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MALIGNANT HYPERTHERMIA

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A 69 year old man presented for Coronary Artery Bypass Grafting (CABG) with a history of:

- non-insulin dependant diabetes
- severe coronary artery disease
- no previous anaesthetic exposures
- no family history
Case History 1

(Firstenberg et al 2010)

- Induction with Fentanyl, Lignocaine & Propofol, Vecuronium
- Maintenance with Isoflurane & Fentanyl infusion
- Heart was arrested with cold antegrade & retrograde blood cardioplegia
- Patient temperature was maintained at 34°C
Case History 1
(Firstenberg et al 2010)

- 4 vessel CABG was performed
- Routine arterial blood gases were taken
- Isoflurane was distilled into the bypass circuit
- Total Isoflurane time was 4.5 hours
Case History 1
(Firstenberg et al 2010)

- On arrival to Intensive Care Unit the patient developed a tachycardia & became hyperthermic
- A chest x-ray was normal
- Haemodynamics were controlled by nicardipine infusion & fentanyl
- Arterial Blood gases revealed severe respiratory acidosis – minute volume was adjusted
Case History 1
(Firstenberg et al 2010)

- Follow-up gases showed increasing CO2 levels
- Hyperkalemia
- Temperature was increasing
- Musculoskeletal stiffness was noted
- Masseter rigidity
- Malignant Hyperthermia was finally suspected
Malignant Hyperthermia remains an important risk for general anaesthesia patients

(Metterlein et al. 2011)
Malignant Hyperthermia

This occurs in genetically predisposed humans

Malignant Hyperpyrexia is a synonymous term
Malignant Hyperthermia
Definition: A catastrophic, often fatal syndrome triggered by;

Anaesthetic Triggers
- Inhalational agents
- Depolarizing muscle relaxants
- ? Rocuronium - 2 cases where Rocuronium was the most likely trigger agent (Aston et al. 2012)
- Incidence 1:3,000 to 1:50,000 anaesthetics (Hirshey Dirksen et al. 2012)
Malignant Hyperthermia

Non Anaesthetic Triggers

- Certain myopathies (ie Evans, King Denborough)
- Emotional stress
- Heat stroke
- Neuroleptic malignant syndrome
- Strenuous exercise
- Trauma
Intracellular skeletal muscle defect

- Excessive amounts of calcium are released from the sarcoplasmic reticulum in skeletal muscle.

- Calcium $\rightarrow$ contraction $\rightarrow$ heat $\rightarrow$ O$_2$ consumption $\rightarrow$ CO$_2$ $\rightarrow$ calcium $\rightarrow$ contraction $\rightarrow$ acid $\rightarrow$ heat.
Ryanodine is a large protein molecule. It covers the opening on the sarcoplasmic reticulum. Ryanodine regulates calcium release. The majority of Malignant Hyperthermia susceptibility individuals have a defect in the ryanodine receptor type 1 (RYR1) gene.

(Hirshey Dirksen et al 2012)
Genetics

- More than 80 genetic defects have been linked to Malignant Hyperthermia (MH)
- Susceptibility is an autosomal dominant inherited disorder of skeletal muscle
- A child or sibling of a susceptible patient has a 50% chance of inheriting a defective gene

(Mitchel-Brown 2012)
Recent research looked at 24 cases of MH in cardio-thoracic patients.

- In 14 cases MH occurred during or shortly after bypass.
- Dantrolene was used in all but 1 case where the patient died.
- All other patients who received Dantrolene survived.

(Metterlein et al. 2011)
Research tells us ....

  - 286 cases studied
  - Young males 74.8%
  - 6.5% had a family history

- ‘77 of 152 patients reported 2 previous unremarkable anaesthetics’ (Larach et al 2010)

- 50% of cases had previous anaesthesia (Blinn 1995)
Research tells us….

- In 10 cases skin liquid crystal temperature probes did not trend ↑ temp.
- Accurate temperature monitoring during general anaesthesia and early Dantrolene administration may decrease MH mortality by 35%.
- 21 experienced haematological/neurological complications with a temp less than 41.6 (human critical thermal maximum).

