Malignant Hyperthermia Resource Kit

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Introduction

Malignant Hyperthermia (MH) is a rare pharmacogenetic disorder. MH reactions are potentially fatal if prompt appropriate treatment is not instituted.

MHANZ (the author of this resource kit) is a group of experts who are involved in malignant hyperthermia testing and research.

The recommendations in this kit are sourced from available evidence, guidelines developed by other groups, simulation testing and accumulated data from MH episodes. In some cases, the recommendations represent refined version of pre-existing documents. MHANZ acknowledges the Southern Health Simulation Centre (Victoria, Australia) and the staff of Palmerston North Hospital (New Zealand) for their contribution to the final package.

An MH crisis is rare. Many anaesthetists will not experience one in their practicing career. There are many high priority tasks that must be attended to simultaneously. The complex coordination required combined with the rarity of an MH crisis and the rapidity of response needed are the reasons for the kit development.

Components of the resource kit

MH Poster – "MH – You've only got a few minutes"

MH Crisis Initial management

MH Crisis coordinators overview

MH Crisis task cards

Instructions for preparing the components

1. MH Poster

Print out the MH poster on A3, laminate and place in strategic places in each operating location

2. MH Crisis Initial management

MH Crisis Initial Management is a page that should be printed, laminated and attached to each anaesthetic machine. This card will assist an anaesthetist in MH crisis diagnosis and initial management while the MH box and extra staff are being mobilised.

3. MH crisis coordinator overview

The **coordinator overview** page should be printed A4 size in colour and laminated.

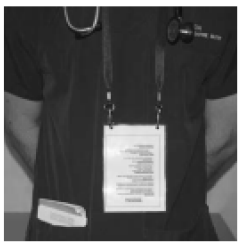
4. MH Crisis Task Cards

The task cards are intended as way to delegate the multiple high priority tasks to available staff. The cards carry simple instructions and are designed for distribution both to staff who may not be familiar with MH crisis management and to skilled clinicians. The cards should be kept with the supply of dantrolene (see contents of an MH emergency box) and distributed by the coordinating anaesthetist to the most appropriate staff members

The printable cards represent a basic template for the management of MH crisis tasks. MHANZ recommends that they are printed and prepared with institutional specifics including locations of dantrolene and other emergency supplies and phone numbers. MHANZ actively encourages hospitals to modify the contents of the cards to suit local needs.

There are seven (7) cards to be printed as A6 and laminated. Holes punched and a suitable neck lanyard is recommended so that cards are easily read, roles are recognised and cards are not misplaced in a crisis. The cards are colour coded so printing in colour is highly desirable.

1. **Anaesthetist 1: resuscitation**
2. **Dantrolene (recommended to print 3 of these) or ryanodex (if it is stocked in your institution)**
3. **Anaesthetic assistant**
4. **Anaesthetist 2: lines and investigations**
5. **Cooling**
6. **Surgical Team**
7. **Logistics**



The poster, cards, coordinators overview and MH crisis initial management pages are available for download from www.malignanthyperthermia.org.au

Dantrolene

Amount of stock

MHANZ recommends that a minimum of 24 (20 mg) vials of **DANTRIUM®** or 2 (250 mg) vials of **RYANODEX ®**are held in any anaesthetising location where triggering anaesthesia is performed. Larger or remote hospitals should carry at least 36 vials as access to further stocks in an MH crisis may be very limited.

Borrowing from other local hospitals

MHANZ does not recommend reliance on dantrolene stocks from other hospitals for initial crisis management. Early and appropriate doses of dantrolene result in lowest morbidity and mortality. Dosing interval is every 10-15 minutes until signs of metabolism are normalised.

Replenishing supplies after use

Each hospital should consider where additional dantrolene for acute management or replacement will be obtained (recurrence of an MH crisis occurs in up to 25% of patients during the first 24 hours).

