A Case of Delayed Awakening
Post Anaesthesia
Mr RS (98368046 UR614424)

64 Male presented with 24/24 history of acute RIF pain scheduled for emergency appendicetomy

Past Anaesthetic History
- Had elective eye operative in UK 35 years ago, developed acute abdo pain 2 weeks afterwards and was told that it was caused by “anaesthetic poisoning”
- Elective laparoscopic cholecystectomy 2002
- Elective inguinal hernia repair 1999
  • Cotham Private
  • Fentanyl/ Midazolam/ Propofol/ Atracurium/ Keflin/ Sevoflurane
- (PONV from morphine and pethidine, otherwise uncomplicated)

Concurrent Medical History
- Alopecia Totalis
- Hypertension (No Medical Rx required)

Preop Ix
- FBE: 155/ 7.5/ 265
- U&E: 134/ 4.3/ 95/ 27/ 16/ 3.8/ 0.07
Anaesthesia

• Induction
  • Midazolam  2 mg
  • Fentanyl  100 mcg
  • Propofol  180 mg
  • Suxamethonium  100 mg

• Maintenance
  • Atracurium
    – 30 mg given after induction
    – followed by another 10 mg 30 min later
  • Sevoflurane/\text{N}_2\text{O}/\text{O}_2
  • Morphine 8mg given in divided aliquots
Operative Findings

- Normal appendix (Subsequently removed)
- ? Inflammatory mass in sigmoid region
- Free peritoneal fluid with fibrinous exudate
- Appendicetomy performed, peritoneal space washed and drains inserted
- Total duration of surgery: 1hr 25 min

- Overall patient was stable intraoperatively, except for a brief episode of extreme bradycardia on stretching of the peritoneum. (Responded with *Atropine 600mcg*)
• Towards end of surgery (approx 30min before extubation)
  – *Propofol* infusion started at 40ml/hr
  – $^E^T$Sevo adjusted to 0.5-0.6%
  – $N_2O$ switched to Air
  – Ondansetron 4mg + *Maxolon* 20mg given

• At termination of surgery
  – *Propofol* and *Sevoflurane* was turned off
  – Full dose reversal (*Neostigmine* 2.5mg/$\textit{Glycopyrrolate}$ 0.4mg) was given
  – Prior to initial extubation, patient had a weak cough with spontaneous eye opening
On Arrival at Recovery

- Patient appeared to be drowsy but able to open eyes on demand.
  - Vital signs:
    - RR 14
    - HR 100
    - BP 140/70
    - SaO₂ 99

- At the same time, he also had a “twitchy” appearance consistent with residual relaxant effect

- A further full dose of reversal was given

- Meanwhile,
  - Patient was able to maintain his oxgenation at 98% with 8 l/min of O₂ via Hudson mask
  - Nerve stimulator study failed to show evidence of fade on TOF or Double Burst (set on 40mA)

- Decision was made to commence the next case
At 25 min after arrival at recovery

• Call by nursing staff to review patient due to delayed awakening

• On examination
  – Patient still appeared to be a bit “twitchy”
  – Still able to open eyes on demand
  – Pin-point pupils
  – Vitals
    • HR 105
    • BP 200/90
    • SaO$_2$ 99%
    • Temp 36.7 °C
Causes of delayed awakening

• Residual drug effects
  Overdose
  Duration and type of anaesthetic given
  Potentiation by other drugs
  Prolonged neuromuscular blockade

• Respiratory failure

• Metabolic Derangements
  Hypoglycaemia/ severe hyperglycaemia
  Electrolyte imbalance
  Hypothermia
  Central Anticholinergic syndrome

• Neurological Complications
  Central hypoxia
  Intracerebral event
Initial Management

- 2 x 100mcg Boluses of Naloxone were given at 2 min interval with minimal effect

