Special Article

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MANAGING MALIGNANT HYPERTHERMIA

Malignant Hyperthermia Association of the United States

Since malignant hyperthermia (MH) was first identified in 1960, each year has brought about a greater understanding of this syndrome. Increased awareness of MH, increased sophistication in patient monitoring, and the introduction of dantrolene in 1979 are responsible for the dramatic decrease in mortality attributed to MH since the 1980s. More is being learned every year about the diagnosis, treatment, pathophysiology and testing for MH.

This brochure is intended as an updated clinical guide to the diagnosis and treatment of MH for anesthesia care providers. 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 Malignant Hyperthermia – An Anesthesia Protocol" and "Man-aging Malignant Hyperthermia - Drugs and Equipment," as well as the recent MHAUS videos.

Not everything is known about MH and its presentation, so some controversies arise concerning the proper clinical management of patients. These controversies are indicated.

DIAGNOSIS OF MH

The most sensitive indicator of potential MH in the OR is an unanticipated increase (e.g. doubling or tripling) of end-tidal CO_2.

The increase in CO_2 may occur over a brief period of time or may develop over 10 to 20 minutes. If cardiac arrest occurs, hyperkalemia should be considered immediately.

The most specific sign of MH is total body rigidity.

Unexpected tachycardia, tachypnea and jaw muscle rigidity are other common signs of MH.

Respiratory and metabolic acidosis usually occur early in MH.

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, axillary or pulmonary artery). We suggest that core temperature be measured whenever general anesthesia is administered for other than very brief procedures.

SUCCINYLCHOLINE IN CHILDREN

The routine use of succinylcholine-for elective surgery is problematic and is best avoided in children. The pharmaceutical companies that manufacture succinylcholine have changed the package insert to indicate that the drug should not be used routinely in children, except for airway emergencies, risk of aspiration and special situations. The reason for the change relates to the complications reported from succinylcholine. These include malignant hyperthermia, masseter muscle rigidity, rhabdomyolysis, and sudden cardiac arrest in patients with undiagnosed myopathies.

MASSETER MUSCLE RIGIDITY (MMR)

MMR is a sustained contracture of the masseter muscles following the use of succinylcholine that may presage MH. A mild increase in masseter muscle tone following succinylcholine with limb flaccidity may be a normal response. It is not possible to determine, clinically, whether that increase in tone represents an MH reaction or not. However, if generalized rigidity also occurs, then MH is highly likely.

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MMR occurs more frequently in children, with or without inhalation agents.
MH may follow MMR immediately, or may be delayed for several minutes.
Clinical signs of MH occur in about 10% of cases of MMR.
Experts are divided as to how to proceed after MMR: Either continue with NON TRIGGER agents or discontinue the anesthetic and postpone elective surgery.
Unless clinical signs of MH appear, dantrolene is not recommended after MMR only.
Because of the likelihood of rhabdomyolysis, and the possibility of an undiagnosed myopathy, CK should be checked every 12 hours, until return to normal.
Myoglobinuria usually occurs 4-9 hours after MMR and should be sought and treated.
Patients experiencing MMR should be observed closely for 12-24 hours.
Discuss muscle biopsy with MH expert.

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

Sudden cardiac arrest, especially soon after the use of succinylcholine, and especially in young males, is likely related to hyperkalemia in a patient with an undiagnosed myopathy. Over 40 such cases have been described since 1990, most with the use of intravenous succinylcholine, but some with intramuscular injection. There is an approximate 50% mortality rate.

Muscle rigidity and/or mild hyperthermia may appear as part of the presentation. Therapy should be directed at treatment of hyperkalemia: calcium chloride, bicarbonate, insulin, glucose and hyperventilation.
Dantrolene therapy should be considered.
Even though the reaction is rare, because of the high mortality, the inability to predict which child may be at risk and the availability of alternative neuromuscular blocking agents, anesthesia providers have been warned not to use succinylcholine except on indication.