Water for mixing DANTRIUM®

It is extremely important that sterile water used for reconstituting dantrolene is not mistakenly infused into the patient. Suggestions to reduce the risk of this life-threatening error include:

- Use of 100 ml water for injections plastic bottles
- Additional labelling of sterile water bags (if 100 ml bottles are not available) in the MH box as “NOT for intravenous infusion”

DANTRIUM® mixing

Mixing dantrolene can be time consuming and rapid administration is critical. As many as 36 vials may be required in the acute treatment of a large adult. It may be worth familiarising staff with dantrolene reconstitution utilising expired stock. Assignment of more than one staff member to the task of mixing may be appropriate if all the other tasks are being managed. This is why 3 dantrolene task cards are printed.

Vial access

Dantrolene reconstitution is ideally performed with a short, wide vial access needle. The *BAXA TWO-FER 16- gauge short needle* or the *BRAUN MICRO PIN (MP2000)* are 2 options tested by MHANZ.

RYANODEX® vs DANTRIUM®

Ryanodex® is dantrolene presented as sterile 250 mg lyophilised powder. Mix Ryanodex® with 5 ml of sterile water for injection to obtain a solution with a concentration of 50 mg/ml

At the time of publication, RYANODEX® was only approved for use in Australia and New Zealand on a TGA exemption when there was a shortage of DANTRIUM®

The following table outlines the differences in preparations of dantrolene in the event that RYANODEX is the preparation that is available.

Product characteristic	**RYANODEX®**	**DANTRIUM®**
Presentation	Sterile **250 mg** lyophilised powder, 20 mL vial injectable suspension for IV use	Sterile **20 mg** lyophilised powder, 65 ml vial for IV use
Formulation	Active: **250 mg** dantrolene sodium; Inactive: 125 mg mannitol, 25 mg polysorbate 80, 4 mg povidone K12, NaOH, HCl.	Active: **20 mg** dantrolene sodium; Inactive 3 g mannitol, NaOH
Dosing	Dose 2.5 mg/kg – MHANZ, MHAUS* recommendation	Dose 2.5 mg/kg – MHANZ, MHAUS* recommendation
Reconstitution/ Administration	Mix with **5 mL** WFI**; produces orange coloured suspension. For Intravenous push. Final concentration = 50 mg/mL, pH 10.3.	Mix with 60 mL WFI. Shake until solution is clear. Continuous rapid Intravenous push. Final concentration ~ 0.33 mg/mL, pH 9.5.
Warning/ Precautions/ Contraindications	Similar. Check full Product Information before prescribing.	Similar. Check full Product Information before prescribing
Storage/ Handling	Use within 6 hrs @ 20C – 25C, Protect from light	Protect from light, use within 6 hrs @ 15C – 25C

*MHAUS – Malignant Hyperthermia Association of the United States

** WFI – water for injection

MH Diagnosis and Differential Diagnosis

Who is susceptible?

MH may occur in any patient given triggering agents, including patients who have previously had uneventful general anaesthesia.

The signs and symptoms

Not all of these need to be present to initiate treatment and **not all** occur in this order

Early

Prolonged masseter spasm
Inappropriately raised end tidal carbon dioxide
Inappropriate tachypnoea during spontaneous ventilation
Inappropriate tachycardia
Cardiac arrhythmias – particularly ventricular ectopic beats

Developing

Rapid rise in temperature (0.5^0C per 15 minutes)
Progressive respiratory and later metabolic acidosis
Hyperkalaemia
Profuse sweating
Cardiovascular instability
Decreased oxygen saturation
Skin mottling
Generalised muscular rigidity unresponsive to non-depolarising muscle relaxant

Late

Cola coloured urine (myoglobinuria)
Generalised muscle aches (awake patient)
Grossly raised serum Creatinine Kinase (CK)
Coagulopathy
Cardiac Arrest

Differential Diagnosis

Inadequate anaesthesia/ machine malfunction
Sepsis or infection
Thyroid Storm
Serotonin Syndrome
Recreational drug use (amphetamines)
Neuroleptic malignant syndrome
Intracerebral infection or haemorrhage
Inadvertent overheating

An arterial blood gas is the single most useful investigation to perform

Recommendations for contents of an MH emergency box

Mobility and accessibility are important considerations for the type of container used. A 50 litre Esky/Chilly Bin on wheels is one suggestion.

