Intravenous anaesthesia in goats: A review

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Intravenous anaesthesia is gradually becoming popular in veterinary practice. Traditionally, general anaesthesia is induced with intravenous drugs and then maintained with inhalation agents. Inhalation anaesthetic agents cause more significant dose-dependent cardiorespiratory depression than intravenous anaesthetic drugs, creating a need to use less of the inhalation anaesthetic agents for maintenance of general anaesthesia by supplementing with intravenous anaesthesia drugs. Better still, if anaesthesia is maintained completely with intravenous anaesthetic drugs, autonomic functions remain more stable intra-operatively. Patient recovery from anaesthesia is smoother and there is less pollution of the working environment than happens with inhalation anaesthetic agents. Recently, a number of drugs with profiles (pharmacokinetic and pharmacodynamic) suitable for prolonged intravenous anaesthesia have been studied, mostly in humans and, to a certain extent, in dogs and horses. There is currently very little scientific information on total intravenous anaesthesia in goats, although, in the past few years, some scholarly scientific articles on drugs suitable for partial intravenous anaesthesia in goats have been published. This review article explored the information available on drugs that have been assessed for partial intravenous anaesthesia in goats, with the aim of promoting incorporation of these drugs into total intravenous anaesthesia protocols in clinical practice. That way, balanced anaesthesia, a technique in which drugs are included in anaesthetic protocols for specific desired effects (hypnosis, analgesia, muscle relaxation, autonomic stabilisation) may be utilised in improving the welfare of goats undergoing general anaesthesia.

Introduction

Total intravenous anaesthesia (TIVA) is becoming a vital technique for general anaesthesia and a well-established anaesthetic concept for some animal species, notably dogs and horses. Information on TIVA protocols for goats is very scarce at the moment; yet, there are situations (field anaesthesia, anaesthesia for MRI, research) when TIVA might be the only practically possible way to achieve general anaesthesia in goats (Carroll, Hartsfield & Hambleton 1997; Larenza *et al.* 2005). This review article highlights the latest developments in intravenous anaesthesia in goats, paying attention to outcomes of recent scientific articles on sedatives, analgesic and/or hypnotic drugs that can be used for TIVA in goats.

In veterinary practice, intravenous anaesthetic drugs are commonly used as induction agents to facilitate endotracheal intubation, whilst inhalation anaesthetic agents form the foundation for maintenance of general anaesthesia (McKenzi 2008; Reid, Nolan & Welsh 1993). Inhalation anaesthesia may not be applicable in all situations where anaesthesia is required. General anaesthesia can then be maintained by intravenous drugs in those situations (Hofer *et al.* 2003). Intravenous anaesthesia (IVA), instead of inhalation anaesthesia, could soon become an established means of anaesthetic provision for both induction and maintenance of anaesthesia in veterinary practice. During early historical times, anaesthesia could only be achieved by inhalation of vapours such as chloroform and ether (Askitopoulou, Ramoutsaki & Konsolaki 2000; Griffith 1934). Following the invention of the hypodermic needle, independently by Charles Gabriel Pravaz in France and by Alexander Wood in England in 1853 (Harvinder & Prausnitz 2007; Kravetz 2005), the technique of intravenous anaesthesia has subsequently grown over the years to a point today, where, propelled by recent major developments in volumetric pump technology and a broader understanding of the pharmacokinetic and pharmacodynamic profiles of relevant drugs, it has become the preferred anaesthetic technique in some instances, especially in commonly anaesthetised animals such as dogs (Mani & Morton 2010; McKenzi 2008; Moens 2004). TIVA is a technique that involves the use of only intravenous anaesthetic drugs to maintain an adequate depth of anaesthesia for a targeted level of central nervous system depression, for example, hypnosis for diagnostic procedures or surgical anaesthesia for noxious interventions (Suarez *et al.* 2012; Waelbers, Vermoere & Polis 2009).

Why intravenous anaesthesia?

There are several advantages of TIVA, especially if the drugs are administered as continuous infusions. These advantages include rapid onset of action independent of ventilation status, reduction of adverse effects of other anaesthetic drugs if used in balanced anaesthesia protocols, allowing for provision of continuous analgesia if needed, smoother recovery from anaesthesia, low costs considering that the minimum requirement is a needle and a syringe, and reduction of the hazards of occupational health and atmospheric pollution (Dundee & McMurray 1984; Hasley 1991; Mani & Morton 2010; Waelbers *et al.* 2009). It must be noted that TIVA anaesthesia also contributes to decreased environmental pollution, to a largely unaccounted extent, through disposal of surplus drugs and excreted metabolites into the environment (Briggs 2003). In remote settings, TIVA would be a very useful method of restraint because it does not necessarily require bulky, sophisticated and expensive equipment such as the anaesthesia machine for inhalation anaesthesia (McKenzi 2008; Waelbers *et al.* 2009).

