MANAGING MH
An MHAUS Online Brochure
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Since malignant hyperthermia (MH) was first identified in 1960, each year has brought a greater understanding of this syndrome. Since the 1980s, increased awareness of MH, major advancements in patient monitoring, and the introduction of dantrolene sodium for injection (in 1979) are responsible for the dramatic decrease in mortality attributed to MH.

This brochure is intended for anesthesia care providers as an updated clinical guide as to the diagnosis and/or treatment of MH. For easy review, it is presented as a bulleted list of specific points. It is intended for use in conjunction with the Malignant Hyperthermia Association of the United States (MHAUS) brochures "Preventing MH – An Anesthesia Protocol" and "Drugs, Equipment and Dantrolene – Managing MH," as well as the MHAUS videos.

Since not everything is known about MH and its presentation, debate exists concerning the proper clinical management of patients. These controversies are indicated below.

DIAGNOSIS OF MH

* The most consistent indicator of potential MH in the OR is an unanticipated increase (e.g., doubling or tripling) of end-tidal CO2 when minute ventilation is kept constant. The increase in CO2 may occur over a brief period of time or may develop over longer periods of time (minutes to hours). If upward adjustments of minute ventilation (tidal volume and frequency) are required to maintain normal end-tidal CO2, the possibility of MH should be considered and promptly evaluated.
* If sudden, unexpected cardiac arrest occurs, especially in a young male, hyperkalemia should be considered immediately and therapy started with calcium, hyperventilation and glucose, and insulin. Plasma potassium concentration should be measured as soon as possible. Sudden unexpected cardiac arrest is not typically due to MH, but to sudden rapid rhabdomyolysis.
* Unexpected tachycardia, tachypnea and jaw muscle rigidity (masseter spasm) are often common signs of MH that follow the significant CO2 increase.
* Respiratory and metabolic acidosis usually indicate fulminant MH. However, metabolic acidosis is not always present prior to severe temperature increase.
* A specific sign of the MH syndrome is body rigidity (i.e., limbs, abdomen and chest). When there is a suspicion of MH, attempts should be made to determine if muscle rigidity is also present.
* Temperature elevation is often a late sign of MH. Temperature change during MH is best detected by core temperature measurement (tympanic, naso- or oropharyngeal, esophageal, rectal, or pulmonary artery). Forehead skin temperature is less acceptable; it is slower in reflecting changes in core temperature and could be influenced by peripheral vasoconstriction. We recommend that core temperature be measured whenever general anesthesia is administered for procedures lasting more than 30 minutes.
* Postoperative rhabdomyolysis without intraoperative signs of MH should be treated with hydration, mannitol and bicarbonate. Plasma potassium concentration should be measured immediately or as soon as possible. The patient should be referred to a neurologist and to an MH testing center to evaluate occult myopathy and determine the need for evaluation of MH susceptibility.
* In the event of an acute MH episode, coagulation profile and creatine should be obtained in addition to electrolytes, arterial blood gas, and CK determinations.
* MH may occur at any time during or emerging from anesthesia, including in the immediate post-operative period.

TREATMENT OF ACUTE MH

* Do not administer volatile anesthetics or succinylcholine once MH has been diagnosed or considered.
* Call for additional help.
* Hyperventilate at two to three times predicted minute ventilation with 100% oxygen.
* Give 2.5 mg/kg of dantrolene sodium for injection. Repeat as often as necessary titrated to control clinical signs of MH. Continue intravenous dantrolene for at least 24 hours after control of the episode (approximately 1 mg/kg q 6 hours).
* Dantrolene sodium does not produce significant cardiac or pulmonary complications when administered acutely. Therefore, there is little harm in administering dantrolene where MH is suspected, but not yet proven.
* Treat acidosis with bicarbonate – if not promptly reversed by dantrolene.

* Avoid calcium channel blockers. Persistent arrhythmias may be treated with any other standard antiarrhythmics. Most arrhythmias respond to correction of hyperkalemia and acidosis by hyperventilation, dantrolene and bicarbonate.

* Monitor core temperature.

* Treat hyperkalemia with glucose, insulin and calcium.

* If hyperthermic or core temperature rises rapidly, cool the subject; employ when possible nasogastric lavage, rectal lavage and/or surface cooling. Cease cooling efforts when temperature has fallen to 38 degrees C.

* Watch for recrudescence by appropriate monitoring in an ICU for at least 24 hours. Recrudescence occurs in about 25% of MH cases. Core temperature should be monitored throughout.

* Avoid parenteral potassium, if possible, during ongoing rhabdomyolysis. Following control of the acute episode, persistent hypokalemia may be treated with careful monitoring of serum potassium level.

* Ensure urine output of at least 2 ml/kg/hr by hydration and diuretics since myoglobinuria is common.