DRUGS AND MH

All volatile inhalation anesthetics (including desflurane and sevoflurane) and succinycholine are MH triggers.
Nitrous oxide, barbiturates, narcotics, tranquilizers, and amide and ester local anesthetics are safe for MH patients.
Calcium channel blockers should not be administered when dantrolene has been given.
Ketamine, propofol, etomidate, vecuronium, pancuronium and atracurium have been determined to be safe drugs for MH patients.
The new muscle relaxants mivacurium, rocuronium, pipecuronium and doxacurium are also considered safe agents. Catecholamines are safe agents.

MANAGEMENT AND PRETREATMENT OF MH-SUSCEPTIBLE (MHS) PATIENTS

MANAGING MH - DRUGS & EQUIPMENT

Preparedness is essential to prevent death from MH. This brochure provides a checklist of drugs and equipment which should be available for all anesthesia departments and operating rooms.
In addition to an anesthesia machine and ECG monitor, all locations where general anesthesia is administered should contain:

A plan to treat MH, such as the wall chart provided by MHAUS
A means to continuously monitor end-tidal CO_2, oxygen saturation and core body temperature by electronic probe
A hypothermia blanket, a machine to manufacture ice, and arefrigerator containing at least 3,000 ml of cold solution

Drugs

A cart or kit containing the following should be immediately accessible to operating rooms:

Dantrolene sodium IV - 36 ampules
2,000 ml sterile water for injection USP (without a bacteriostatic agent) to reconstitute dantrolene
50-cc ampules sodium bicarbonate 8.4% x 5
20% mannitol 500 ml x 2 (or ten 50 ml vials)
Furosemide 4 ml x 2 (40 mg/amp)
50% glucose 50 ml x 2
Regular insulin 100 units/ml x 1 (refrigerated)
10% calcium chloride x 2

Cooling Equipment

50 ml syringe x 2
Nasogastric tube x 2

Large, clear plastic bags for ice
Bucket for ice

Equipment

Blood pump x 2
CVP line set x 2
Urinary Foley catheter (several sizes)
Urimeter x 2
Mini spike IV additive pins to facilitate mixing water with dantrolene or Multi Ad fluid transfer sets for reconstituting dantrolene
Anesthesia breathing circuits

Anesthesia Machine Preparation For MH Patient

It has been shown that after replacing the anesthesia circuit and fresh gas hose, flows of 10 L/min of O_2 will effectively purge the anesthesia machine of inhalation agents in 10 minutes. During this time, a breathing bag should be attached to the Y-piece of the circle system and the ventilator set to inflate the bag. Therefore, a separate anesthesia machine for MH-susceptible patients is not required.

Tubes For Laboratory Tests

Blood tubes (Red stopper) for six repeat CK, LDH, Na, K, Cl, Ca, Mg, myoglobin determinations
Heparinized 5 ml blood gas syringes x 6
Tubes for coagulation studies (e.g., PT, PTT, platelet count, fibrinojen and Fibrin-split product)
Urine specimen containers to measure myoglobin
Urine dip stick for hemoglobin
A treatment plan for MH should be available.
All facilities where general anesthesia is administered (including ambulatory surgery centers) should stock 36 vials of dantrolene sodium.
Do not use MH-triggering agents with MHS patients or their relatives.
Prophylactic dantrolene should be used with caution in patients with muscle weakness or muscle disease, as muscle weakness may be exacerbated.
Dantrolene prophylaxis may be omitted if the patient will receive sedation or regional anesthesia or general anesthesia with appropriate intra-operative monitoring (including continuous temperature and continuous end-tidal CO_2 monitoring) and dantrolene is readily available for administration.
The anesthesia machine should be prepared by changing soda lime and breathing circuit, removing or inactivating vaporizers, and flushing with Oxygen or air at 10 liters/min for 10-20 minutes. See "Preventing MH" for further details.
The MHS patient undergoing outpatient surgery may be discharged on the day of surgery if the anesthetic has been uneventful and no dantrolene has been given. A minimum of 4 hours in the PACU is suggested.

