:: Malignant hyperthermia

Synonyms:
malignant hyperpyrexia, hyperthermia of anesthesia

Syndromes with higher risk of MH:

- King-Denborough syndrome
- central core disease (CCD, central core myopathy)
- multiminicore disease (with or without *RYR1* mutation)
- nemaline rod myopathy (with or without *RYR1* mutation)
- hypokalemic periodic paralysis

Definition:
Malignant hyperthermia (MH) is a rare disorder of skeletal muscles related to a high release of calcium from the sarcoplasmic reticulum which leads to muscle rigidity in many cases and hypermetabolism. Abrupt onset is triggered either by anesthesic agents such as halogenated volatile anesthetics and depolarizing muscle relaxant such as succinylcholine (MH of anesthesia), or, occasionally, by stresses such as vigorous exercise or heat. In most cases, mutations of *RYR1* and *CACNA1S* genes have been reported.
MH is characterized by tachycardia, arrhythmia, muscle rigidity, hyperthermia, skin mottling, rhabdomyolysis (cola-colored urine) metabolic acidosis, electrolyte disturbances especially hyperkalemia and coagulopathy.
Dantrolene is currently the only known treatment for a MH crisis.

Further information:
See the Orphanet abstract

PRE-HOSPITAL EMERGENCY SERVICES

Synonyms

- malignant hyperpyrexia, hyperthermia of anesthesia

Aetiology

- disorder of skeletal muscles related to a high release of calcium from the sarcoplasmic reticulum
- triggers: anesthetic agents, vigorous exercise, heat

Special risks in emergency situations

- prompt life-threatening emergency
- arrhythmia
- rhabdomyolysis
- metabolic acidosis
- coagulopathy
- hyperkalemia
- if untreated mortality ~ 90%, whereas if treated with dantrolene mortality < 10-20%

Frequently used long term treatments

- no long term treatment

Complications

- MH can be delayed

Specific medical care prior to hospitalization

- intravenous access (multiple if possible), normal saline
- aggressive and rapid cooling at home and/or during transport to hospital in case of severe hyperthermia
- intubation and hyperventilation when required
- administration of dantrolene if available

HOSPITAL EMERGENCY DEPARTMENTS

Emergency issues

- Anesthesia of a known susceptible patient
- Management of an acute MH crisis

Emergency recommendations

1. Anesthesia of a known MH susceptible patient

- MH can occur if trigger anesthetics and/or succinylcholine are used in any location, such as ERs, dental surgery offices, surgeon's offices or intensive care units
- Be familiar with the signs and treatment of MH
- **No triggering anesthetics** (see annexes):
  - **No halogenated anesthetic agents**
  - **No succinylcholine**
- All the other total intravenous anesthetic agents and local anesthetics are safe to use

- dantrolene is not indicated prior to anesthesia

- During surgery:
  - Use a clean anesthesia machine or any Mapleson system connected to an oxygen tank or wall outlet
  - Continuously monitoring:
    - exhaled CO_2 concentration
    - core temperature
  - **Have an MH kit with an adequate supply of dantrolene**

2. Management of an acute MH crisis

- Call for help early. Teamwork is critical
- **Emergency diagnosis measures**
  - **Emergency laboratory investigations**
    - continuous monitoring:
      - temperature
      - heart rate
      - respiratory rate
      - intra-arterial blood pressure if possible
      - SpO_2
      - $ETCO_2$
      - urinary output
    - repeat q 15 minutes until process normalizes
      - arterial blood gas
      - serum electrolytes
      - coagulation studies
      - urine collection for urine myoglobin
  - Diagnosis based on circumstances of onset, clinical presentation and biology:
    - patient medical history
    - medication history
    - toxicology history

- clinical presentation:
  - tachycardia
  - hypercarbia
  - hyperCKemia
  - mottling
  - rigidity
  - acidosis
  - myoglobinuria
- emergency laboratory investigations (*see above*)
  - MH onset can be delayed and may occur in the post anesthesia care unit

Emergency therapeutic measures

- Immediately stop triggering agents
- O_2 hyperventilation (open-circuit): objective $ETCO_2 < 55$ mm Hg
- Change the tubing of anesthesia breathing circuit (potent inhalation agents are highly soluble)
- As soon as MH is diagnosed, administration of dantrolene:
  - initial dose 2.5 mg/kg
  - then 1-2.5 mg/kg q 6h or infusion if intolerant of bolus medication and guided by clinical signs for no less than 24 h in a critical care unit setting since recrudescence may occur in 25% of cases
  - continue until temperature has defervesced or CK values are declining
  - the dose of dantrolene is increased if the patient is not responding to the current dose:
    - the aggregate dose of 10 mg/kg/day of dantrolene is an average number. The dose can be increased until the patient's CK, hyperkalemia and acidosis stabilize or improve clinically.
- Correct all abnormalities:
  - hyperthermia:
    - cool the body externally including large body surfaces such as torso as well as axilla and groin. There is no body surface to necessarily avoid. Use ice packs.
    - cool, if possible, body cavities including stomach, urinary bladder and open abdomen with ice-cold physiological saline perfusion
  - hyperkalemia:
    - sodium bicarbonate. Doses are the same with or without arterial blood gas values.
    - glucose:
      - for adults: glucose 50 GM plus regular insulin 10 units
      - for children: glucose 25 GM plus regular insulin 5 units
  - inappropriate sinus tachycardia usually does respond to treatment of acidosis and hyperkalemia:
    - use standard drugs, **except calcium channel blockers** which may cause hyperkalemia or cardiac arrest in the presence of dantrolene
  - rhabdomyolysis: copious intravenous fluid, diuretics
  - hypocalcemia: calcium gluconate or chloride
- If untreated: mortality approaches 90%. If treated with dantrolene, mortality is less than 10-20%