There are some disadvantages to the use of TIVA that include the need for infusion pumps as the ideal modality of IVA delivery, difficulty of aligning infusion rates to depth of anaesthesia, tendency for the drug plasma concentrations to increase with duration of IVA time, and pain on injection of some drugs (Mani & Morton 2010; Waelbers *et al.* 2009). Even though the equipment required to deliver inhalation anaesthetic agent is expensive, the cost of IVA drugs used could prove more expensive, especially for very long anaesthetic procedures. Yet, in the author's opinion, when all is considered, the advantages of TIVA far outweigh the disadvantages, especially when patient comfort is considered.

Basic requirements for anaesthesia in goats

Anaesthetic management in goats is usually uncomplicated, with the primary notable risk being regurgitation with potentially fatal pulmonary aspiration (Hall, Clarke & Trim 2001). Mature goats have a multi-compartmental stomach with a large rumen that does not empty easily (Riebold 2007). Withholding food for 12–18 h may decrease rumen fermentation and decrease the risk of regurgitation, but does not result in a real reduction in the volume of ruminal contents (Abrahamsen 2008; Taylor 1991; Valverde & Doherty 2008). Water can be withheld for 6–12 h (Fulton, Clarke & Farris 1994). It is essential to prevent aspiration of rumen contents, even after following the precautions suggested above, by prompt placement of an endotracheal tube and inflation of the cuff of the tube after induction of general anaesthesia in mature goats (Abrahamsen 2008; Galatos 2011; Riebold 2007). Endotracheal intubation in goats is difficult because of the long, narrow oral cavity and distant laryngeal opening. Using a long-bladed laryngoscope to facilitate visualisation and a non-flexible stylet makes placement of the tube into the trachea much easier (Caulkett 2003; Taylor 1991).

Prior to an anaesthestic procedure, a physical examination should be performed. It is not uncommon for goats to develop hypoxaemia with general anaesthesia (Hall *et al.* 2001). Normal eructation in the goat is hampered by anaesthesia and by dorsal or lateral recumbent positioning. As a result, gas accumulates in the rumen, causing ruminal tympany or bloat, and the distended rumen exerts pressure on the diaphragm causing the lung capacity to decrease (Fulton *et al.* 1994; Galatos 2011). Pressure on the major vessels then impedes venous return to the heart. Cardiac output, blood pressure and tissue perfusion are also compromised and this can lead to possible ventilation-perfusion mismatch. Hypoxaemia and hypercarbia may result and can be life threatening. Passing a stomach tube after intubation can help resolve gaseous distension (Riebold 2007).

Supportive therapy during anaesthesia should ideally include intravenous fluid administration for maintenance and replacement needs, heat conservation and supplementation and oxygen supplementation (Abrahamsen 2008). Fluid maintenance can be achieved with a balanced electrolyte solution such as Lactated Ringers at a flow rate of 4 mL/kg/h – 6 mL/kg/h through an intravenous catheter placed in the cephalic vein (Fulton *et al.* 1994).

Techniques for intravenous anaesthesia

Intravenous anaesthetic drugs are usually first administered as a large bolus to fill the volume of distribution of the central compartment, which is then followed by continuous lower dosages to maintain effective drug plasma concentrations for the duration of the anaesthetic procedure (Beths 2008; Waelbers *et al.* 2009). Administration of intravenous anaesthetic drugs for maintenance of anaesthesia can be achieved by multiple bolus injections or continuous infusion at a fixed or variable rate (Beths 2008; Waelbers *et al.* 2009). Intermittent multiple bolus injection of IVA drugs is very simple, but is characterised by inconsistent drug plasma concentrations, variable anaesthetic depth and may result in poor and/or prolonged recovery from anaesthesia (Beths 2008; Joubert 2009). Continuous administration of intravenous anaesthetic drugs can be achieved by using a drug-spiked intravenous fluid bag, buretrol or a syringe controlled by a basic volumetric pump (syringe driver) or computer-controlled pump (Beths 2008; Waelbers *et al.* 2009). If intravenous anaesthetic drugs are administered from a drug-spiked fluid bag or a buretrol, the rate of administration is calculated to drops per second and adjusted over time to achieve a desired anaesthetic effect (analgesia, hypnosis, surgical anaesthesia). However, administration of intravenous anaesthetic drugs can be undertaken in a more sophisticated manner by the constant rate infusion (CRI) technique using the conventional syringe driven by a pump, or by the target-controlled infusion (TCI) technique using a highly sophisticated computer-controlled pump that adjusts the rate of drug administration so as to maintain a user-defined target plasma or effect site drug concentration (Mani & Morton 2010; Waelbers *et al.* 2009).

In human practice, a number of TCI systems have been developed for popular IVA drugs (Beths 2008; Sneyd 2004), but, in veterinary practice, research towards development of TCI system for propofol has only been conducted for dogs (Beths 2008; Joubert 2009). Ideally, the effect of a selected drug and the dose or plasma concentration at which the effect occurs should be known (Mama 2006). However, administration of intravenous anaesthetic drugs by the TCI technique is still a far-fetched wish in ruminant anaesthesia practice because of unavailability of infusion systems and limited population pharmacokinetics of suitable drugs (Hatschbach *et al.* 2008). The rate of intravenous anaesthetic drug administration will continue to be influenced by less sophisticated and cheaper equipment for years to come in veterinary practice.

