INTRODUCTION

This chapter will be looking at the following types of anaesthetic agents: Nitrous oxide, (a gas used to supplement anaesthetic agents such as Halothane), and neuromuscular agents (Suxamethonium, Alcuronium, Neostigmine).

Remember that it is best to know a few drugs really well than to know many drugs not so well.

1. NITROUS OXIDE

Nitrous oxide is a gas that is commonly given as a mixture with oxygen. In this combination it is sometimes known as Entonox, and is used in obstetrics for women during labour.

Uses

In anaesthetics, nitrous oxide is used in combination with oxygen and an anaesthetic gas such as Halothane or Isoflurane. Its main effects are to:

- act as an analgesic;
- reduce the amount of Halothane, Isoflurane or Enflurane that is necessary for general anaesthesia. For many operations, only 0.521% of Halothane is needed when combined with nitrous oxide.

Nitrous oxide is often administered in a 60:40 or 50:50 mixture with oxygen. However, the patient must always get 100% oxygen during induction, and at the end of anaesthesia.

Side effects

- Because of its chemical properties, a patient who switches from breathing a nitrous oxide/oxygen mixture to breathing air, can develop what is called 'diffusion hypoxia'. In order to prevent this, it is imperative that at the end of all anaesthetics during which nitrous oxide has been used, the patient breathes 100% oxygen for at least 10 minutes before breathing normal air.
- Because of its chemical properties, nitrous oxide can cause air-containing spaces within the body to expand. For example, when nitrous oxide is administered in a concentration of 75%, the volume of a cavity can increase by as much as three times its original volume within 30 minutes. For this reason, nitrous oxide should not be administered in a patient suspected of having a pneumothorax or an air embolism.
- Nitrous oxide has toxic effects, and should not be used for more than six hours at any one time.

2. NEUROMUSCULAR BLOCKING AGENTS

Neuromuscular blocking agents are sometimes known as 'muscle relaxants'. They are used to abolish the muscular activity which will occur as reflex responses to surgery or tracheal intubation, and also to abolish muscular tone which may hinder surgery or make artificial ventilation difficult.

Before the development of muscle relaxants, large doses of anaesthetic drugs had to be given to reduce muscular tone. This would cause problems related to cardio-respiratory depression, other dose-related side-effects, and would also cause patients to take much longer periods of time to recover. With muscle relaxants, smaller doses of anaesthetic agents can be used with fewer side effects.

There are two groups of muscle relaxants:

a. Depolarising (short-acting) relaxants, eg Suxamethonium.
GOLDEN RULES FOR THE USE OF MUSCLE RELAXANTS

Because a muscle relaxant will effectively paralyse a person, you should never give a neuromuscular blocking agent without pre-oxygenating the patient, and without being sure of your ability to ventilate the patient.

Because the cessation of respiratory effort is often the first noticeable sign of cardio-respiratory arrest, you should never give a neuromuscular blocking agent without monitoring the patient’s pulse during artificial ventilation.

b. Non-depolarising (medium and long-acting) relaxants, e.g. Alcuronium, Vecuronium, Atracurium and Pancuronium.

Suxamethonium

Suxamethonium (often referred to as Scoline) is a short-acting ‘depolarising’ agent that causes profound paralysis. It is quick acting with an onset time of about 20 seconds.

Prior to paralysis, all the muscles in the body will undergo contract (fasciculation). It will then cause apnoea for 4-5 minutes, and takes about 10 minutes for complete and spontaneous recovery of hand function.

Indications

- To provide brief muscle relaxation to enable tracheal intubation.
- To provide complete muscular relaxation for short procedures that last a few minutes only. For example, reducing a dislocated hip or shoulder.

Dosage

The recommended dose is 1mg/kg. However, it is quite safe to give a standard dose of 100mg for all adults.

If intubation has been unsuccessful, a second dose may be given. In children, this must always be accompanied by a paediatric dose of atropine (50mcg/kg) to prevent bradycardia.

In adults, you should have a drawn-up syringe of atropine ready for administration in case of bradycardia.

Never give a second dose of Suxamethonium until after you have fully oxygenated the patient again. Never give a second dose of Suxamethonium to children without giving atropine before hand. Never give a third dose of Suxamethonium.

Side effects

‘Scoline apnoea – Suxamethonium is normally broken down by plasma cholinesterase. Some people lack this enzyme, which will result in paralysis for two hours or more. This is rare, but these patients will need to be ventilated until they recover. They should be warned not to have Suxamethonium in future anaesthetics.

