

DELAYED AWAKENING OR EMERGENCE FROM ANAESTHESIA

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At the end of anaesthesia and surgery the patient should be awake or easily rousable, protecting their airway, maintaining adequate ventilation and with their pain under control. Time to emerge from anaesthesia is very variable and depends on many factors related to the patient, the type of anaesthetic given and the length of surgery.

CAUSES OF DELAYED AWAKENING

Residual Drug Effects

- **Overdose.** Too much drug may have been given or the patient is unduly susceptible. Frail, small or elderly patients generally require lower doses than fit, normally sized adults. Delayed drug metabolism occurs in renal or hepatic failure, and smaller doses may be required. In certain conditions there may be increased sensitivity to particular agents. For example there is greatly increased sensitivity to non-depolarising muscle relaxants in myasthenia gravis.

- **Duration and type of anaesthetic given.** For inhalational anaesthetic agents the speed of emergence is directly related to alveolar ventilation. Therefore hypoventilation is a frequent cause of delayed emergence. Speed of emergence is also inversely related to the blood gas solubility of the agent, so the less soluble agents eg: nitrous oxide and halothane are eliminated more rapidly than ether. When the duration of anaesthesia is prolonged, emergence also depends on the total tissue uptake of the drug which is related to drug solubility, average concentration used and the duration of exposure.

For intravenous anaesthetic agents, immediate recovery depends mainly on redistribution from blood and brain into muscle and fat. Patients given propofol for induction and /or maintenance recover faster than those receiving other agents because propofol is rapidly metabolised by the liver and possibly also at other extrahepatic sites. Elimination half life is relatively fast (10 to 70 minutes), and it does not accumulate.

With thiopentone however, whilst the initial drug effect is terminated by redistribution within 5 to 15 minutes. Elimination is by oxidative metabolism in the liver

at a rate of 15% per hour. It therefore has a long elimination half life of 3.4 to 22 hours and as much as 30% of the dose may remain in the body at 24 hours. Cumulative effects may therefore become apparent when more than one dose is given. For most other intravenous anaesthetic drugs the termination of drug action depends on the time required to metabolise or excrete the drug (elimination or metabolic half life) and in this situation, advanced age or renal or hepatic disease can prolong drug action.

- **Potentiation by other drugs.** Prior ingestion of sedative premedication such as benzodiazepines, or alcohol, will potentiate the central nervous system depressant effects of anaesthetic and analgesic drugs, and may delay emergence from anaesthesia.

- **Prolonged neuromuscular blockade.** Residual neuromuscular blockade results in paralysis which may be perceived as unresponsiveness though the patient may be fully conscious and aware. This may occur secondary to overdose or incomplete reversal of non-depolarising muscle relaxants or in a patient with suxamethonium apnoea. A nerve stimulator will assist the diagnosis. Alternatively inability to maintain head lift for 5 seconds in a patient who could normally comply with this request indicates residual block of greater than 30% of receptors. The typical twitchy movements of partial reversal may also be seen, and the patient may become distressed and agitated.

Prolonged apnoea following suxamethonium “scoline apnoea” is due to an abnormal or absent plasma cholinesterase enzyme. In pregnancy and liver disease, levels of this enzyme also tend to be lower and suxamethonium may produce longer lasting muscle relaxation. Repeated doses of suxamethonium (>6-8mg/kg total dose) may produce a “dual block” which is prolonged and slow to recover. The newer muscle relaxant mivacurium is also metabolised by plasma cholinesterase and ‘mivacurium apnoea’ may occur rarely.

Patients with myasthenia gravis are very sensitive to non-depolarising muscle relaxants, doses of only 10 to 50% of the usual dose are required and long acting agents like pancuronium should be avoided. In the

PRACTICE POINT - Relaxants

- Avoid excessive doses of relaxants.
- Intermediate acting drugs such as atracurium or vecuronium are easier to use than long acting ones.
- Only give repeat doses when necessary (when there is evidence of muscle activity).
- When giving repeat doses use 20-25% of the initial dose.
- Wherever possible use a nerve stimulator to guide doses and assess reversal.

muscular dystrophies there is also increased sensitivity to muscle relaxants and to all respiratory depressant drugs.

In renal failure there is reduced elimination of non depolarizing muscle relaxants such as pancuronium and vecuronium. Large doses of aminoglycoside antibiotics (gentamicin etc) can prolong muscle relaxant action. Acidosis can also have this effect.

Respiratory Failure

Patients who do not breathe effectively during or after anaesthesia may become hypercarbic (raised CO₂) to a level that may produce sedation or even unconsciousness. Risk factors include underlying respiratory disease, particularly those with CO₂ retention preoperatively, high dose opioids, obstructed airway and poor relaxant reversal. The diagnosis is usually suspected clinically and may be confirmed by arterial blood gas analysis or measurement of the end tidal CO₂. Note that patients receiving oxygen may have normal SpO₂ readings even with significantly raised CO₂ readings.

Metabolic Derangements

An underlying metabolic disorder may be responsible for delayed recovery after anaesthesia. Conditions include:

- **Hypoglycemia.** Can occur in small children and those who have been given insulin or oral hypoglycaemic drugs. It may also occur in liver failure, in the presence of alcohol excess and in septicaemia and malaria.