Drugs available for prolonged intravenous anaesthesia in goats

To avoid misunderstandings, prolonged intravenous anaesthesia is defined, in this review article, as an anaesthetic procedure lasting at least 60 min, or long enough to require a drug or drugs to be topped up more than once to maintain general anaesthesia at a desired level.

For an anaesthetic drug to be deemed suitable for prolonged IVA it should, (1) be stable in solution, (2) water soluble, (3) lipid soluble and potent as an anaesthetic agent, (4) have a rapid onset of action, (5) have few adverse effects, (6) be rapidly cleared from body tissues and (7) cause short, smooth and predictable recovery from anaesthesia (Beths 2008; Dzikiti 2010; Joubert 2009; McKenzi 2008). Based on these criteria, drugs that can currently be used in prolonged IVA include general anaesthetics (propofol, ketamine, alfaxalone), opioids (fentanyl, remifentanil), benzodiazepines (diazepam, midazolam) and some anaesthetic adjuncts (lidocaine, glycerol guaicolate). In food animals such as goats, it is essential for administered drugs to have short half-lives to ensure short withdrawal times and that way restrict presence of excess drug residues in meat or milk to a very short period of time (Fajt 2011).

General anaesthetic agents for intravenous anaesthesia in goats

Goats are not amongst the commonly anaesthetised animals, which is partly why information on goat anaesthesia is scarce. General anaesthesia can be induced in goats using the same drugs commonly used in other species. These induction agents include thiopentone, propofol and ketamine, which can be administered with or without premedication at dosages of 5 mg/kg – 20 mg/kg, 3 mg/kg – 7 mg/kg and 4 mg/kg – 15 mg/kg, respectively (Dzikiti *et al.* 2010; Dzikiti *et al.* 2009; Galatos 2011; Prassinos, Galatos & Raptopoulos 2005; Taylor 1991). It is recommended to premedicate goats so that they are calm before administering these induction agents (Galatos 2011). Once induced, goats should have their tracheas intubated with a cuffed endotracheal tube to protect against aspiration of regurgitated ruminal contents (Dzikiti 2010; Galatos 2011; Reid *et al.* 1993; Taylor 1991). Of these induction agents, propofol and possibly ketamine possess pharmacokinetic profiles that make them suitable for TIVA for maintenance of general anaesthesia in goats.

Propofol

Propofol provides a rapid and smooth onset of induction that easily facilitates intubation in the goat (Dzikiti *et al.* 2010; Dzikiti *et al.* 2009; Larenza *et al.* 2005; Prassinos *et al.* 2005; Reid *et al.* 1993). Propofol causes induction apnoea more frequently than other general anaesthetics (Bettschart-Wolfensberger *et al.* 2000; Carroll *et al.* 1998; Langley & Heel 1988; Pablo, Bailey & Ko 1997), especially if administered too rapidly and at a high dose (Galatos 2011). Propofol causes dose-dependent cardiovascular and respiratory depression, implying a need to monitor these systems and take necessary corrective measures (intravenous fluid infusion, ventilation support) if required (Hodgkinson & Dawson 2007). Rapid metabolism and high body clearance make propofol suitable for IVA in goats either by intermittent incremental boluses or continuous infusion (Reid *et al*. 1993). In goats, propofol can be administered for TIVA on its own at a dose of 0.3 mg/kg/min – 0.6 mg/kg/min (12 mg/kg/h – 36 mg/kg/h), or in combination with other anaesthetic drugs at lower dosages adjusted to the effect required (Carroll *et al.* 1998; Dzikiti *et al.* 2010; Dzikiti, Stegmann, Cromarty, Dzikiti & Hellebrekers 2011; Larenza *et al.* 2005). Propofol should be combined with analgesic drugs in anaesthesia protocols for noxious procedures because it is devoid of any substantial analgesic effects (Beths 2008; Langley & Heel 1988; Sneyd 2004).

Ketamine

Ketamine is a commonly used general anaesthetic agent in veterinary practice that has recently gained greater popularity because of its suitability for use as an analgesic agent to prevent development of chronic pain when administered at sub-anaesthetic doses by continuous infusion (Valverde & Gunkel 2005; White, Way & Trevor 1982). It is a dissociative anaesthetic agent which has major advantages in comparison with other general anaesthetic agents because it mildly stimulates cardiovascular function via sympathomimetic effects and also provides analgesia as already stated (White *et al.* 1982). The major drawback with ketamine is inability to relax skeletal muscles, which has given rise to a need to always co-administer it with benzodiazepines to facilitate adequate muscle relaxation to enable intubation and minimise muscle excitation (Ghurashi *et al.* 2009; Prassinos *et al*. 2005). Ketamine causes less induction apnoea and respiratory depression in comparison with propofol in goats (Prassinos *et al*. 2005). Ketamine possesses most of the characteristics required for suitability for continuous IVA, lending itself well for field anaesthesia, but is longer acting and slightly more cumulative than propofol (Hodgkinson & Dawson 2007). Goats regain the swallowing reflex after more than 11 min following an intravenous bolus of ketamine (Prassinos *et al*. 2005), in comparison with less than 5 min

