SUXAMETHONIUM APNOEA

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Introduction

Suxamethonium (succinylcholine) apnoea occurs when a patient has been given the muscle relaxant suxamethonium, but does not have the enzymes to metabolise it. Thus they remain paralysed for an increased length of time and cannot breathe adequately at the end of an anaesthetic.

This article describes the action of suxamethonium, the inheritance of suxamethonium apnoea, and the non-inherited conditions that can also cause it. The presentation and treatment of the condition are discussed. The post-operative care of patients and their families is outlined. Finally mivacurium, a short-acting, non-depolarising muscle relaxant, which can cause similar problems, is discussed with a case report.

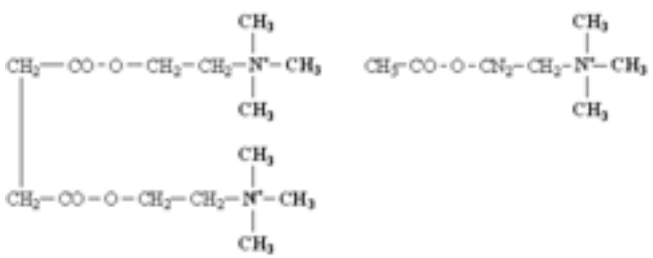
Suxamethonium

Suxamethonium is a depolarising muscle relaxant, which has the fastest onset of all the muscle relaxants. Its length of action is 2-6 minutes. It acts by mimicking acetylcholine at the neuromuscular junction and binds to the post-synaptic membrane of the junction thus preventing acetylcholine from binding. It is an example of non-competitive binding. Unlike non-depolarising muscle relaxants, it cannot be reversed, and recovery is spontaneous. Suxamethonium is mainly metabolised by plasma cholinesterase (previously called pseudo-cholinesterase) and the kidneys excrete 10%. Anticholinesterases such as neostigmine prolong the action of suxamethonium by inhibiting plasma cholinesterases and so should not be given with suxamethonium.

The structure of suxamethonium and acetylcholine.

The two nitrogen-containing groups (**shown in bold**) bind to the alpha (α) subunit of the post-synaptic acetylcholine receptor at the neuromuscular junction. This causes an ion channel to open in the post-synaptic membrane and depolarisation of the muscle and fasciculations (visible muscle twitches) to occur. The suxamethonium stays bound to the membrane: it remains depolarised and further action potentials cannot pass to the muscle. All muscles go flaccid, which facilitates intubation. The action of suxamethonium is terminated by plasma cholinesterase.

Figure 1: The structure of suxamethonium and acetylcholine



Suxamethonium *Acetylcholine*

Spontaneous breathing cannot occur until the action of suxamethonium has ceased.

The indications for suxamethonium

Suxamethonium is used to intubate patients rapidly. This is useful in patients who have full stomachs as in an emergency or for the treatment of laryngospasm. The dose used is 1.0 - 1.5mg/kg. If more than one dose is given the heart rate may slow. In children this can occur with the first dose. This can be prevented and treated by intravenous atropine.

Suxamethonium in these situations is useful because it acts and wears off quickly. If a patient has been adequately pre-oxygenated for 3 minutes, and proves impossible to intubate, the patient can be turned on their side and spontaneous respiration rapidly regained. Patients with suxamethonium apnoea do not recover muscle function rapidly after suxamethonium.

Suxamethonium apnoea

Suxamethonium apnoea is rare. It can be inherited, or it can appear spontaneously in a person with no family history. In cases where suxamethonium apnoea is inherited the level of plasma cholinesterase is reduced. In the acquired condition the level of plasma cholinesterase is normal but its activity is reduced.

Inherited suxamethonium apnoea

The genes for the inheritance of plasma cholinesterase are autosomal. There are several variations from the normal enzyme $E1^U$. The most common of these is $E1^a$. This abnormal gene is carried by 4% of the Caucasian population. This figure is higher in Asians and those from the Middle East and lower in Africans [1,2]. People who are heterozygous for the genes ($E1^uE1^a$) have an increased recovery time from suxamethonium (approximately 30 minutes). Homozygotes ($E1^aE1^a$) have reduced functioning of plasma cholinesterase and can take 2 hours or more to recover from suxamethonium. There are other more rare abnormal enzyme genes such as $E1^f$ (the fluoride plasma cholinesterase) and $E1^s$ (the silent). In $E1^s$ there is little plasma cholinesterase activity and therefore recovery from suxamethonium can take over 3 hours. In these people non-specific plasma esterases help to clear suxamethonium from the blood. There are ethnic differences in the silent type atypical enzyme ($E1^s$). Studies have suggested that this gene is more common in Asian populations.