TREATMENT OF ACUTE MH

Stop volatile anesthetics and succinylcholine
Hyperventilate with 100% O2.
Give 2.5 mg/kg of dantrolene IV. Repeat as necessary titrated to signs of MH. Suggested upper limit is 10mg/kg, but this may be exceeded as necessary.
Avoid calcium channel blockers. Persistent arrhythmias may be treated with other standard any antiarrhythmic. Most arrhythmias respond to correction of hyperkalemia and acidosis.
Monitor core temperature.
Cool by nasogastric, rectal lavage and surface cooling—but avoid overcooling.
Continue dantrolene for at least 36 hours after control of the episode.
Watch for recrudescence by monitoring in an ICU for 24-36 hours. Recrudescence occurs in about 25% of MH cases.
Avoid parenteral potassium.
Follow coagulation profile—DIC may occur.
Measure CKs every 12 hours until normalized.
Refer patients and families to MHAUS for information.
For consultation to help with patient management, call the MHAUS Hotline at (800) MH-HYPER.
Report acute MH episodes to the North American Malignant Hyperthermia Registry: (717) 531-5437).

TESTING FOR MH

There are only 11 centers in North America. There are over 20 in Europe. Those performing muscle biopsy tests in the U.S. and Canada have

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standardized the test and the sensitivity and specificity of the contracture test. Molecular genetic testing for MH susceptibility is not a realistic expectation for the near future, since multiple genes or mutations have been demonstrated in many families.

PREVENTING MH - AN ANESTHESIA PROTOCOL

This protocol is intended as a guide for anesthesia practioners and other health care professionals to be prepared to recognize, treat and prevent malignant hyperthermia (MH).

Routine Pre-Operative Questioning

All patients about to undergo general anesthesia should be asked these specific questions as part of a medical history:

Is there a family history of MH?

Have there been unexpected deaths or complications arising from anesthesia (including the dental office) with any family members?

Is there a personal history of a muscle disorder (e.g. muscle weakness)?

Is there a personal history of dark or cola-colored urine following anesthesia?

Is there a personal history of unexplained high fever following surgery?

Intra-Operative Preparedness

The following precautions should be taken in order to detect MH in its early stages, when it is usually amenable to treatment without sequelae:

Planning Ahead:

A written treatment plan should be posted in a conspicuous place. A plan is available from MHAUS.

A kit or cart containing drugs necessary for the treatment of MH should be immediately available to all operating rooms. Each kit should contain 36 vials of dantrolene, bacteriostatic water for injection, and bicarbonate. MHAUS offers a brochure listing the recommended supplies.

A refrigerator unit near the operating room should be stocked with iced saline. Ready access to an ice machine is important.

All operating and recovery room personnel should be trained in the recognition and treatment of MH. Periodic dry-runs of an MH emergency are recommended. In-service materials can be provided by MHAUS.

During Surgery

Evaluate any unexpected hypercarbia, tachycardia, tachypnea or arrhythmia (e.g. arterial and venous blood gases). Avoid suppressing tachycardia with beta blockers until MH has been ruled out.

Core temperature should be monitored in all patients given general anesthesia for 30 minutes or more. Acceptable core temperature sites include: distal esophagus, nasopharynx, axilla, rectum, bladder and pulmonary artery. Skin temperature may not adequately reflect core temperature during MH episodes. Consider MH in the differential diagnosis of any temperature rise.

Stop inhalation anesthetic and succinylcholine if masseter rigidity occurs. If surgery must continue, immediately switch to non-triggering anesthetics.

Do not give triggering agents to patients with Duchenne Dystrophy, Central Core Disease, Myotonia and other forms of muscular dystrophy.

Sudden cardiac arrest in a young male with normal oxygenation should be considered as secondary to hyperkalemia and so treated.

Treating The Known Or Suspected MH-Susceptible Patient

Pre-operative Preparations:

Anesthesia machine:

Remove vaporizers, if possible. Otherwise, drain and disconnect or tape in the off position.

Flow 10 L/m O_2 through circuit for at least 20 minutes. If fresh gas hose is replaced, 10 minutes is adequate. During this time a breathing bag should be attached to the Y-piece of the circle system and the ventilator set to inflate the bag.

Use new or disposable breathing circuit.

Take a preoperative creatine kinase (CK) and CBC.
Place a cooling blanket on the table.

Dantrolene Prophylaxis:

Dantrolene prophylaxis should be considered on an individual patient basis but is not recommended for most MH susceptibles. When used, dosage is 2.5 mg/kg IV starting 30 minutes prior to anesthesia. For consultation, contact MHAUS.

