TOTAL INTRAVENOUS ANAESTHESIA (TIVA) AND PARTIAL INTRAVENOUS ANAESTHESIA (PIVA)

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Introduction

The requirements of total intravenous anaesthesia are similar to those for any general anaesthetic, - to provide hypnosis, analgesia and muscle relaxation as required for the procedure concerned, whilst maintaining the patient’s cardiopulmonary function. Respiratory depression can be counteracted by administering oxygen, and by intermittent positive pressure ventilation (IPPV) if required. The equipment requirement is therefore as for inhalation, other than replacing the vaporiser with an infusion syringe, and the need for monitoring is equal.

This presentation will examine the drugs suitable for TIVA and modes of administration. It will then discuss the addition of supplementary IV agents to animals anaesthetized with inhalation agents (PIVA) - does it improve cardiopulmonary function? The range of possible drug doses and combinations is enormous, but in the verbal communication some dose regimens for practical clinical use will be presented.

Agents used for TIVA

The requirements are that the drugs or combinations can provide adequate anaesthetic conditions (as above) with minimal cardiovascular depression for as long as is required, (surgeons often take longer than expected) but still result in a smooth rapid recovery. There are two major methods of achieving this (a) by using agents which do not have a context sensitive half-life (ie are non cumulative) and (b) by using reversible combinations. With this second option care is needed that the duration of antagonist and agonist match and that if the analgesic component is reversed, provision is made for post-operative pain control.

Propofol This, given as constant rate infusion (CRI) has been the mainstay of TIVA in man and in dogs. In dogs it can be infused for prolonged periods for anaesthesia and recovery is still relatively rapid. Major disadvantages at clinical doses are (a)respiratory depression- oxygen supplementation is essential and (b)lack of analgesia. This latter means that whilst it is adequate on its own for non-painful procedures, for surgery it needs to be given with a potent analgesic. Analgesics can be given as a heavy premedicant, but it is preferable to give them
as a CRI. Agents suitable for such a CRI are fentanyl, medetomidine or dexmedetomidine, and ketamine. In the cat, the potential problems of propofol toxicity and accumulation mean it is not the best agent for TIVA of more than approximately 30 minutes.

**Alfaxalone** Alfaxalone has been used very satisfactorily for TIVA in both cats and dogs, both by means of ‘top-ups’ and as CRIs. Although there were clinical trials for licencing, there is surprisingly published papers on the clinical use of TIVA for surgery, making it difficult to assess if extra analgesia is required. In one study reported by the pharmaceutical company, 37 feral cats underwent neutering procedures; premedication was with medetomidine (20 mcg kg⁻¹) and morphine 0.3-0.5 mg kg⁻¹. Mean induction dose of alphaxalone was 1.8+SD6 mg kg⁻¹ and mean maintenance infusion 0.18+0.04 mg kg⁻¹ minute⁻¹. In study of ovariohysterectomy in bitches [1] premedication was with Acepromazine 0.01 mg kg⁻¹ and morphine 0.4 mg kg. Mean alphaxalone induction dose was 1.9 mg kg⁻¹ and infusion dose 0.11 mg kg⁻¹.

**Ketamine** Ketamine (or tiletamine) is used widely by IM injection, most usually in combination with an alpha 2 adrenoceptor agonist, in cats to obtain anaesthesia adequate for ovariohysterectomy. However, in (non feral) dogs, it is more usually given by IV injection after heavy premedication, or in combination with a benzodiazepine (eg diazepam). Ketamine is very analgesic, and can be used as a CRI in combination with less analgesic hypnotics (propofol, or inhalation agents) to provide analgesia and reduce the dose of the other agents.

**Reversible ‘anaesthesia’**

The three types or reversible agents are the opioids (major antagonist, -naloxone), the alpha 2 adrenoceptor agonists (major antagonist- atipamezole) and the benzodiazepines (antagonists- flumazenil, sarpazenil). None of these agents are in themselves anaesthetics but combinations do produce a state close to anaesthesia. Reversal is expensive and is not always used if prolonged recovery is acceptable. A huge number of such combinations are in use, but some common ones are;

(a) Medetomidine/dexmedetomidine and ketamine - reverse the alpha 2 if necessary at the end of surgery. This of course means that there is no remaining ‘cover’ for ketamine ‘hallucinatory’ or ‘movement’ side effects.