following a bolus of propofol (Dzikiti *et al.* 2009; Prassinos *et al*. 2005). Ketamine is used extensively in dogs (Aguado, Benito & Gómez de Segura 2011; Wilson *et al.* 2008) and horses (Enderle *et al.* 2008; Kruger & Stegmann 2009; Vallaba, Santiago & Gómez de Segura 2011) in sub-anaesthetic doses for partial intravenous anaesthesia (PIVA), but there are very few scientific reports on its use for the same purpose in goats. Previous studies report administration of ketamine for PIVA at doses of 0.03 mg/kg/min – 0.05 mg/kg/min (1.8 mg/kg/h – 3.0 mg/kg/h) in goats (Doherty *et al.* 2007; Larenza *et al.* 2005). Studies in other species have demonstrated that the major metabolic product of ketamine, norketamine, possesses significant anaesthetic effects, but has a shorter half-life than racemic ketamine (Hijazi & Boulieu 2002; Larenza *et al.* 2007). Following prolonged intravenous infusion, this active metabolite might accumulate and result in more pronounced anaesthetic effects. It is prudent therefore to monitor depth of anaesthesia carefully and consider reducing the infusion rate during very long ketamine infusions.

Alfaxalone (previously a component of saffan)

Intravenous administration of alfaxalone is characterised by a rapid onset of action, rapid redistribution and a short terminal half-life (Ferré *et al.* 2006; Suarez *et al*. 2012). It fulfils most properties of an ideal intravenous infusion anaesthetic agent and has several advantages over other drugs, including a very high therapeutic index that is even greater than that of propofol (Muir *et al.* 2008). Alfaxalone has recently been used as an induction agent in sheep (Andaluz *et al.* 2012). In that study, alfaxalone administered as an intravenous bolus at 2 mg/kg produced minimal adverse effects and uneventful recovery from anaesthesia. The few publications leaning towards alfaxalone in goats (Amer *et al.* 1989, 1990; Camburn 1982; Gibbons 1986) are outdated, as they are based on saffan, which has since been discontinued because of the histamine release that was linked to its stabiliser (Child *et al.* 1971; Dodman 1980; Sear *et al.* 1983). Alfaxalone was first introduced in 1971 as althesin and saffan, which were composed of a mixture of the two neurosteroids, alfaxalone and alfadolone acetate (Child *et al.* 1971; Sear *et al.* 1983), solubilised in 20% polyethoxylated castor oil (Cremophor-EL). A new formulation has since been developed for use in dogs and cats from alfaxalone (without alfadolone) solubilised in 2-hydroxypropyl-beta cyclodextrin (HPCD) (Ferré *et al.* 2006; Suarez *et al*. 2012). In future, alfaxalone could become useful for prolonged IVA in goats as well, if more research-based data on its pharmacokinetic profile in this species become available and its cost decreases.

Thiopentone

Thiopentone's pharmacokinetic profile makes it unsuitable for prolonged IVA. Maintaining general anaesthesia with thiopentone for any longer than 15 min progressively results in its accumulation in body tissues, which might result in delayed recovery from anaesthesia (Galatos 2011). For this reason, thiopentone should be used only for intravenous induction that would be followed by maintenance of general anaesthesia with other anaesthetic drugs, usually inhalation anaesthetic agents (Taylor 1991).

Sedative and analgesic agents for intravenous anaesthesia in goats

Opioids: Fentanyl

Opioids are used extensively for premedication, for analgesic supplementation during regional and general anaesthesia, as primary anaesthetic agents and as analgesics for postoperative pain (Clutton 1998; Stanski 2000). Whilst many opioids of high analgesic potency are suitable for prolonged IVA, fentanyl is currently commonly preferred in veterinary practice as it offers clinically desirable effects over a wide dose range and has a wide therapeutic margin (Mama 2006). Fentanyl, a synthetic μ-opioid agonist, is commonly used for the treatment of moderate to severe pain (Carroll *et al.* 1999; Lamont & Mathews 2007; Plumb 2005). The onset of action of fentanyl is rapid following intravenous administration, with analgesia, sedation, ataxia, respiratory depression and hyperaesthesia developing in 3 min – 8 min (Carroll *et al.* 1999; Lamont & Mathews 2007). It has a short duration of action, with the peak effect lasting less than 30 min (Carroll *et al.* 1999; Lee, Papich & Hardie 2000). Fentanyl has been administered intravenously as an adjunct to general anaesthetic drugs at doses of 0.002 mg/kg/h – 0.030 mg/kg/h in mechanically ventilated goats and at 0.020 mg/kg/h in spontaneously breathing goats without severely affecting vital physiological functions, although some insignificant signs of excitement (specifically tail-wagging) were observed at high dose rates (Andel *et al.* 2000; Dzikiti *et al.* 2010; Dzikiti, Stegmann, Dzikiti & Hellebrekers 2011a). Studies in humans and dogs have shown that fentanyl alone does not result in complete general anaesthesia, but can be combined with benzodiazepines or sub-anaesthetic doses of a general anaesthetic agent such as propofol to achieve satisfactory levels of general anaesthesia (Carroll *et al.* 1999; Stanski 2000).