* Follow coagulation profile - disseminated intravascular coagulation (DIC) may occur.

* Measure CKs every 6 hours until decreased. CK may remain elevated for 2 weeks if event was severe. After the patient has improved and stabilized, CK should be measured on a declining time basis until it is normal (e.g., every 4 hours during the acute episode to every week during convalescence). This is important because it is elevated normally in some myopathies, and this should be recognized as a part of overall evaluation and treatment.

* For consultation to help with patient management, call the MH Hotline: 1-800- MH-HYPER (1-800-644-9737) or 1-315-464-7079 if outside the U.S.

* Report patients who have had acute MH episodes to the North American MH Registry of MHAUS: 1-412-692-5464 by means of a confidential AMRA report. The patient can call this number to add their name to the Registry database. (See www.mhreg.org)

* Refer patients and families to MHAUS for information.

DRUGS AND MH

* All volatile inhalation anesthetics (halothane, enflurane, isoflurane, desflurane, sevoflurane, ether, methoxyflurane and cyclopropane) and succinylcholine are MH triggers. Nitrous oxide is not a trigger.

* Calcium channel blockers should not be administered when dantrolene has been given.

* All other currently used anesthetics and life-support drugs are considered safe.

SUCCINYLCHOLINE IN CHILDREN

* Routine use of succinylcholine for elective surgery is best avoided in children.

* The FDA ordered the pharmaceutical companies that manufacture succinylcholine to change the package insert to indicate that the drug should not be used routinely in children. Some indications for succinylcholine are: airway emergencies, risk of aspiration and procedures where it is advisable that paralysis be induced within 60 seconds of induction of anesthesia. The reason for the change relates to complications such as masseter muscle rigidity, rhabdomyolysis, and sudden hyperkalemic cardiac arrest in patients with undiagnosed myopathies (i.e., may be in preclinical stage). Rhabdomyolysis may occur in as many as 40% of children given IV succinylcholine, whether clinical or “subclinical.”

MANAGEMENT AND PRETREATMENT OF MH-SUSCEPTIBLE (MHS) PATIENTS

* A treatment plan for MH should be available in every anesthetizing location.

* All facilities, including ambulatory surgery centers and offices, where MH triggering anesthetics (desflurane, sevoflurane, isoflurane, halothane, enflurane, ether, methoxyflurane, cyclopropane or succinylcholine) are administered, should stock a minimum of 36 vials of dantrolene sodium for injection. If potent volatile agents are not used, and succinylcholine is available for an emergency situation such as to facilitate obtaining an airway that is lost or difficult, a minimum of 36 vials of dantrolene sodium should be available. If none of these is used or available, then dantrolene sodium need not be present.

* Do not use MH-triggering agents on patients susceptible to MH or their undiagnosed relatives.

* Dantrolene prophylaxis is not recommended for most MH-susceptible patients. Dantrolene can worsen muscle weakness in patients with muscle disease and should be used with caution. For most procedures, including those requiring general anesthesia, dantrolene prophylaxis may be omitted.

* The anesthesia machine to be used for a patient susceptible to MH should be prepared in the following way: Ensure that anesthetic vaporizers are disabled by removing or taping in the "OFF" position. Some consultants recommend changing CO_2 absorbent (soda lime or baralyme). Flow 10L/min O_2 through circuit for at least 20 minutes. If fresh gas hose is replaced, 10 minutes is adequate. During this time a disposable, unused breathing bag should be attached to the Y-piece of the

circle system and the ventilator set to inflate the bag periodically. Use new or disposable breathing circuit. The expired gas analyzer will indicate absence of volatile agents in the anesthesia circuit.

* The patient susceptible to MH undergoing outpatient surgery may be discharged on the day of surgery if the anesthetic has been uneventful. A minimum period of 1.0 hour in PACU monitoring vital signs at least every 15 minutes and 1.5 hours in phase 2 PACU/step down is recommended.

TESTING FOR SUSCEPTIBILITY TO MH

* There are a small number of centers in North America. A complete list is available from MHAUS or at www.mhaus.org.
* Muscle specimens for MH testing must be isolated fresh at the biopsy center.
* Muscle biopsy centers in the U.S., Canada and Europe have standardized the contracture test and determined its sensitivity and specificity. The muscle biopsy is highly sensitive for the detection of susceptibility to MH and currently is the only valid definitive test to determine the diagnosis of MH susceptibility or its absence.
* Molecular genetic testing for MH susceptibility is progressing steadily. To date, there are about 50 mutations identified as being causal for MH, and only genotypes have been identified in less than 50% of these. In some MH families where a specific gene has been clearly associated with susceptibility in several members, DNA testing may be used for determining susceptibility in other individuals. Such testing may be available on a limited basis in the U.S. . At any time, a genetic test of the Ryanodine receptor may be offered in a clinical diagnostic genetics laboratory. But it is expected that this test will be much less sensitive than the muscle contracture test. If the exam of the Ryanodine receptor gene does not identify a mutation causative for MH, the patient must still be considered MH susceptible until a muscle contracture test demonstrates that individual is NOT susceptible. In vitro muscle biopsy contracture testing is still the gold standard for MH diagnosis.