NOTE: Dantrolene can worsen muscle weakness in patients with muscle disease and should be used with caution. For procedures with local anesthesia only, dantrolene prophylaxis may be omitted.

Intra-operative Considerations

Techniques of choice
Spinal, epidural, regional or local, if possible.
Safe drugs
Local: No local anesthetics trigger MH; thus any type of regional anesthesia is safe for MH susceptibles.
General: Benzodiazepines, opioids, barbiturates, propofol, ketamine, nitrous oxide, etomidate. Pancuronium, atracurium, vecuronium, pipecuronium, mivacurium, doxacurium, or curare may be used for relaxation. Neostigmine and atropine are used for reversal by some; others disagree on their safety.
Unsafe drugs/MH triggers
Halothane, Enflurane, Isoflurane, Desflurane, Methoxyflurane, Ether, Cyclopropane, Sevoflurane, Ether. Succinylcholine
Monitoring
Essential: blood pressure, central temperature, ECG, pulse oximeter, and capnograph or capnometer
Strongly suggest respirometer
Use arterial line, CVP or other invasive monitors as appropriate for the surgery

Post-operative Procedure

If the anesthetic course has been uneventful:
Continue to monitor temperature and ECG for 1 to 2 hours. No further dantrolene is necessary.
If MH has occurred:
Recover patient in an ICU for 24-48 hours.
Continue IV dantrolene for 48-72 hours, titrated to alleviation of muscle rigidity, tachycardia, acidosis, and CK levels.
Suggested dantrolene dosage is at least 1 mg/kg q 6 hours IV.
After that, 1 mg/kg may be given q 6 hours orally x 24 hours.
Monitor the patient's coagulation status, watching for DIC.
Look for myoglobinuria and renal failure, and treat as needed.
Use potassium-containing solutions with caution.
Monitor potassium and CK levels q 6 hours at least.
Monitor urine output.
Register patient with North American MH Registry. Forms are available by contacting North American MH Registry, Penns-ylvania State University, College of Medicine, Dept of Anesthesia, PO Box 850, Hershey, PA 17033-0850, (717) 531-6936.
Alert family to the dangers of MH in other family members.
Refer for testing at nearest center (list available from MHAUS).

OTHER ISSUES

Several muscle diseases predispose to MH. There has been a clear association with Central Core Disease. Case reports have also linked MH to Muscular Dystrophy and forms of Myotonia.

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INFORMATION RESOURCES

Forms For Reporting Mh Episodes Available From North American Mh Registry

Pennsylvania State University
College of Medicine
Anesthesia Dept
PO Box 850
Hershey, PA 17033-0850
(717) 531-6936 or 531-5937

MHAUS Hotline

Names and phone numbers of on-call anesthesiologists available to consult in MH emergencies may be obtained 24 hours a day through:

1 800 MH HYPER
(1 800 644-9737)
Outside the United States call:
315-428-7924

MHAUS provides educational and technical information to patients and health care providers. All MHAUS literature is available 24-hours a day, 7 days a week through the MHAUS Fax-On-Demand system at 1-800-440-9990.

The North American MH Registry, an operating unit of MHAUS registers information about specific patients and their families. Health care providers are encouraged to report MH episodes to the Registry. Forms may be obtained from:

North American MH Registry Pennsylvania State University Department of Anesthesia P.O. Box 850 Hershey, PA 17033-0850 (717) 531-5737

Medic Alert Foundation International

(209) 634-4917 Ask for Index Zero

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This brochure was written and produced by the MALIGNANT HYPERTHERMIA ASSOCIATION OF THE UNITED STATES (MHAUS). MHAUS serves MH-susceptible individuals and medical professionals. MHAUS is a non-profit organization under IRS Code 501(c)(3). Its services are provided free. It operates solely on contributed funds. All contributions are tax-deductible and should be sent to:

MHAUS
32 S Main St Box 1069, Sherburne, NY 13460
(607) 674-2420

There is still much that is not known about malignant hyperthermia. Research is continuing. Contact MHAUS Hotline for current information. MMHP-1(6/94/12K)