MALIGNANT HYPERTHERMIA

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NOVEMBER 2015

MALIGNANT HYPERTHERMIA (MH)

- An ***inherited*** disorder which causes sensitivity of skeletal muscle to certain inhaled anesthetic agents and/or depolarizing muscle relaxants
- Abnormally large amounts of calcium released from skeletal muscle leading to a life-threatening hypermetabolic state
- If not identified and treated promptly, it may progress and cause irreversible organ damage or death
- May occur at any time during the anesthesia process – including the early recovery phase
- MH-susceptible patients are ***always*** at high risk, even if they have had previous anesthesia without a reaction

TRIGGERING AGENTS

- **Inhaled General Anesthetic Agents:**

  Halothane (Fluothane)

  Desfulrane (Suprane)

  Enflurane (Ethrane)

  Isonflurane (Forane)

  Sevoflurane (Ultane)

  Ether

- **Depolarizing Neuromuscular Blocking Agents:**

  Succinylcholine (Anectine)

MH-SUSCEPTIBLE PATIENTS

- An inherited autosomal dominant genetic disorder
- Personal or Family history of:
  - Malignant Hyperthermia
  - Unexplained death during anesthesia
  - A fetus with a paternal history of MH-sensitivity (even if maternal history is negative)
  - Patients exhibiting prolonged Masseter muscle spasm (Trismus), or muscle rigidity after a triggering agent
- Predisposing disorders associated with MH-susceptibility:
  - Central core disease
  - Duchenne's or Becker's Muscular dystrophy
  - King-Deneborough syndrome
  - Myotonia
- Incidence rate: Adults 1:100,000 Children 1:50,000

PATHOPHYSIOLOGY

Trigger

↓

Large quantities of Calcium released

(from sarcoplasmic reticulum in skeletal muscle)

↓

Sustained increased calcium levels within the skeletal muscle

↓

Excessive stimulation of aerobic and anaerobic glycolytic metabolism

↓

Increased Carbon Dioxide production/Decreased Oxygen Supply

↓

Respiratory and metabolic acidosis

↓

Sustained muscle contractions

↓

Increased metabolism and heat production

↓

ATP stores within the cells are depleted

↓

Cells die

↓

Large amounts of potassium released into circulation

Hyperkalemia

↓

Cardiac Dysrhythmias

Myoglobin released

↓

Renal Failure

Signs and Symptoms

EARLY	LATE
1. Tachycardia (usually 1st symptom – mistaken for light anesthesia)	1. Fever (up to > 110° - 114° F)
2. Masseter spasm or trismus (severe, sustained contraction of jaw making intubation difficult)	2. Sympathetic Nervous System activation
3. Increase in end-tidal carbon dioxide (>100 mmHg – unable to correct it)	3. Edema (Cerebral/Peripheral)
4. Tachypnea (pt's attempt to correct hypercarbia)	4. Cyanosis/Mottled Skin
5. Hypoxia	5. Myoglobinuria/Rhabdomylysis
6. Acidosis (pH < 7.0)	6. DIC
7. Hyperkalemia	7. Multiorgan Failure (Cardiac/Renal)
8. Hypertension	8. Cardiac Arrhythmias
	9. Sudden Cardiac death in young patients

Operating Room or PACU

In the event of a MH emergency in the OR:

* Hyperventilate with 100% O_2 in an attempt to meet the requirements of the body during the crisis period.
* The Circulating RN shall call for additional help from the other OR suites, or from PACU
* Anesthesia staff will retrieve the Malignant Hyperthermia cart from the Anesthesia Work Room, and bring it to the OR
* Additional staff shall assist Anesthesia, mix the Dantrolene, assist with cooling the patient, deliver specimens to the Clinical Laboratory, documentation, run for supplies, etc.
* The surgeon should close the surgical wound, if possible. If not, the surgeon should pack the wound with saline-soaked surgical towels or laparotomy sponges. The Circulating RN should document, on the Intraoperative Nurses' Notes, the number of towels/lap sponges used to pack the wound.
* Notify the Pharmacy

Operating Room or PACU

* **The Malignant Hyperthermia cart contains:**
  - 54 vials of Dantrolene
  - Sterile water to reconstitute the Dantrolene (w/o bacteriostatic agent)
  - Ice packs
  - Various sizes of syringes and needles; 60 ml, 10ml, 3 ml
  - Toomey Syringes

- At least 3 one liter bags of 0.9NS are kept in the refrigerator at all times
- Instructions for reconstituting the Dantrolene are taped to top of the MH cart
- The "Emergency Therapy For Malignant Hyperthermia" protocol, by MHAUS,
  is taped to the top of the MH cart