Suggested contents:

Dantrolene

At least 24 vials of Dantrium ® (20 mg per vial)
Sterile water for injection – either 100 ml bottles or, if larger bags are used these need to be clearly labelled as "not for intravenous infusion"
Drawing up needles (see vial access – page 4)
60 ml syringes (5-10)
Or
At least 2 vials of Ryanodex ® (250 mg per vial)

Include local information on where to source additional dantrolene including contact details

Drugs

8.4% sodium bicarbonate (1 mmol/ml)
50% dextrose 50 ml
Lignocaine 1%
Amiodarone 300 mg

Cold Box (in fridge)

2 litres Saline for IV use
Actrapid insulin

Pathology collection tubes with prewritten requests (if appropriate) for:

Haematology
Coagulation profile
Electrolytes, creatinine, urea, creatinine kinase (CK)
Blood cross match
Blood gases
Urine myoglobin (urine sample pot)

Task Cards

As described in the Resource Kit instructions

Guidelines for managing the elective MH susceptible patient

Who should receive trigger free anaesthesia?

Patients with one of the following should be treated as susceptible

1. Previous malignant hyperthermia reaction
2. Positive in vitro contracture test (IVCT) from muscle biopsy designated MHShc, MHSh or MHSc
3. Positive genetic test for MH
4. If an IVCT has not been done and the patient has a relative with a positive IVCT or suspected clinical reaction
5. Patient has a negative genetic test for MH (but has not yet had a confirmatory IVCT)

Patients in whom it is not necessary to treat as susceptible

1. Patient has had a negative in vitro contracture test
2. Patient's parent (from the MH susceptible side of the family) has had a negative IVCT and there is no evidence of MH in the other parents' family.

Preparing the operating theatre

Prepare the anaesthesia workstation (see below)

Add "Susceptible to Malignant Hyperthermia" to the surgical safety checklist and make all personnel aware of the precautions required

Remove volatile anaesthetic cassettes or canisters from the workstation

Remove suxamethonium from the specific operating room anaesthetic drug trolley

Intraoperative monitoring

Standard ANZCA intraoperative monitoring with temperature monitoring

The post anaesthesia care unit

Patients susceptible to MH may be managed in the normal post anaesthetic care unit and do not need to be isolated from other post-operative patients. Volatile anaesthetic levels in parts per million safe for occupational exposure are also safe for susceptible patients.

Standard post-operative monitoring as per ANZCA guidelines including standard PACU discharge criteria is appropriate

Anaesthesia Workstation preparation

Different workstations require different preparation depending on their internal components. The table below summarises some workstations where flushing times to safe levels of volatile agent have been determined. If your workstation is not listed, contact the manufacturer for appropriate flushing times.

Many anaesthesia workstations contain silicone parts that can retain small amounts of volatile agent. Maintenance of high fresh gas flows for the duration of a trigger free anaesthetic will minimise the chance of significant concentrations of volatile agent reaching the patient.