(Larach et al 2010)
TRIGGERING

- 12 Anaesthetics and triggered fatally on the 13th (Blinn 1995)
- MH is most likely to occur in the operating theatre (Hommertzheim 2006)
- It can also present in the PACU and possibly up to 12 hours post-operatively (Hommertzheim 2006)
- Suspected case using Deflurane only presented 6 hours post-operatively (Papadimos 2004)
TRIGGER AGENTS

Volatile Inhalational agent
- Isoflurane
- Sevoflurane
- Desflurane
- Halothane
- Enflurane
- Ether, Cyclopropane

Depolarizing muscle relaxants
- Suxamethonium Chloride
Safe Agents

Intravenous agents
- Propofol
- Barbiturates
- Benzodiazepines
- Opiates

Muscle relaxants
- Non-depolarizing (Rocuronium)

Inhalation agents
- Nitrous oxide

Local anaesthesia - Amides / esters
SIGNS OF MALIGNANT HYPERTHERMIA

Early (s+s may be seen in any order)

- Tachycardia
- Tachypnoea
- Sweating
- Sudden rise in end – tidal CO₂
- Temperature
- Ventricular extra systole
- Unstable B/P
- Rigidity (immediately after sux)
- Masseter muscle rigidity
SIGNS OF MALIGNANT HYPERTHERMIA

Research showed frequent early signs were:

- Hypercarbia
- Sinus tachycardia
- Masseter spasm

In 63.5% temp was the 1st to 3rd sign  
(Larach et al 2010)
SIGNS OF MALIGNANT HYPERTHERMIA

Late
- Cyanosis
- Skin mottling
- Hyperkalemia
- Myoglobinuria
- Elevated Creatine Kinase
TREATMENT

- Stop trigger agents immediately
- Change anaesthetic machine/circuit
- Change catheter mount (if old black liquorice stick)
- Stop or expedite surgery
- Administer 100% oxygen – hyperventilate
- Call for help – press emergency bell
- Obtain malignant hyperthermia kit
- Administer Dantrolene 2.5mg/kg up to 10mg/kg
Notify nursing supervisor & pharmacy department
Send orderly for buckets of ice
Cool patients and monitor temperature
Ice to axilla and groin
Cool I.V. fluids
Cooling blanket (Polar Bear)
Assist in line insertion
Central line
Arterial line
ASSIST IN TREATMENT OF:

Arrhythmia’s
Electrolyte imbalance
Maintenance of cardiac function
Urinary catheterisation

- Careful observation of output and colour of urine
Dantrium is a skeletal muscle relaxant
Decreases the amount of calcium released by the sarcoplasmic reticulum
Reverses the pathophysiology of Malignant Hyperthermia
Case fatality rate has fallen from 70% in the 1970’s to less than 10 % in 2006

Preparation: 20mg vials – powder to be mixed with 60mls sterile water
Sterile warm water or room temperature
Sodium Hydroxide and 3g Mannitol
DANTROLENE SODIUM (Dantrium)

- Initial dose 2.5mg x 70kg = 175mg = 9 vials
- 10mg x 70kg = 700mg = 35 vials
- 12 vials cost ?? Ireland ??
- The median dose of Dantrolene was 5.9mg/kg (Larach et al., 2010)
DANTROLENE SODIUM (Dantrium)

- Subsequent doses may be required over the coming hours or days - 1mg/kg 6 hourly for the first 24-48 hours (Carter – Templeton 2006)
- MH symptoms re-occur in 25% of patients after episode if there is no further Dantrolene (Mitchel-Brown 2012)
- pH 9.5 – care must be taken to; prevent extravasation, be watchful for thrombophlebitis
- Solution must be protected from light and used within 6 hours
Dantrium® Intravenous
(dantrolene sodium for injection)

For treatment of malignant hyperthermia
For intravenous use only.

CAUTION: Federal law prohibits dispensing without prescription.