Acquired Suxamethonium apnoea

Plasma cholinesterase is normal in these subjects, but activity is reduced. Acquired suxamethonium apnoea can occur in the following situations;

- Pregnancy
- Hypothyroidism
- Liver disease
- Renal disease

- Carcinomatosis
- Cardiopulmonary bypass
- Anticholinesterases
- Monoamine oxidase inhibitors
- Methotrexate

In these cases the action of suxamethonium is lengthened by minutes rather than hours.

Presentation of suxamethonium apnoea

Suxamethonium apnoea is not usually apparent until it is time to wake the patient up. At the end of the procedure the patient makes little effort to cough or breathe spontaneously. The pulse rate and blood pressure rise. Patients may sweat and the pupils may dilate. This occurs because the patient becoming aware but is still paralysed. At this stage a nerve stimulator (if available) can be used to determine whether the patient is still paralysed. If the patient is still paralysed but unable to move they should be re-anaesthetised.

Treatment of suxamethonium apnoea

The patient should be anaesthetised and ventilated. Neuromuscular transmission should be monitored with a nerve stimulator. As the suxamethonium wears off they should regain four strong twitches with no fade when tested with a nerve stimulator using a "train of four" (set at 2Hz over 2 seconds). If a nerve stimulator is not available then the patient should be kept anaesthetised until they are breathing spontaneously. The patient may have experienced a phase of awareness in the initial waking phase, and will need to have this explained to them when they are fully recovered. The patient should remain ventilated and anaesthetised until breathing spontaneously. They should be extubated awake when they are able to obey commands, can grip tightly and raise their head off the pillow for 10 seconds. Do not be tempted to extubate them deeper or earlier than this, as they may become tired quickly and might need reintubation.

Case Report

A 72 year old lady was admitted for direct laryngoscopy under the ENT surgeons. She had possessed a hoarse voice for a number of months and a vocal cord nodule had been seen on indirect laryngoscopy and needed removing. She had undergone many anaesthetic procedures in the past with no problems. None of these were as emergencies. As this was a short procedure but required full paralysis she was given mivacurium. The procedure went well and took 12 minutes. Neostigmine was given to reverse the mivacurium. The anaesthetic gases and ventilator were stopped. Her pulse rate began to rise to 100 beats per minute and her blood pressure rose from 90/60 to 160/100. She was visibly sweating. She had made no effort to breathe spontaneously. Nerve function was tested using a peripheral nerve stimulator. There were no twitches. It was concluded that she was still paralysed and she was re-anaesthetised and put back on a ventilator. She was taken to recovery where she was monitored closely. She began to breathe spontaneously and was finally taken off the ventilator 2 hours later. Blood tests later revealed that she had very low levels of plasma cholinesterases. She is undergoing genetic tests but the levels are so low it is suspected she is a homozygote for the abnormal plasma cholinesterase genes. Her family is also being tested.

This lady now has a red triangle on the front of her notes and her and her GP have been informed that she is to avoid suxamethonium (and mivacurium) in the future.

Post-operative care of patient and families

If a person has had an episode of suxamethonium apnoea then they ought to be warned to avoid suxamethonium in the future. A warning card can be carried by the patient to show doctors in the future. It must be explained that this condition can be inherited and if available both the patient and their direct family should have a blood test to measure the level of plasma cholinesterases to confirm whether they have the inherited form or the acquired. The method for detecting structurally abnormal plasma cholinesterases was first described by Kalow and Genest in 1957. If the plasma of normal patients is added to a benzoylcholine solution light is emitted at a specific wavelength, which can be measured. If dibucaine is also added no light is emitted as the reaction is inhibited. The inhibition of light production is given as a percentage and referred to as the dibucaine number. A normal patient has a number of 77-83. Hetrozygotes for the abnormal plasma cholinesterase gene have a number of 45-68. Homozygotes (both genes abnormal) have a number of less than 30. In this way the patient and the family can all be tested.

Mivacurium

This is the shortest-acting non-depolarising muscle relaxant available. It is relatively new and therefore expensive. Its advantages over suxamethonium are that it does not cause muscle pains after administration. It can be used for short procedures that require full muscle relaxation for airway manipulation such as ENT surgery. It cannot be used in emergency cases to allow rapid intubation (as in a rapid sequence induction), because its time of onset is slow, like most other non-depolarising muscle relaxants. It is metabolised by plasma cholinesterase (like suxamethonium). As non-depolarising muscle relaxants like mivacurium bind **competitively** with the postsynaptic membrane of the neuromuscular junction, they can be reversed with anticholinesterase drugs such as neostigamine. Anticholinesterases increase the concentration of acetylcholine at the neuromuscular junction and therefore facilitate reversal of the blockade. If decreased levels of plasma cholinesterase are either inherited or acquired (as discussed above) the length of action of mivacurium is increased as with suxamethonium apnoea.

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