- Arterial blood gas collected + BSL checked
- **BSL:** 8.4 mmol/L

- **ABG:**
  - pH: 6.95
  - $\text{PaCO}_2$: 125 mmHg
  - $\text{PaO}_2$: 166 mmHg
  - $\text{HCO}_3^-$: 27 mmol/L
  - BE: -9.2
  - $\text{SaO}_2$: 98%
  - $\text{Na}^+$: 137 mmol/L
  - $\text{K}^+$: 4.4 mmol/L
  - $\text{Cl}^-$: 103 mmol/L
  - $\text{Ca}^{2+}$: 1.26 mmol/L
  - Lactate: 0.9 mmol/L
  - Hb: 161 g/L
Subsequent Mx

• Patient re-intubated with no medication with ease (approximately 35 min after arrival at recovery)

• Second on-call opinion seeked with possibility of suxamethonium apnoea suggested

• Threshold measured on nerve stimulator = 27mA

• Arrangement made for transfer to ICU for respiratory support overnight

• Meanwhile, with initiation of IPPV, patient became visibly more alert and was able to communicate by blinking his eyes. Concurrent to this, his blood pressure fell back to 140/80 mmHg

• Patient’s condition was explained to him and he was re-sedated with propofol 100mg/hr and morphine 1mg/hr
Follow up

• Blood collected for Dibucaine test
• Initial review at 7 hours postoperatively
  – Able to open eyes spontaneously
  – Able to move all limbs with difficulty but unable to sustain hand grip > 5 sec
  – Nerve stimulator threshold 20 mA

• At 10 hours postoperatively
  – Nerve stimulator threshold 17-18mA
  – Still unable to perform sustained hand grip
  – Decision made to give FFP

• Further review at 12 hours postoperatively
  – FFP still thawing
  – Able to perform sustained 10 sec hand grip

• At 15 hours postoperatively
  – Extubated successfully after FFP was given
Follow up (day 3 post op)

- Patient interviewed regarding recollection of events and stated that he could only remember the anaesthetist telling him to “Wake up!”
- Patient counseled on implications of his condition on himself and immediate family members
- Was told by patient that one of his sisters might have had some difficulty with anaesthesia in the past requiring ICU admission
Follow up (Day 8 Post op)

- Patient developed subacute small bowel obstruction post-operatively and presented again for laparotomy on day 8 post-operatively

- Patient was induced this time around with a modified rapid sequence technique with *Rocuronium/ Propofol/ Fentanyl* and *Midazolam*

- Extent of neuromuscular blockade was monitored with nerve stimulator

- Procedure lasted for 2 hours

- Patient extubated at the end of procedure wide awake with reversal of neuromuscular blockade confirmed with nerve stimulation
Follow up (3 weeks Post op)

- Blood result from RMH
  - Pseudocholinesterase: 177 IU/L (650-1500)
  - Dibucaine No: 19% (69-80)
  - Fluoride No: 25L% (46-60)

- Patient contacted regarding his result. On his discharge from BHH, he was supplied with a red medical alert card warning against future use of suxamethonium.

- After discharge, patient managed to contact his sister in England and confirmed that she had also suffered from an episode of suxamethonium apnoea 10 years earlier on.
Suxamethonium Apnoea

- Atypical plasma cholinesterase first described by Kalow in 1957
- Dibucaine test subsequently described by Kalow and Genest in the same year
Dibucaine Test

• Dibucaine inhibits hydrolysis of benzoylcholine by the normal enzyme by 70% or more
• With atypical variant, this is reduced to 30% or less
• Individuals can be separated into three groups
  – Dibucaine no >70
    • Homozygote with 2 normal gene
  – Dibucaine no 40-70
    • Heterozygote
  – Dibucaine no <30
    • Homozygote with 2 abnormal gene (incidence 1:2,500)
Variant atypical plasma cholinesterase

- Fluoride resistant variant
- Silent Variant
- J, K, H Variants
- Newfoundland Variant
- High activity variant
- Variants id by techniques of molecular genetics
Fluoride and Silent Variant

**Fluoride Variant**
- Extremely rare
- Found in high frequency in a Punjabi pop
- Variant has some ability, though less to hydrolyze sux