TREATMENT

ACUTE PHASE TREATMENT

- ✓ Dantrolene should be administered ***within 10 minutes*** of the diagnosis
  - initial dose 2.5 mg/kg IV
  - repeat dose q 5 minutes until reversal of the reaction occurs *OR* a total dose of 10mg/kg has been given
  - dissolve 20 mg in each vial with at least 60ml sterile-water (warming may speed it up)
- ✓ Halt the triggering event- If surgery must continue, maintain general anesthesia with IV non-triggering anesthetics (e.g. propofol)
- ✓ Hyperventilate with 100% Oxygen- To flush volatile anesthetics and ETCO2
- ✓ Draw labs and ABGs
- ✓ Anti-arrhythmic agents for dysrhythmias (Do NOT use Calcium Channel Blockers)
- ✓ Cold saline IV, lavage with cold fluids, and cooling blanket (for a core temperature > 39° C)
- ✓ Glucose/insulin, calcium, sodium bicarb for hyperkalcemia

DANTROLENE

Mechanism of Action

- Classified as a direct-acting, muscle relaxant – specific to skeletal muscle only
- Disassociates the excitation-contraction coupling within the muscle cells by acting on the rayodene receptor. (Where gene mutations occur)
- Interferes with the release of calcium from the Sarcoplasmic Reticulum, thus suppressing the rise in calcium in the muscle cells that triggers the MH crisis
- Reestablishes the normal level of ionized calcium in the myoplasm

Dosage and Administration

- Supplied in 36 ml vials
- Each vial contains 20 mg of Dantrolene Sodium, 3 grams of Mannitol, and Sodium Hydroxide (Sodium Hydroxide increases the pH to 9.5)
- Reconstitute with 60 mls of sterile water for injection, ***without*** Bacteriostatic Agent
- Vial is shaken until solution is clear - ***THIS MAY TAKE 2 – 4 MINUTES***
- Give 2.5mg/kg ***RAPID IV Push*** (use a micron filter)

Dantrolene Dosage and Administration

- Large bore IV/Central line → inject close to the IV insertion site
- Its effects should be noticed within 2-3 minutes
- Repeat dose Q 5 minutes until MH crisis subsides
- Maximum doses 10 mg/kg - 30mg/kg
- Should be given via a separate line, ***not compatible*** with 0.9NS, D5W, or LR
- Primary line must be flushed with sterile water for injection USP (*without a bacteriostatic agent)* ***before*** administering the Dantrolene and ***after*** administration
- Tissue necrosis with IV extravasation (due to the high pH of the Dantrolene)
- Protect from light
- Use within 6 hours of mixing
- Half life is variable = 4°- 8°
- Shelf life of Dantrolene = 28 months
- Post Acute Treatment → Dantrolene 1mg/kg q 4-6 hours IV, 8 mg/kg/day in 4 divided doses, or 0.25 mg/kg/hr by continuous IV infusion until symptoms completely stop

DANTROLENE

Side Effects

- Lethargy
- Muscle weakness (↓ grip strength, Lower Extremities s affected more)
- ↓Respiratory function
- Dizziness
- Double vision
- Nausea, vomiting, diarrhea
- Can potentiate the effects of NMB agents
- CV collapse if given with a Calcium Channel Blocker

Indications

- For relief of spasms, cramping, and tightness of muscles caused by certain medical conditions such as:

  - MS
  - Cerebral Palsy
  - Stroke
  - Spinal Injuries

POST ACUTE PHASE TREATMENT

- ✓ ICU monitoring for 24-36 hours
- ✓ Dantrolene 1 mg/kg q 4-6 hours or 0.25 mg/kg/hr by infusion for at least 24 hours
- ✓ Frequent ABG, BMP, CPK, CBC, and PT/PTT levels drawn until normalized
- ✓ Follow standard ICU therapy for acute rhabdomyolysis ad myoglobinuria
  - alkalinazation of urine with bicarb drip
  - urine output > 200 ml/hr

For help with an Emergency Situation call:
The Malignant Hyperthermia Hotline
1-800-644-9737

(Non-Emergency Information: 1-800-986-4287)

Conditions That Mimic MH

- Post surgery sepsis
- Thyrotoxicosis
- Duchenne's dystrophy
- Becker's musculodystrophy
- Myotonic dystrophy
- Neuroleptic malignant syndrome
- Iatrogenic hyperthermia
- Head trauma
- Drug toxicity
- Hyperthyroidism
- Hypokalemic periodic paralysis
- Pheochromocytoma
- Rhabdomyolysis
- Ventilation problems

- These conditions can mimic Malignant Hyperthermia, but are ***NOT*** actually MH.
- May have many similar signs and symptoms, but the mechanism responsible is not the same as MH.