Management approach

Where?

- Transfer to a PACU or Critical Care Unit (including Emergency Departments)

When?

- When the patient is sufficiently stable to be transferred

How? Standard transfer precautions should be taken, especially:

- Full resuscitation medications
- Invasive monitoring of intra-arterial pressure and central venous pressure when possible

Drug interactions

- Interactions with dantrolene:
  - Complications of dantrolene treatment: muscle weakness, phlebitis, gastrointestinal upset, respiratory failure (muscle weakness), excessive secretions
  - **No calcium channel blockers** as it may cause cardiac arrest and/or hyperkalemia in the presence of dantrolene
- **No volatile anesthesia agents**
- **No succinylcholine**

Anesthesia

- See "Anesthesia of a known MH susceptible patient"

Preventive measures

- Avoid triggering anesthetics in the susceptible patient
- Recrudescence occurs in 25% of MH crises even with dantrolene treatment
- Known patients should have ID tag and be informed of anesthesia precautions that must be taken:
  - No volatile anesthesia agents except nitrous oxide
  - No succinylcholine
  - All the other anesthetic agents are safe to use

Additional measures

- Contact family members for genetic testing or specialized muscle biopsy which is available at only certain diagnostic centers. Those centers are listed on the web site of the European MH Group (www.emhg.org) or the Malignant Hyperthermia Association of the United States (www.mhaus.org).

Phone numbers

- Emergency calls:
  - USA, Canada: 1-800-644-9737 (1-800-MH HYPER)
  - Mexico: 209-417-3722
- Routine calls in North America : +607-674-7901
- UK:
  - 07947 609601
  - or 0113 2433144 and ask for MH consultant on call

Annexes

Forbidden anesthetic agents
ether
halothane
enflurane
isoflurane
sevoflurane
desflurane
succinylcholine

References

- www.mhaus.org
- Rosenberg H, Davis M, James D *et al.*: **Malignant Hyperthermia**. *Orphanet Journal of Rare Diseases* 2007, 2: 21.
- McAllen KJ, Schwartz DR. **Adverse Drug Reactions Resulting in Hyperthermia in the Intensive Care Unit**. *Crit Care Med* 2010, 8: S244-S252.
- Wappler F: **Anesthesia For Patients with a History of Malignant Hyperthermia**. *Curr Opin Anaesthesiol* 23: 417-422.
- Brandom B: **Ambulatory Surgery and Malignant Hyperthermia**. *Curr Opin Anaesthesiol* 2009, 22: 744-747.
- Capacchione JF, Muldoon SM: **The Relationship Between Exertional Heat Illness, Exertional Rhabdomyolysis, and Malignant Hyperthermia**. *Anesth Analg* 2009; 109: 1065-1069.
- Litman RS, Rosenberg H: **Malignant Hyperthermia: Update on Susceptibility Testing**. *J Am Med Assoc* 2005, 293: 2918-2924.
- Brandom BW, Larach MG, Chen MSA *et al.*: **Complications Associated with The Administration of Dantrolene 1987 to 2006: A Report from the North American Malignant Hyperthermia Associate of the United States**. *Anesth Analg* 2011, 112: 1115-1123.
- Rosenberg H, Sambuughin NK, Dirksen R: **Malignant hyperthermia susceptibility** in *GeneReviews* Edited by Pagon RA, Bird TD, Dolan CR Stephens K. Seattle (WA): University of Washington; 2011.
- Larach MG, Gronert GA, Allen GC, Brandon BW, Lehman EB: **Clinical presentation, treatment and complications of malignant hyperthermia in North American from 1987 to 2006**. *Anesth Analg* 2010, 110: 498-507.

These recommendations have been compiled by Dr. Andrew HERLICH – UPMC Mercy Hospital, Pittsburgh, PA, USA – *and the malignant hyperthermia association of the United States (MHAUS), in collaboration with Dr. Henry ROSENBERG* – Department of Medical Education and Clinical Research, Saint Barnabas Medical Center, Livingston, NJ, USA –, *Dr. Gilles BAGOU* – SAMU-69, Lyon –, *the « Société française de médecine d'urgence » (SFMU) and Prof. Renée KRIVOSIC* – CHU Lille.

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