The principles of anaesthesia

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Abstract

The understanding and safety of anaesthesia has advanced significantly over the last two centuries, facilitating most of the surgical advances seen in this period. This article covers essential elements of both general and local anaesthetic agents, describing the anaesthetic triad, the component parts of a typical general anaesthetic, and adjunctive drugs and techniques.

Keywords Inhalational agents; intravenous agents; local anaesthetics; muscle relaxants

Background

Before the advent of anaesthesia, the most important skill a surgeon possessed was speed. Surgery was a horrific last resort, reserved only for superficial procedures, amputations (Figure 1), or removal of fungating tumours. Patients were often plied with alcohol then strapped to the table to be restrained. Surgery was quick, bloody and often inaccurate. Surgery in body cavities was virtually impossible.

The discovery of anaesthesia allowed surgeons to become more skilled, perform more complex operations, and also to perform surgery within the abdomen and chest.

Although Humphrey Davy had demonstrated the analgesic properties of nitrous oxide in 1800, it was in 1846 in Boston that the first documented 'modern day' anaesthetic was administered by a dentist, William Morton. He administered ether to a patient undergoing tooth extraction. He went on to demonstrate his discovery at Massachusetts General Hospital by successfully anaesthetizing a patient having a neck tumour removed.[1] Following the success of his demonstration many others adopted his techniques, and the search for better anaesthetic agents began. Chloroform was the next inhalation anaesthetic to be widely used, with the first documented case in 1847. It was easier and more pleasant to administer than ether, but had a worse side effect profile, including liver damage and sudden death. Its popularity was boosted after famously being used by Queen Victoria during childbirth. The next major advance in anaesthesia came in 1877 with the discovery of the local anaesthetic properties of cocaine by Koller, an Austrian ophthalmologist.

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Figure 1 Leg amputation, by an unknown artist. 18th century painting, from a collection of the Royal College of Surgeons, London.

In today's clinical practice, the term 'balanced anaesthesia' is used to describe the concept of using combinations of techniques and drugs to provide the optimal conditions to facilitate surgery. The triad of anaesthesia is analgesia, anaesthesia and muscle relaxation. Rather than using a large dose of a single agent to achieve the anaesthetic triad, smaller, safer doses of multiple drugs, each with specific actions are used. This allows the beneficial effects of each drug to be used, while avoiding dose related adverse side effects.

Mechanism of action of drugs used for general anaesthesia

Balanced anaesthesia involves the use of multiple different drugs together to achieve adequate analgesia and anaesthesia and muscle relaxation. These drugs can be broadly divided into the following categories:

- intravenous induction agents
- inhalational anaesthetic agents
- muscle relaxants
- opioids.

Intravenous induction agents

Induction of anaesthesia is the transition from an awake to an anaesthetized patient. It is most commonly achieved by the use of an intravenous agent, although inhalational induction is also possible and used commonly in children (to avoid difficult or distressing venous cannulation). Although a diverse range of drugs are used as induction agents, they share the properties of achieving anaesthesia in one arm—brain circulation and are fat soluble so that penetration of the blood—brain barrier is possible. The drugs commonly used are discussed here.

Thiopental sodium (thiopentone) is a short-acting barbiturate and has been used in anaesthesia since the 1930s. It is also used in the treatment of status epilepticus. It works by increasing the conductance of chloride ions into nerve cells, mediated by γ-aminobutyric acid (GABA) channels.[2] This results in hyperpolarization and neuronal inhibition. Given at a dose of 3–6 mg/kg, thiopentone reliably induces anaesthesia within one arm—brain circulation, with anaesthesia lasting around 5–10 minutes. It also produces dose-dependent respiratory depression. A

reduction in cardiac output and systemic vascular resistant (SVR) results in a drop in blood pressure and tachycardia. Thiopentone should be avoided in patients with porphyria as it can precipitate a crisis. Inadvertent intra-arterial injection can have devastating consequences as precipitation of crystals can cause distal ischaemia.

Propofol is a phenolic derivative that is prepared as an oil −water emulsion, and is highly lipid-soluble. As well as its use as an induction agent, its quick recovery profile means it can also be used as an infusion for total intravenous anaesthesia and for sedation on the intensive care unit. Propofol obtunds upper airway reflexes more readily than thiopentone so is an ideal agent to use with the laryngeal mask airway (LMA). Unlike thiopentone, the mechanism of action is not on GABA receptors but is thought to be by a reduction in the opening time of sodium channels.[2] Common side effects are pain on injection, fall in SVR and blood pressure, and respiratory depression and apnoea. Excitatory effects can occur, with involuntary movements. Propofol infusion syndrome has been reported in patients receiving high doses for sedation in the intensive care unit (ICU). This can result in multi-organ failure and often proves fatal. It is more common in children and propofol sedation is therefore not licensed for children.

