers and patients, including evidence-based
The Malignant Hyperthermia Association of the United States: Services and Research

The Malignant Hyperthermia Association of the United States (MHAUS) was established in 1981 to educate both healthcare professionals and lay communities. Its mission is to reduce death and injury from malignant hyperthermia (MH) by improving medical care related to MH, providing support information to patients, and improving the scientific understanding and research related to MH and other heat-related syndromes.

**Highlights of Services and Educational Materials**

- The MHAUS hotline, 1-800-MH HYPER, provides medical professionals with access to anesthesiologists who specialize in MH-crisis treatment 24 hours a day, 365 days per year. These anesthesiologists provide expertise and support for successfully managing an MH crisis.
- MHAUS publishes a quarterly newsletter, the Communicator, providing the latest news on MH.
- MH procedure manual is a new program offering comprehensive protocols and a training video for use in hospitals, ambulatory surgery centers, and office-based surgery practices.
- A variety of educational information is available at the association’s Web site (http://www.mhaus.org).
- Emergency medical identification tags, to alert healthcare providers to a patient’s MH status, may be obtained through MHAUS.

**Scientific Research**

MHAUS maintains the North American MH Registry (http://www.mhreg.org), which is used to analyze and disseminate patient-specific clinical and laboratory information of MH-susceptibility to scientific investigators and physicians caring for MH-susceptible patients.


**Notes**


(See Self-Assessment Questions on next page.)
Self-Assessment Questions

The following questions about this article may be useful for internal education and assessment. You may use the following examples or come up with your own.

1. All of the following are clinical manifestations of malignant hyperthermia (MH) EXCEPT?
   a. Increased temperature
   b. Tachycardia
   c. Fluctuating blood pressure
   d. Fine muscle twitching and rigidity

2. Which is the definitive means to determine the presence of MH?
   a. DNA analysis
   b. Caffeine-halothane contracture test
   c. Ionized calcium levels
   d. 12-lead electrocardiogram

3. Dantrolene sodium administered by continuous rapid intravenous (IV) push is the treatment of choice for MH.
   a. True
   b. False

4. The components of the treatment plan when MH is suspected and/or diagnosed include which of the following?
   a. Withdrawing all anesthetics and administering 100% oxygen
   b. Discontinuing IV fluids and assessing urine output
   c. Obtaining 12-lead electrocardiogram to identify and treat arrhythmias
   d. Maintaining temperature in the operating room

5. All of the following risk reduction strategies may reduce harm to patients that develop MH EXCEPT?
   a. Conducting annual drills and providing MH emergency management kits to the surgical team
   b. Displaying posters that include the clinical manifestations of MH and the Malignant Hyperthermia Association of the United States hotline number.
   c. Cancelling all procedures on patients with a family history of MH
   d. Obtaining an anesthesia history that identifies any previous reactions to anesthesia
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