The plasma concentration of fentanyl declines mainly as a result of redistribution to a large volume following a single bolus or a brief intravenous infusion (Mani & Morton 2010; Roberts & Freshwater-Turner 2007). If fentanyl is administered at a constant rate for a period longer than 3 h in humans, it attains a steady state (elimination occurring at the same rate as administration), in which case redistribution becomes less important and a rise in context-sensitive half-life (plasma half-life after a specified period of time) ensues (Roberts & Freshwater-Turner 2007). It is therefore not recommended to administer fentanyl at a constant rate for periods longer than 3 h, but rather by the TCI technique to avoid fentanyl accumulation in tissues (Mani & Morton 2010; Roberts & Freshwater-Turner 2007). For opioids with small volumes of distribution, such as remifentanil, redistribution is very limited and the context-sensitive half-life changes very little even after very long periods of CRI (Roberts & Freshwater-Turner 2007; Sneyd 2004).

Benzodiazepines: Midazolam and Valium

Midazolam and diazepam are the most commonly used benzodiazepines (Galatos 2011; Posner 2007). Both

benzodiazepines are fast-acting with short elimination half-lives (Lemke 2007; Posner 2007) making them suitable for prolonged IVA. Being water-soluble, midazolam can be administered by the intramuscular route as well as the intravenous route as it is non-irritant to tissues, unlike diazepam (Kanto 1985; Posner 2007). Diazepam, being insoluble in water, is delivered in propylene glycol, an organic solvent that causes pain with subcutaneous, intramuscular and intravenous injections and makes absorption after subcutaneous or intramuscular administration unpredictable (Posner 2007). Midazolam also has a shorter context-sensitive half-life than diazepam making it a better choice for prolonged IVA (Posner 2007). For premedication in goats, both midazolam and diazepam are usually administered at doses of 0.1 mg/kg – 0.5 mg/kg (Dzikiti *et al.* 2009; Ghurashi *et al.* 2009; Lemke 2007). Benzodiazepines cause mild and transient cardiovascular and respiratory effects and are commonly used as mild tranquillisers, potent muscle relaxants and anticonvulsants (Galatos 2011; Lemke 2007). The sedative and hypnotic effects of benzodiazepines are dose-dependent, with hypnosis attainable at intravenous doses of about 0.6 mg/kg following midazolam administration (Stegmann & Bester 2001). Midazolam has been administered intravenously as an adjunct to general anaesthetic drugs at doses of 0.1 mg/kg/h – 0.9 mg/kg/h in mechanically ventilated goats and at 0.3 mg/kg/h in spontaneously breathing goats, without adversely affecting vital physiological functions (Dzikiti *et al.* 2010; Dzikiti, Stegmann, Dzikiti & Hellebrekers 2011b).

Alpha-2 adrenergic agonists

Use of α_2-adrenoceptor agonists in small ruminants is highly controversial at the moment. Development of profound hypoxaemia in goats, but especially in sheep, has been documented with anaesthetic protocols that included α_2-adrenoceptor agonists such as xylazine, romifidine, detomidine and medetomidine (Celly *et al.* 1997; Kumar & Thurmon 1979; Mogoa, Stegmann & Guthrie 2000). For this reason, it is recommended to exercise caution when using these drugs in small ruminants (Carroll *et al.* 2005; Galatos 2011). Because the suitability of use of α_2-adrenoceptor agonists in goats is currently debatable, the author decided not to include literature on IVA with these drugs in goats in this review.

Intravenous anaesthesia adjuncts

In addition to the drugs discussed above, there are other non-anaesthesia specific drugs that can be incorporated into TIVA protocols for specific purposes in goats. Lidocaine and glycerol guaicolic ether (GGE) are amongst these adjuncts.

Lidocaine is traditionally used as a local analgesic and anti-arrhythmic agent (Cassutto & Gfeller 2003; Gintant, Hoffman & Naylor 1983), but has lately been administered by intravenous infusion in various species as an antioxidant and inflammatory modulator useful in preventing reperfusion injury (Cassutto & Gfeller 2003) and for reduction of requirements of inhalation anaesthetic agents during general anaesthesia in various species, including rats (DiFazio, Niederlehner & Burney 1976), ponies (Doherty & Frazier 1998), horses (Dzikiti, Hellebrekers & Van Dijk 2003), dogs (Mannarino *et al.* 2012; Valverde *et al.* 2004), cats (Pypendop & Ilkiw 2005) and calves (Vesal *et al.* 2011). Intravenously administered lidocaine depresses the central nervous system, specifically causing sedative, analgesic and anti-epileptic effects (Rademaker & De Vries 2008). In goats, intravenous lidocaine, administered as a bolus dose at 2.5 mg/kg followed by a CRI dose of 6.0 mg/kg/h, was reported to cause a clinically significant reduction in the concentration of isoflurane required for maintenance of general anaesthesia (Doherty *et al.* 2007).