(b) A benzodiazepine, climaazolam, with a specific antagonist, sarmazenil, is licenced for use with ketamine in dogs and cats in some European countries.

(c) Powerful opioids plus sedatives (the extreme is phenothiazine/etorphine- ‘Immobilon’), then the opioids is reversed with naloxone or diprenorphine. With this technique opioids cannot be used to provide post-operative analgesia.

**Modes of Administration**

1. **Intramuscular** (eg alpha 2/ketamine in cats; darting wild animals) This is always ‘second best’ to a CRI, or even ‘top ups’. However, analgesia (eg morphine) additional to the main anaesthetic can be given very effectively by this route.

2. **Intravenous** A well secured venous access - preferably a catheter, is essential.

   (a) **Top ups’** These have been used very successfully by many veterinarians. However, they cause peaks and troughs of anaesthetic concentration and depth.

   (b) **Constant rate infusion (CRI)** This can be given by varying degrees of sophistication. It can be
administered simply via an infusion set - although for small animals this making the volume practicable may be difficult. An increase of sophistication is to incorporate a specific volume pump.

Preferable is via a CRI syringe driver. These are very easy to use and very practicable. They can be set to deliver a certain pre-calculated rate- if the anaesthesia is light it can deliver a bolus, or the rate can be changed as required according to the depth of anaesthesia.

Target Controlled Infusion. For TIVA with propofol (and later for remifentanyl) in human anaesthesia, target controlled infusers eg the DiprifusorTM have been developed. Physical factors of the patient are set, and then the infuser injects the propofol to a ‘target’ plasma concentration, based on pharmacokinetic calculations. The group at Glasgow developed this further for dogs [3]. Currently a company ‘RugloopTM’ have developed a computer programme to drive infuser syringes, not just for propofol but also for other agents. Their software has been modified by incorporating the Glasgow pharmacokinetic model for dogs and appears to have been used successfully.

**Partial Intravenous Anaesthesia (PIVA) or can we get the best of both?**

The background for this idea is that all inhalation anaesthetic agents cause dose dependent cardiovascular depression, and therefore if the dose can be reduced by the CRI of an analgesic agent, there will be less depression. The problem is (a) the original concept was when halothane was the inhalation agent used- at MAC (minimal alveolar concentration) it caused greater cardiac depression than do the currently used agents. (b) the definition of cardiovascular depression-improved blood pressure is often the result of vasoconstriction, which can reduce blood flow. What matters is that cardiac output is improved and tissue blood flow increased. In the majority of cases there is little evidence that the combinations improve cardiac output compared with the inhalation agent alone, and in some cases (lidocaine in the cat ref) the combination makes things worse. There are numerous studies to show that infusions of lidocaine, opioids (at least in dogs), ketamine, combinations of all three (MLK), or medetomidine reduce MAC - many demonstrate improved blood pressure, but have not measured cardiac output. CRIs of analgesics during inhalation anaesthesia may be advantageous for other reasons- preventing surgical response and ‘wind up’, contributing to post-operative analgesia, but the case for better cardiovascular stability is not proven.

**Commonly used CRIs**

**Opioids** Fentanyl or morphine infusions effectively reduce MAC of inhalation agents in both cats and dogs. Respiratory depression means that IPPV is necessary. Potent opioids cause bradycardia- if this is not corrected (use of an anti-cholinergic) then cardiac output falls.

**Lidocaine** Lidocaine reduces MAC in dogs and cats, and it use currently is very ‘fashionable’. However, it is contraindicated in anaesthetised cats as it reduces cardiac output (ref). Studies in horses suggested no change in cardiac output compared with inhalation agents alone.

**Ketamine** Ketamine’s sympathetic stimulation effects mean that its use increases blood pressure, but I have been unable to find a cardiac output study with inhalation agents. When used with propofol TIVA in dogs, despite greatly reducing the propofol required, cardiac output was the same as when a larger dose of propofol alone was employed (ref). Long periods of high dose ketamine results in prolonged recovery.
**Medetomidine** Infusions of low doses reduce MAC, and maintain blood pressure. However bradycardia probably means that blood flow is not improved. Further studies are needed with and without anti-cholinergic agents.

**References**