Workstation	Fresh gas Flow (FGF) for flushing (litres per minute)	Numbers of minutes to flush	Maintainence FGF during case (litres per minute)	Components to change	Other instuctions	Reference article
Ohmeda modulus 1	10	5		remove vaporiser, replace disposable tubing, replace reservoir bag and change CO2 absorber		Beebe JJ, Sessler DI: Preparation of anesthesia machines for patients susceptible to malignant hyperthermia. Anesthesiology 1988; 69:395– 400
Ohmeda modulus 2	12	15				McGraw TT, Keon TP: Malignant hyperthermia and the clean machine. Can J Anaesth 1989; 36:530 –2
Ohmeda Exel 210	10	7				Prinzhausen H, Crawford MW, O'Rourke J, Petroz GC. Preparation of the Drager Primus anesthetic machine for malignant hyperthermia-susceptible patients. Can J Anaesth 2006; 53:885–90
Datex/Ohmeda AS/3	10	30				Schonell LH, Sims C, Bulsara M: Preparing a new generation anaesthetic machine for patients susceptible to malignant hyperthermia. Anaesth Intensive Care 2003; 31:58 – 62
Narkomed GS	10	20				Gunter JB, Ball J, Than-Win S. Preparation of the Drager Fabius anesthesia machine for the malignant hyperthermia susceptible patient. Anesth Analg 2008; 107:1936 – 45
Drager Primus (accelerated)	10	5	10		replace ventilator diaphragm and integrated breathing system with autoclaved components, replace non-disposable ventilator tube with new or autoclaved	Crawford MW, Prinzhausen H, Petroz GC: Accelerating the washout of inhalational anesthetics from the Drager Primus anesthetic workstation: Effect of exchangeable internal components.Anesthesiology 2007; 106:289 –94
Drager Primus	10	70	10			Prinzhausen H, Crawford MW, O'Rourke J, Petroz GC. Preparation of the Drager Primus anesthetic machine for malignant hyperthermia-susceptible patients. Can J Anaesth 2006; 53:885–90
Drager Fabius	10	36	10		replace ventilator diaphragm and integrated breathing system with autoclaved components,replace non-disposable ventilator tube with new or autoclaved	Shanahan, H. O'Donoghue, R. O'Kelly, P. Synnott, A. O'Rourke, J. Preparation of the Drager Fabius CE and Drager Zeus anaesthetic machines for patients susceptible to malignant hyperthermia. European Journal of Anaesthesiology. 29(5):229-34, 2012 May
Drager Zeus	10	90	10			Shanahan, H. O'Donoghue, R. O'Kelly, P. Synnott, A. O'Rourke, J. Preparation of the Drager Fabius CE and Drager Zeus anaesthetic machines for patients susceptible to malignant hyperthermia. European Journal of Anaesthesiology. 29(5):229-34, 2012 May
Drager Fabius GS	10	104	10			Whitty RJ, Wong GK, Petroz GC, Pehora C, Crawford MW: Preparation of the Drager Fabius GS workstation for malignant hyperthermia-susceptible patients. Can J Anaesth 2009; 56:497–501
Datex Ohmeda Aisys	10	90	10			Jones,C. Bennett, K., Kim,T. W., Bulger T. F., Pollock, N. Preparation of Datex-Ohmeda Aestiva® and Aisys® anaesthetic machines for use in malignant hyperthermia susceptible patients Anaesth Intensive Care 2012; 40: 490-497

Charcoal Filters

MHANZ Recommendations the following for the use of activated charcoal filters (ACF) in the preparation of anaesthetic workstations for patients at risk for MH susceptibility:

1. Remove vaporisers from the anaesthetic machine
2. Flush circuit for 90 seconds with oxygen or air at 10 litres/min using the ventilator with a 2-litre test lung attached.
3. Change full breathing circuit and soda lime whilst maintaining flushing at 10 litres/min (the ventilator is left unchanged).
4. Insert activated charcoal filters on both the inspiratory and expiratory ports of the breathing system.
5. Maintain fresh gas flow of 10 litres/min for 90 mins from the commencement of the anaesthetic.
6. After 90 mins it is safe to reduce FGF to 3 litres/min.
7. ACFs can be used at 3 litres/min until a total of 12 hours has elapsed from the commencement of the anaesthetic.
8. ACFs are single use items.
9. In the event of an MH crisis the addition of ACFs to the anaesthetic machine may be of benefit, but this has not yet been proven clinically.
    - Clinical priorities in an MH crisis remain: dantrolene administration (2.5mg/kg), high fresh gas flows, treatment of arrhythmia/acidosis and active cooling.

Up to date information on referrals, contacts, genetics and in vitro contracture testing is available on the MHANZ website

www.malignanthyperthermia.org.au