**Silent Variant**
- Extremely rare
- Occur with high frequency in several Alaskan Eskimo groups, in Afrikaner South Africans, and in the Vysya caste group of Andhra Pradesh, India
- Most homozygote have no cholinesterase activity
J, K, H Variants

- Variants cholinesterase have normal catalytic activity but have reduced number of molecules in plasma
- Variants have normal inhibition characteristics
- **J Variant**
  - Frequency of homozygotes: 1:150,000
  - 66% reduction in activity
- **K Variant**
  - Frequency of homozygotes: 1:65
  - 33% reduction in activity
- **H Variant**
  - Only reported in 4 families
  - 90% reduction in activity
Other variants

- **Newfoundland Variant**
  - High dibucaine number but reduced ability to hydrolyze sux

- **High Activity Variant**
  - Marked resistance to sux
  - Cholinesterase activity 3 times normal
  - Normal Dibucaaine and F numbers
  - Maybe related to increased production of enzymes
  - Reported in
    - Cynthiana, Kentucky (1st report)
    - 2 x families in Germany
    - Johannesburg
Causes of variation in plasma cholinesterase activity

- Physiological
  - Reduction in activity is not clinically significant unless it falls below 30% of normal
  - Individual variation: 57% to 143% from the mean
  - Male > Female
  - No age related variation in adult
  - With pregnancy, there is a drop in 20% activity from the 1st trimester. In day 2-4 postpartum, this is further reduced to 33% from normal.
Acquired variation

- Diseases associated with decreased activity
  - Liver disease
  - Malignancy
  - Malnutrition
  - Heart Disease
  - Renal Disease
  - Burns
- Diseases associated with increased activity
  - Hyperthyrodisim
  - Nephrotic syndrome
  - Obesity
  - Mental retardation and illness
Other causes of variation

- **Plasmapheresis**
  - Reduces activity by 64%
- **Cardiopulmonary bypass**
  - Reduces by 56% (persist for 7 days)
- **Oral contraceptives**
  - Reduces by 20%
- **Noncompetitive cholinesterase inhibitors**
  - Ecothiopate eye drops
  - Organophosphate
- **Competitive cholinesterase inhibitors**
  - Pyridostigmine
  - Tacrine
  - Pancuronium
  - Metaclopramide
Adverse Reaction From Suxamethonium

- Cardiovascular
- Increases
  - Intraocular pressure
  - Intragastric pressure
  - ICP
- Hyperkalaemia
- Myoglobinemia
- MH
**CVS effect**

- **Dysrhythmias**
  - Usual sequence of bradycardia and hypotension followed by tachycardia and hypertension 15-30s later
  - Bradycardia more pronounced in paediatrics
    - Nodal rhythm and VE have been reported at up to 80% of children
  - Incidence of dysrhythmias is increased with repeated dose

- **Pulmonary oedema and haemorrhage**
  - Has been reported in young children receiving IM sux
  - Related to acute increase in ↑ SVR and ↓ in PVR
Intraluminal pressure

- **Intragastric Pressure**
  - Increase proportional to extent of fasciculation
  - Can be as high as 40 cm H$_2$O

- **Intraocular Pressure**
  - Related to contraction of extraocular muscle
  - Rise begins in 60s, peak at 2-3min, normalizes in 5-7min

- **Intracranial Pressure**
Hyperkalaemia

- K+ usually ↑ by 0.3-0.5 mmol/L
- This may be exaggerated with
  - Burns
  - Massive Trauma
  - Stroke
  - Spinal Cord Injury

- Association with occult myopathies
  - 1992 MH assoc of US received reports of cardiac arrest in healthy children given sux. Many of them were boys with undiagnosed Duchenne or unspecified myopathy
  - Cardiac dysrhythmias usually occurred abruptly at a median time of 18 min
Malignant Hyperthermia

• Incidence estimated at 1:4,000 to 40,000
• Trismus is rare
• Nonetheless, trismus or masseter spasm accompanied by the entire body may be associated with high incidence of MH