Malignant hyperpyrexia – This is a rare and potentially fatal condition caused by an inherited abnormality in skeletal muscle. Exposure to Suxamethonium can precipitate a rapid rise in body temperature (2°C/hr) muscle rigidity, tachycardia, tachypnoea, hypoxaemia and cyanosis. If this happens, stop the anaesthetic, give 100% oxygen, cool the patient with ice packs and send patient to the nearest ICU. (If you are in a regional or tertiary hospital IV Dantrolene should be available and given as soon as possible.

Hyperkalaemia – Suxamethonium causes a transient rise in serum potassium concentration. Some patients (see below) may develop a dangerous hyperkalaemia, and should not receive any Suxamethonium.

Muscle pain – Up to 50% of patients can experience muscular pain after administration of Suxamethonium. It particularly affects young, ambulant women.

Bradycardia – This is a side-effect that commonly follows repeat doses of Suxamethonium.

Contra-indications

In all these cases, the need to facilitate intubation as a life-saving procedure will outweigh the complications and side-effects of Suxamethonium.

- Patients with severe burns from first week to three months. (May cause dangerously high hyperkalaemia.)
- Patients with extensive muscle damage from first week onwards. (Hyperkalaemia.)
- Paraplegic patients from first week of injury. (Hyperkalaemia.)
- Patients with severe peripheral neuropathy. (Hyperkalaemia.)
- Patients with penetrating eye injuries. (Suxamethonium causes a transient rise in intra-ocular pressure.)

Alcuronium (Alloferin)

Alcuronium is one of about seven different types of non-depolarising neuromuscular blocking drugs that are available. These drugs work by blocking the acetylcholine receptors on the muscle fibre, and have a longer duration of action than Suxamethonium. The main difference between the various non-depolarising muscle relaxants is in their duration of action, and the main points described here about Alcuronium are relevant to the other agents.

Dosage

The onset of paralysis and its dura-
tion of action depends on the dose that is used. However, there is a lot of variation from one individual to another.

**Initial dose:**
0.2 mg/kg

**Onset of action:**
Three to five minutes (longer than Suxamethonium).

**Duration of effect:**
Very variable, but usually 20-30 minutes.

**Maintenance dose:**
0.1 mg/kg every 20-30 minutes.

There are a number of factors that can prolong the duration of action. These are:
- poor renal function;
- liver disease;
- hypokalaemia;
- acidosis;
- myasthenic disease; and
- aminoglycoside antibiotics.

**Side-effects of Alcuronium**
The main side-effect is related to prolonged paralysis (see below).

Moderate hypotension.

**Reversing Alcuronium**
After you have paralysed a patient, it is vital that when the operation and anaesthetic is finished, the patient should start breathing spontaneously without any residual paralysis. Residual paralysis, however, may cause the patient to struggle for breath, and cause post-operative hypoxaemia.

Although the effects of Alcuronium will wear off by itself, the reversal of neuro-muscular blockade is usually facilitated by giving the patient Neostigmine.

However, it is dangerous to give Neostigmine too soon after the last dose of any non-depolarising muscle relaxant because this may actually cause a prolongation of the paralysis. In some hospitals, nerve stimulators are used to judge the appropriate time for giving Neostigmine. In hospitals which do not have nerve stimulators available, the following rules of thumb will help prevent complications:

- Do not attempt to start spontaneous respiration or administer Neostigmine within 20 minutes of the last dose of Alcuronium.
- Be cautious with patients who may be acidosis, who have renal or hepatic disease, or who have had gentamicin given to them recently. Wait for 30 minutes before trying to reverse the effects of Alcuronium in these patients.
- Do not give subsequent doses of Alcuronium to a patient unless you have to.
- Make a note of the time when you give Alcuronium.

**3. NEOSTIGMINE**
As explained above, Neostigmine is used to reverse the effects of non-depolarising muscle relaxants. It works by increasing the concentration of acetyl choline at the neuromuscular junction.

It also stimulates the muscarinic receptors which will cause bradycardia, intestinal peristalsis and spasm, salivary secretions and bladder contraction. These effects can be counteracted by Atropine (20 mcg/kg), and it is therefore common to administer Neostigmine in combination with Atropine. This is especially vital in cases of abdominal surgery where there has been bowel anastomosis.

**Dosage**

**Onset of action**
Three to five minutes. Because Atropine works more quickly, it should be given a minute or so later.

**Duration of action**
Twenty minutes. If significant concentrations of Alcuronium remain in the circulation after this time, a second dose of Neostigmine may be necessary.

**Dose**

Adults: 2.5 mg (up to a total dose of 100 mcg/kg).

Children: 60 mcg/kg.