Glycerol guaicolate is a central-acting muscle relaxant with a role in equine and bovine anaesthesia that is similar to that of the benzodiazepines (Galatos 2011; Hall *et al.* 2001; Riebold 2007). It is usually used in combination with induction agents such as ketamine to induce and maintain IVA of short duration (less than 1 h) (Riebold 2007). When it is administered for muscle relaxation just before induction of anaesthesia, the dose of GGE is about 50 mg/kg, whilst the infusion rate for PIVA is 50 mg/kg/h – 100 mg/kg/h (Hall *et al.* 2001; Riebold 2007). Endotracheal intubation and oxygen supplementation are recommended when GGE-incorporating anaesthetic protocols are used to minimise development of respiratory depression and hypoxaemia (Hall *et al.* 2001; Riebold 2007). Not much scientific information exists at present on the effects of GGE in goats, but its profile makes it suitable for continuous PIVA of short duration (up to 1 h long) if artificial ventilation cannot be provided.

Drug combinations for total intravenous anaesthesia in goats

In practical terms, the groups of drugs described above as suitable for IVA in goats can be used to achieve TIVA-based, balanced anaesthesia by utilising specific combinations to target individual components of the anaesthetic state (unconsciousness, analgesia, muscle relaxation) to achieve any desired purpose of anaesthesia in goats. Unconsciousness can be obtained from the propofol and ketamine, analgesia from fentanyl, ketamine and lidocaine, and muscle relaxation from benzodiazepines and possibly GGE. For TIVA in goats, propofol or ketamine can be combined with midazolam and fentanyl for both induction and maintenance of general anaesthesia. Table 1 summarises the dosages at which these drugs can be administered for the initial bolus and subsequent intermittent boluses or continuous infusion.

Monitoring the total intravenous anaesthesia -anaesthetised goat

Anaesthetised goats should be carefully monitored to ensure an appropriate anaesthetic depth and assessment of associated peri-anaesthetic complications, mostly involving the digestive system (tympany, regurgitation, excessive salivation) and the cardiorespiratory system (choking, hypercarbia, hypotension, hypoxaemia) (Galatos 2011; Taylor 1991). An appropriately anaesthetised goat may

TABLE 1: Summary of referenced dosages of drugs utilisable for intravenous anaesthesia in goats.

Drug	Dosage		
	Induction bolus (mg/kg)	Top-up bolus in already anaesthetised goats (mg/kg)	Infusion rate (mg/kg/h)
Propofol	3–7[a,b,c,d,e,f]	0.500–2.000[g,h]	12.000–36.000[a,b,e,f]
Ketamine	4–10[e]	1.500–3.000[i,h]	1.800–3.000[i,h]
Fentanyl	-	0.005–0.030[j,k]	0.002–0.030[j,j,k]
Midazolam	-	0.100–0.900[m]	0.100–0.900[m]
Lidocaine	-	2.500[i]	6.000[i]

Sources: [a], Bettschart-Wolfensberger *et al.* 2000; [b], Carroll *et al.* 1998; [c], Dzikiti *et al.* 2009; [d], Pablo, Bailey & Ko 1997; [e], Prassinos, Galatos & Raptopoulos 2005; [f], Reid, Nolan & Welsh 1993; [g], Dzikiti Stegmann, Cromarty, Dzikiti & Hellebrekers 2011; [h], Larenza *et al.* 2005; [i], Doherty *et al.* 2007; [j], Dzikiti *et al.* 2010; [k], Dzikiti, Stegmann, Dzikiti & Hellebrekers 2011a; [l], Andel *et al.* 2000; [m], Dzikiti Stegmann, Dzikiti & Hellebrekers 2011b.
For more information, please see the full reference list of the article, Dzikiti, T.B, 2013, 'Intravenous anaesthesia in goats: A review', *Journal of the South African Veterinary Association* 84(1), Art. #499, 8 pages. http://dx.doi.org/10.4102/jsava.v84i1.499

display sluggish palpebral and pedal reflexes as well as stable autonomic responses (Galatos 2011; Garcia 2012). If a goat is too deeply anaesthetised, the palpebral reflex and even corneal reflex will be absent, the cornea will dry up and severe bradypnoea and even apnoea may be observed. On the other hand, a lightly anaesthetised goat might blink, lachrymate, vocalise, salivate excessively, breathe more rapidly, swallow or even move its extremities (Galatos 2011; Garcia 2012). The rate of administration of intravenous drugs for maintenance of general anaesthesia should be guided by the signs of anaesthetic depth displayed by individual patients and not necessarily by known theoretical infusion rates.