Ketamine is a phencyclidine derivative, which can be used as an induction agent if given at the dose of 1−2 mg/kg. It also has the advantage of being a potent analgesic agent. Ketamine is effective if given intramuscularly (5−10 mg/kg), and may also be used orally. Unlike the other induction agents, it stimulates the sympathetic nervous system so cardiac output, blood pressure and heart rates increase. It is the only induction agent that does not cause respiratory depression, and laryngeal reflexes are generally well preserved. These qualities mean that it is most commonly used for analgesia and anaesthesia in the shocked patient and outside the hospital such as the battlefield. It's routine use is limited by the unpleasant emergence phenomena and hallucinations associated with its use. Ketamine exerts its effect via the N-methyl-D-aspartate (NMDA) receptor, by antagonizing the excitatory neurotransmitter glutamate. It also has some effect on opioid receptors.

Inhalational anaesthetic agents

Inhaled anaesthetic agents are most commonly used for the maintenance of anaesthesia. One of the oldest agents is nitrous oxide (N_2O), which also has the advantage of analgesic qualities. However, N_2O is not potent enough to be used as sole anaesthetic agent and is therefore most commonly used as a carrier gas for the other volatile gases, or as an analgesic gas in the form of entonox where it is delivered with 50% oxygen. Nitrous oxide has many disadvantages including causing expansion of gas-filled cavities, emetogenic properties, and interference with DNA synthesis, so its use is becoming less popular.

The remaining volatile anaesthetic agents in popular use are all halogenated hydrocarbons. They share several properties, in that they all have relatively rapid recovery profiles, and they all cause a drop in systemic vascular resistance and therefore blood pressure.

Halothane is an anaesthetic agent with a side effect profile (hepatitis, cardiac arrhythmias) which limits its use in many countries. It is non-irritable to the airway so can be used for gaseous induction which is especially useful in the paediatric population.

The introduction of sevoflurane replaced the common use of halothane, as sevoflurane also is non-irritant so therefore can be used for gaseous induction. It does not have the arrhythmogenic properties of halothane, but is more expensive than other volatiles and has theoretical toxicity implications with the production of compounds within the breathing circuit that can cause renal toxicity.

Isoflurane and desflurane are both irritant to the airway so cannot be used for gaseous induction. Desflurane is relatively less fat soluble and therefore has a very rapid recovery time, which can be useful in anaesthetizing obese patients, or when postoperative neurology needs to be quickly and reliably assessed, such as in neurosurgery. Isoflurane is also a widely used agent, and has the advantage of being significantly cheaper than sevoflurane and desflurane.

Muscle relaxants

Muscle relaxants are used in order to facilitate tracheal intubation and provide optimal operating conditions. Not all operations require muscle relaxation; superficial and distal surgery can be done with the patient not relaxed and spontaneously breathing. Muscle relaxants work by exerting their effect on the neuromuscular junction (Figure 2).

The neuromuscular junction allows propagation of the action potential from a nerve across the muscle, therefore allowing contraction. The action potential from the nerve causes vesicles containing acetylcholine to empty into the synaptic cleft. Binding of acetylcholine (ACh) to postsynaptic ACh receptors results in sodium influx into the motor endplate to produce an endplate potential, which results in contraction of the muscle. Acetylcholinesterase breaks down the ACh, therefore terminating its action.

Suxamethonium is the most commonly used depolarizing muscle relaxant, and exerts its effect by mimicking the action of ACh, attaching to nicotinic ACh receptors at the neuromuscular junction. The molecule stays in situ and causes persistent depolarization which results in muscle relaxation. The rapid and predictable onset of suxamethonium means it is useful to facilitate rapid intubation of the trachea, which can be useful in situations such as an unfasted patient. Suxamethonium is broken down rapidly by plasma cholinesterases so the muscle relaxation is short lived, usually less than 5 minutes. Suxamethonium does have some unpleasant side effects, the fasciculations can result in myalgia, and hyperkalemia. Anaphylaxis is well described and prolonged duration of paralysis can result if the patient has reduced plasma cholinesterase activity such as in suxamethonium apnoea.

Non-depolarizing muscle relaxants are competitive antagonists at ACh receptors. As more receptors are occupied, then neuromuscular transmission becomes less effective and eventually fails. The drugs used to achieve muscle relaxation can be short, medium, or long acting.

Short-acting non-depolarizing muscle relaxants are useful for quick surgical procedures. The most commonly used drug in this category is mivacurium. Mivacurium is, like suxamethonium, broken down by plasma cholinesterases so patients with either an acquired or genetic deficiency of these can have prolonged muscle relaxation following its administration.