MUSCLE DISEASE ISSUES

* Several muscle diseases may predispose to susceptibility to the MH syndrome or hyperkalemic reactions to MH-trigger agents. MH susceptibility is genotypically associated with Central Core Disease. Patients with Central Core Disease should not be given MH-triggering anesthetics.
* Importantly, patients with Duchenne or Becker's muscular dystrophy are at risk for developing life-threatening hyperkalemia when administered succinylcholine or potent volatile agents. Potent volatile agents have on relatively rare occasions resulted in hyperkalemic arrest in Duchenne/Becker patients. As a result, many recommended their use only until an intravenous is established. Subtypes of myotonia, specifically sodium channel forms of myotonia and cold-induced myotonia, may predispose to MH. Hyper- and hypokalemic paralyses have also been associated with MH-like anesthetic reactions. . Mitochondrial myopathies do not appear to predispose to MH.

MASSETER MUSCLE RIGIDITY (MMR)

* MMR is a sustained contracture of the jaw muscles following the administration of succinylcholine and, if considered abnormally long in duration, may be a forewarning of MH. A mild increase in masseter muscle tone with limb flaccidity following succinylcholine may be a normal response. It is not possible to determine, clinically, whether that increase in tone represents an MH reaction, some other myopathic response, or not. However, if generalized rigidity also occurs, then MH is highly likely. Immediately check potassium and blood gas.
* MMR occurs more frequently in children, with or without inhalation agents.
* Clinical signs of MH occur in about 20% of cases of MMR. These signs may follow immediately or be delayed. Temperature monitoring should be employed, if not yet done so.
* Experts are divided as to how to proceed after MMR: i.e., either continue with anesthetic agents that will not trigger MH or discontinue the anesthetic and postpone elective surgery.
* Unless clinical signs of MH appear, dantrolene is not recommended following the occurrence of MMR only.
* Because of the likelihood of rhabdomyolysis, and the possibility of an undiagnosed myopathy, CK and urine color should be checked every 6 hours, until return to normal. Also test electrolytes; rapidly developing rhabdomyolysis includes rapid increases in potassium and slowly developing rhabdomyolysis is less dangerous, since potassium is re-distributed more quickly than blood levels can increase.
* Hyperkalemic cardiac arrhythmias may follow MMR and presage severe rhabdomyolysis. Myoglobinuria may occur within a few hours after MMR and should be sought and treated to prevent acute tubular necrosis and obstructive nephropathy.
* Patients experiencing MMR with associated clinical signs/symptoms of MH should be observed closely (temperature monitoring) for at least 24 hours in an ICU.

* Discuss muscle biopsy with an MH expert.

SUDDEN, UNEXPECTED CARDIAC ARREST: MH OR AN OCCULT MYOPATHY?

* Sudden cardiac arrest, especially soon after the use of succinylcholine in young or adolescent males, is likely caused by hyperkalemia in a patient with an undiagnosed myopathy. Many such cases have been described since 1970, most with the use of intravenous or intramuscular succinylcholine. Initial reports indicated a high mortality. Muscle rigidity and/or hyperthermia may also be present.
* Therapy should be directed at treatment of hyperkalemia: calcium chloride, bicarbonate, insulin, glucose and hyperventilation. Dialysis and cardiopulmonary bypass may be required.
* If hyperkalemia is successfully treated, a good outcome may be attained even after prolonged resuscitation.
* Even though hyperkalemic cardiac arrest is uncommon, because of the extremely high mortality in such cases, the inability to predict which child may be at risk, and the availability of alternative neuromuscular blocking agents, anesthesia providers have been warned against elective use of succinylcholine in children.

INFORMATION RESOURCES

* MHAUS provides educational and technical information to patients and health care providers. Contact MHAUS at 607-674-7901 or e-mail to info@mhaus.org
* Information is available via the Internet at: http://www.mhaus.org

NORTH AMERICAN MH REGISTRY of MHAUS

* The North American MH Registry of MHAUS registers information about specific patients and their families. The Registry is located at Children's Hospital of Pittsburgh at the University of Pittsburgh and Dr. Barbara Brandom is the director. Health care providers are encouraged to report MH and MH-like episodes to the Registry. Contact the Registry office at 1-888-274-7899 for forms or information. (See www.mhreg.org.)