- **Severe hyperglycemia.** May occur in decompensated diabetics ie: hyperosmotic hyperglycaemic diabetic coma, or diabetic ketoacidosis.

- **Electrolyte imbalance.** This may be secondary to the underlying illness or as a consequence of the surgical procedure e.g. hyponatraemia occurring with trans-urethral resection of prostate (where glycine or other hypotonic fluid is used for irrigation).

- **Hypothermia.** Severe hypothermia may lead to reduced conscious level. A core temperature of less than 33°C has a marked anaesthetic effect itself and will potentiate the CNS depressant effects of anaesthetic drugs. In addition hypothermia reduces the MAC value of inhalational agents, antagonises muscle relaxant reversal and limits drug metabolism.

- **Central anticholinergic syndrome** may rarely follow the use of anticholinergic drugs especially hyoscine, but also antihistamines, antidepressants, phenothiazines and pethidine. It has also been reported after volatile anaesthetic agents, ketamine and benzodiazepines. Thought to be due to a decrease in inhibitory anticholinergic activity in the brain, it may be manifest as confusion, restlessness, hallucinations, convulsions and coma, and therefore as delayed awakening from anaesthesia. Peripheral anticholinergic effects; dry mouth, tachycardia, blurred vision etc may also be present. Treatment is with physostigmine 0.04mg/kg slowly iv which acts within 5 minutes, but features may return after 1-2 hours.

Neurological Complications

- **Cerebral hypoxia** of any cause will result in reduced conscious level which may first present as delayed awakening from anaesthesia, especially if the hypoxic insult has occurred during anaesthesia.

- **Intracerebral event** such as haemorrhage, embolism or thrombosis. This is very rare except in neurosurgery, cardiac surgery, cerebrovascular and carotid surgery.

EVALUATION AND MANAGEMENT**Immediate care**

- **Airway** - maintain a clear airway and give oxygen. Reintubate if indicated.

- **Breathing** - ensure adequate respiration. If indicated ventilate the patient effectively via an endotracheal tube. Monitor SpO₂.

- **Circulation** - assess blood pressure, heart rate, ECG, peripheral perfusion, conscious level and urine output. Resuscitate as indicated.
- **Review** the history, investigations, and perioperative management, including the anaesthetic chart and the timings of drug administration, looking for a possible cause of the delay in recovery.
- **Assess for persisting neuromuscular blockade**, using a nerve stimulator if available. Alternatively if the patient is awake enough to obey commands ask them to lift their head off the pillow for 5 seconds. If the patient is still paralysed they should be sedated or kept anaesthetised, and ventilated until the block is fully reversed. A further dose of reversal agent eg; neostigmine 2.5mg plus glycopyrrolate 0.5mg or atropine 1mg may be tried. Where there is prolonged neuromuscular block in suxamethonium apnoea, prolonged ventilation (up to 12 - 36 hours) may be required.
- **Look for signs of opioid narcosis** - pin point pupils and slow respiratory rate. In this situation a test dose of naloxone may be given: iv increments of 100 to 200 micrograms are usually sufficient. (child = 10 micrograms/kg, subsequent dose of 100 micrograms/kg if no response.). If too much is given the analgesic effect of the opioid will be antagonised and the patient will be in pain. The dose should therefore be titrated to effect. The duration of action of naloxone is approximately 20 minutes and this may be shorter than the effect of the opioid. Subsequent doses of naloxone may therefore be required, and these may be given intramuscularly, or a naloxone infusion may be required (800 micrograms in 500 mls of normal saline over 6 hours).
- Where it is suspected that the delayed recovery is due to an excess of **benzodiazepine** (diazepam or midazolam) or other drugs, management is supportive, with maintenance of airway and ventilation until the drug has been metabolised. Where the specific

benzodiazepine antagonist flumazenil is available it can be tried (iv increments of 0.1mg to a maximum adult dose of 1mg). However, Flumazenil is expensive, and may cause arrhythmias, hypertension and convulsions. It's use is generally not indicated.

- **Measure the patient's temperature**, and warm if necessary. Forced air warming with a Bair hugger or similar device is the most effective method. However wrapping in blankets, and / or tin foil sheets, ensuring the room is kept warm, and giving warmed iv fluids, will also help.
- **Check blood glucose** - and correct with iv dextrose if it is less than 3mmol/l. Hyperglycaemia should be managed as described in Update in Anaesthesia No 11.
- **Measure and correct plasma electrolytes** - hyponatraemia should be corrected slowly, as there is a risk of subdural haemorrhage, central pontine myelinolysis and cardiac failure if correction is too rapid. The optimal rate is uncertain, but a maximum safe rate of 5 -10 mmol/l/day has been suggested, or up to 2mmol/l/hour until the plasma sodium is 120 mmol/l.
- If no other cause can be found for delayed emergence from anaesthesia, an intracerebral event may be suspected and a full neurological examination should be performed, looking particularly for localising signs. However radiological imaging (CT or MRI scan) is often required to confirm the diagnosis.

Summary

Delayed awakening of varying degrees is not uncommon after anaesthesia, and may have a number of different causes, individual or combined, which may be both drug or non - drug related. The primary management is always support of airway, breathing and circulation, whilst the cause is sought and treated as outlined above.