MH Hotline
1-800-644-9737
Outside the US:
1-315-464-7079

EMERGENCY THERAPY FOR
MALIGNANT HYPERTHERMIA

DIAGNOSIS

Signs of MH:

- Increased $ETCO_2$
- Trunk or total body rigidity
- Masseter spasm or trismus
- Tachycardia/tachypnea
- Acidosis
- Increased temperature (may be late sign)

Sudden/Unexpected Cardiac Arrest in Young Patients

- Presume hyperkalemia and initiate treatment (see #6)
- Measure CK, myoglobin, ABGs, until normalized
- Consider dantrolene
- Usually secondary to occult myopathy (e.g., muscular dystrophy)
- Resuscitation may be difficult and prolonged

Trismus or Masseter Spasm with Succinylcholine

- Early sign of MH in many patients
- If limb muscle rigidity, begin treatment with dantrolene
- For emergent procedures, continue with non-triggering agents; consider dantrolene
- Follow CK and urine myoglobin for 36 hours at least. Check CK immediately and at 6–hour intervals until returning to normal. Observe for cola colored urine. If present, test for myoglobin.
- Observe in PACU or ICU for at least 12 hours

ACUTE PHASE TREATMENT

GET HELP. GET DANTROLENE –

1 Notify Surgeon.
- Discontinue volatile agents and succinylcholine.
- Hyperventilate with 100% oxygen at flows of 10 L/min. or more.
- Halt the procedure as soon as possible; if emergent, use non-triggers.

(The circle system and CO_2 absorbent need not be changed.)

2 Dantrolene 2.5mg/kg rapidly IV through large-bore IV, if possible

To convert kg to lbs for amt of dantrolene, give patients 1 mg/lb (2.5 mg/kg approximates 1 mg/lb).

- Repeat until there is control of the signs of MH.
- Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary.
- Dissolve the 20 mg in each vial with at least 60 ml **sterile preservative-free water** for injection. Prewarming (not to exceed 38°C) the sterile water will speed solublization of dantrolene.
- The crystals also contain NaOH for a pH of 9; each 20 mg bottle has 3 gm mannitol for isotonicity.

3 Bicarbonate for metabolic acidosis.
- 1-2 mEq/kg if blood gas values are not yet available.

4 Cool the patient with core temperature >39°C. Lavage open body cavities, stomach, bladder, or rectum. Apply ice to surface. Infuse cold saline intravenously. Stop cooling if temp. <38°C and falling to prevent drift <36°C.

5 Dysrhythmias usually respond to treatment of acidosis and hyperkalemia.
- Use standard drug therapy **except calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.**

6 Hyperkalemia - Treat with hyperventilation, bicarbonate, glucose/insulin, calcium.
- Bicarbonate 1-2 mEq/kg IV.
- For **pediatric**, 0.1 units insulin/kg and 1 ml/kg 50% glucose **or** for **adult**, 10 units regular insulin IV and 50 ml 50% glucose.
- Calcium chloride 10 mg/kg or calcium gluconate 10-50 mg/kg for life-threatening hyperkalemia.
- Check glucose levels hourly.

7 Follow $ETCO_2$, electrolytes, blood gases, CK, core temperature, urine output and color, coagulation studies. If CK and/or K+ rise more than transiently or urine output falls to less than 0.5 ml/kg/hr, induce diuresis to >1 ml/kg/hr urine to avoid myoglobinuria-induced renal failure.
- Venous blood gas (e.g., femoral vein) values may document hypermetabolism better than arterial values.
- Central venous or PA monitoring as needed and record minute ventilation.
- Place Foley catheter and monitor urine output.

POST ACUTE PHASE

A Observe the patient in an ICU for at least 24 hours, due to the risk of recrudescence.

B Dantrolene 1 mg/kg q 4-6 hours or .25 mg/kg/hr by infusion for at least 24 hours. Further doses may be indicated.

C Follow vitals and labs as above (see #7)
- Frequent ABG
- CK every 6 hours

D Follow urine myoglobin and institue therapy to prevent myoglobin precipitation in renal tubules and the subsequent development of Acute Renal Failure. Follow standard intensive care therapy for acute rhabdomyolysis and myoglobinuria (urine output > 200 ml/h, alkalinization of urine with Na-bicarbonate infusion with careful attention to both urine and serum pH values, etc.).

E Counsel the patient and family regarding MH and further precautions; refer them to MHAUS. Fill out and send in the Adverse Metabolic Reaction to Anesthesia (AMRA) form (www.mhreg.org) and send a letter to the patient and her/his physician. Refer patient to the nearest Biopsy Center for follow-up.

CAUTION: This protocol may not apply to all patients; alter for specific needs.

Non-Emergency Information

MHAUS
11 East State Street
PO Box 1069
Sherburne, NY 13460-1069
Phone
1-800-986-4287
(607-674-7901)
Fax
607-674-7910
Email
info@mhaus.org
Website
www.mhaus.org

Since 1981
MHAUS
MALIGNANT HYPERTHERMIA ASSOCIATION OF THE UNITED STATES
Dedicated to Patient Safety

References

1. Malignant Hyperthermia Association of the United States. *Emergency Therapy for Malignant Hyperthermia.* http://www.mhaus.org

2. Malignant Hyperthermia Association of the United States. *Official MHAUS Home Page.* http://www.mhaus.org

3. Martin, C. A Practical Guide for Malignant Hyperthermia Management. ORNurse2009. www.ORNurseJournal.com