Other basic parameters that can be monitored include heart rate, colour of the mucous membranes, capillary refill time, respiratory rate and body temperature (Galatos 2011; Garcia 2012; Taylor 1991). Symptomatic corrective therapy, which might include oxygen, fluids, electrolytes, specific drugs and patient therapy, should be instituted, where necessary, especially to ensure that circulation, respiration and body temperature stay within normal physiologic limits (Galatos 2011; Garcia 2012; Taylor 1991). During recovery from general anaesthesia, it is still essential to monitor the goat throughout, especially to avoid complications associated with the digestive and respiratory systems. The goat should be supported to sternal recumbency and the endotracheal tube only removed after the swallowing and coughing reflexes return (Galatos 2011; Garcia 2012; Taylor 1991).

Ethical considerations

This is a literature review article summarising observations from several scientific papers that were published in journals that require that the involvement of animals in research be conducted in accordance with relevant national and international ethical guidelines and that the research protocols be approved by the authors' institutional and relevant ethics committee.

Conclusion

General anaesthesia is used to produce unconsciousness, analgesia and muscle relaxation, but might also suppress autonomic reflex activities and consequently lead to inadequate function of vital physiological systems such as the cardiovascular and respiratory system (Antognini & Carstens 2002; Rees & Gray 1950). Use of inhalation anaesthetic agents to maintain general anaesthesia is associated with dose-dependent depression of the cardiopulmonary systems (Antognini & Eisele 1993; Hall *et al.* 2001; Hikasa *et al.* 2002). Balanced anaesthesia, a technique in which several drugs are combined at reduced dosages to decrease adverse effects of each drug, is used to limit cardiopulmonary depression associated with use of inhalation anaesthetic agents at high dosages to maintain general anaesthesia (Toner 2005). Incorporation of intravenous anaesthetic drugs in goat anaesthetic protocols would go a long way towards attaining balanced anaesthesia because the currently available inhalation anaesthetic agents do not have any significant muscle-relaxing or analgesic effects in goats. When applying balanced anaesthesia techniques, it is important to define the purpose of each drug used. Recent scientific papers have provided information on dosages of some drugs that can be successfully utilised for prolonged IVA in goats. It is envisaged that future scientific research will be conducted to provide more information on pharmacokinetic and pharmacodynamics profiles of currently suitable IVA drugs and other potential IVA drugs such as alfaxalone and remifentanil in goats.

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Competing interests

The author declares that he has no financial or personal relationships which may have inappropriately influenced him in writing this article.

References

Abrahamsen, E.J., 2008, 'Ruminant field anaesthesia', *Veterinary Clinics of North America: Food Animal Practice* 24, 429–441. http://dx.doi.org/10.1016/j.cvfa.2008.07.001, PMid:18929950

Aguado, D., Benito, J. & Gómez de Segura, I.A., 2011, 'Reduction of the minimum alveolar concentration of isoflurane in dogs using a constant rate of infusion of lidocaine-ketamine in combination with either morphine or fentanyl', *Veterinary Journal* 189, 63–66. http://dx.doi.org/10.1016/j.tvjl.2010.05.029, PMid:20594878

Amer, H.A., Ahmed, A.S., Gohar, H.M. & Abdel Mamid, M.A., 1989, 'Effects of steroid anaesthesia on some liver function tests in goats', *Journal of Steroid Biochemistry* 32, 475–476. http://dx.doi.org/10.1016/0022-4731(89)90225-2

Amer, H.A., Ahmed, A.S., Gohar, H.M. & Abdel Mamid, M.A., 1990, 'Biochemical effect of steroid anaesthesia on some liver function tests in goats', *Archiv für Experimentelle Veterinärmedizin* 44, 361–366. PMid:2241474

Andaluz, A., Felez-Ocana, N., Santos, L., Fresno, L. & Garcia, F., 2012, 'The effects on cardio-respiratory and acid-base variables of the anaesthetic alfaxalone in a 2-hydroxypropyl-β-cyclodextrin (HPCD) formulation in sheep', *Veterinary Journal* 191, 389–392. http://dx.doi.org/10.1016/j.tvjl.2011.03.017, PMid:21543243

Andel, H., Bayer, G.S., Ciovica, R., Monsivais, J., Bacso, M., Zimpfer, M. *et al.*, 2000, 'Depressive effect of isoflurane on motor evoked potentials in the Nubian goat', *Canadian Journal of Anaesthesia* 47, 81–86. http://dx.doi.org/10.1007/BF03020739, PMid:10626726

Antognini, J.F. & Carstens, E., 2002, '*In vivo* characterization of anaesthesia and its components', *British Journal of Anaesthesia* 89, 156–166. http://dx.doi.org/10.1093/bja/aef156, PMid:12173227

Antognini, J.F. & Eisele, P.H., 1993, 'Anaesthetic potency and cardiopulmonary effects of enflurane, halothane and isoflurane in goats', *Laboratory Animal Science* 43, 607–610. PMid:8158989