Procter & Gamble
PHARMACEUTICALS
Testing

Caffeine Halothane Contractility test

- Very sensitive and detects virtually all patients with MH
- Costly
- Requires fresh muscle biopsy

Molecular genetic diagnostic test

- Blood sample
- DNA testing
- Not all patients with MH have DNA change
- Test will only detect 30% of sufferers
CASE PRESENTATION No.2

- The Friday Night Call Back”

- A Theatre Nurses Challenge
Principle Diagnosis
Supra condylar # Left Humerus

- 12 year old boy
- Admitted to theatre for – Reduction +/- internal fixation of Left elbow
- No medical history
- No medications
- Nil known Allergies
- Weight estimated by mother a 35-40kgs
Pre Induction Obs

- Temp: Afebrile 36.5
- Pulse: 80 beats/min
- BP: 103 systolic
- SaO2: 99%
1915hrs

Anaesthetic Induction

- Decided by Anaesthetist – GA with no initial Muscle Relaxant
- LMA #3 Airway
- Dipravan 180mg
- Midazolam 2mg
- Fentanyl 100mg

- Anaesthesia Maintenance
  Isoflurane 0.6% - 1.8% with
  50% O2
- Patient initially spontaneously ventilated
Increasing End Tidal CO2 – another monitor required with capnography
1930 - 1935hrs

- Surgeon confident that he could reduce Pt fracture with manipulation
- However, he required that the Pt be given Muscle Relaxant due to muscle tightness
- 1935hrs 15mgs Rocuronium given IV
1935 - 1940hrs

- Unstable tachycardia
- Pt requiring manual ventilation to help blow off CO2
- Noted by Nursing Staff, Anaesthetist and Surgeon that there was marked rigidity despite being given muscle relaxant
- Pt now flushed and perspiring
Diagnosis MH 1935 - 1940hrs

- Tympanic temp: 39.9
- Pulse: 140-160 beats/min
- ETCO2: 92mmHg
Everyone was given a job

- **Scout & Scrub nurse & radiographer** mixed Dantrolene immediately
- **Anaesthetic nurse** changed circuit and organised art line box, then became scribe
- **Supervisor** to check availability of Dantrolene from other hospitals and be outside legs
- **ICU nurse** to assist in insertion of art line and sampling of ABG’s
- **Nurse attendant** to get buckets of ice
1945hrs

- 5 mins after diagnosis
- 1st dose Dantrolene given
- 2.5mg/kg (2.5mg x 35kg = 87.5mg)
- Given initially as a bolus then as titrated doses
- Dantrolene given as IV bolus into L & R dorsal foot vein
- Art line was accessed, 1st ABG taken
- Pt cooled with ice packs to groin and axilla, warmed IV fluid replaced with cool
1955hrs

- Nasopharyngeal temp probe inserted
- Temp 38.1
- Urine output – measured and monitored
- Output greater than 100mls/hr
- Monash Medical Centre phoned for further enquiries
2005hrs

1st ABG – 20mins Post Diagnosis

- pH : 7.06 (7.35/7.45)
- PaO2 : 313mmHg (80/100)
- PaCO2 : 58mmHg (35/45)
- HCO3 : 13mmol/L (22/31)
- BE : -15.7 mmol/L (-3.3/+1.2)
- SaO2 : 99%
- Respiratory and Metabolic Acidosis
2015hrs

- Rapid response to Dantrolene
- Last dose of Dantrolene given
- Intra Op 19 amps given
- Total = 380mgs
2020hrs

- Temp: 36.5
- Pulse: 116 beats/min
- ETCO2: 34mmHg
- BP: 90 systolic
- Ice packs removed from Pt to prevent Hypothermia
- Surgeon reduced fracture successfully
- POP to L arm and collar and cuff applied
Dantrolene stocks:

- ‘The MHANZ group recommends that a minimum of 24 (20mg) vials of Dantrolene are held in any anaesthetising location where triggering anaesthesia is performed. Larger or remote hospitals should carry 36 vials.

- This stock level represents 2-3 x 2.5mg/kg doses for an average sized adult and is a reasonable compromise between clinical need and economy.

- Dantrolene cost is approximately AUD $900 and NZD $1600 for 12 ampoules’.

(ANZCA Guidelines January 2007)


References