Askitopoulou, H., Ramoutsaki, I.A. & Konsolaki, E., 2000, 'Analgesia and anesthesia: Etymology and literary history of related Greek words', *Anesthesia Analgesia* 91, 486–491. PMid:10910873

Beths, T., 2008, 'Total intravenous anaesthesia in dogs: Development of a target-controlled infusion (TCI) scheme for propofol', PhD thesis, Department of Companion Animal Sciences, University of Glasgow, viewed 14 June 2012, from http://theses.gla.ac.uk/354/01/2008bethsphd.pdf

Bettschart-Wolfensberger, R., Semder, A., Alibhai, H., Demuth, D., Aliabadi, F.S. & Clarke, K.W., 2000, 'Cardiopulmonary side-effects and pharmacokinetics of an emulsion of propofol (Disoprivan) in comparison to propofol solved in polysorbate 80 in Goats', *Journal of Veterinary Medicine A* 47, 341–350. http://dx.doi.org/10.1046/j.1439-0442.2000.00289.x

Briggs, D., 2003, 'Environmental pollution and the global burden of disease', *British Medical Bulletin* 68, 1–24. http://dx.doi.org/10.1093/bmb/ldg019, PMid:14757707

Camburn, M.A., 1982, 'Use of alphaxalone-alphadolone in ruminants', *Veterinary Record* 111, 166–167. http://dx.doi.org/10.1136/vr.111.8.166, PMid:7135786

Carroll, G.L., Hartsfield, S.M., Champney, S.M., Geller, S.C., Martinez, E.A. & Haley, E.L., 2005, 'Effect of medetomidine and its antagonism with atipamezole on stress-related hormones, metabolites, physiologic responses, sedation, and mechanical threshold in goats', *Veterinary Anaesthesia and Analgesia* 32, 147–157. http://dx.doi.org/10.1111/j.1467-2995.2005.00187.x, PMid:15877661

Carroll, G.L., Hartsfield, S.M. & Hambleton, R., 1997, 'Anesthetic effects of tiletamine-zolazepam, alone or in combination with butorphanol, in goats', *Journal of the American Veterinary Medical Association* 211, 593–597. PMid:9290827

Carroll, G.L., Hooper, R.N., Boothe, D.M., Hartsfield, S.M. & Randoll, L.A., 1999, 'Pharmacokinetics of fentanyl after intravenous and transdermal administration in goats', *American Journal of Veterinary Research* 60, 986–991. PMid:10451210

Carroll, G.L., Hooper, R.N., Slater, M.R., Hartsfield, S.M. & Matthews, N.S., 1998, 'Detomidine-butorphanol-propofol for carotid artery translocation and castration or ovariohysterectomy in goats', *Veterinary Surgery* 27, 75–82. http://dx.doi.org/10.1111/j.1532-950X.1998.tb00101.x, PMid:9449181

Cassutto, B.H. & Gfeller, R.W., 2003, 'Use of intravenous lidocaine to prevent reperfusion injury and subsequent multiple organ dysfunction syndrome', *Journal of Veterinary Emergency and Critical Care* 13, 137–148. http://dx.doi.org/10.1046/j.1435-6935.2003.00080.x

Caulkett, N., 2003, 'Anaesthesia of ruminants', *Large Animal Veterinary Rounds* 3(2), viewed 20 June 2012, from http://www.larounds.ca/crus/laveng_0203.pdf

Celly, C.S., McDonell, W.N., Young, S.S. & Black, W.D., 1997, 'The comparative effect of four α_2-adrenoceptor agonists (xylazine, romifidine, detomidine and medetomidine) in sheep', *Journal of Veterinary Pharmacology and Therapeutics* 20, 464–471. http://dx.doi.org/10.1046/j.1365-2885.1997.00097.x, PMid:9430770

Child, K.J., Currie, J.P., Dis, B., Dodds, M.G., Pearce, D.R. & Twissell, D.J., 1971, 'The pharmacological properties in animals of CT1341 – A new steroid anaesthetic agent', *British Journal of Anaesthesia* 43, 2–13. http://dx.doi.org/10.1093/bja/43.1.2-a, PMid:4251319

Clutton, R.E., 1998, 'New drugs in companion animal anesthesia', *Waltham Focus* 8, 9–16.

DiFazio, C.A., Niederlehner, J.R. & Burney, R.G., 1976, 'The anesthetic potency of lidocaine in the rat', *Anesthesia and Analgesia* 55, 818–821. http://dx.doi.org/10.1213/00000539-197611000-00016, PMid:1033700

Dodman, N.H., 1980, 'Complications of saffan anaesthesia in cats', *Veterinary Record* 107, 481–483. http://dx.doi.org/10.1136/vr.107.21.481, PMid:6160674

Doherty, T.J. & Frazier, D.L., 1998, 'Effect of lidocaine on halothane minimum alveolar concentration in ponies', *Equine Veterinary Journal* 30, 300–303. http://dx.doi.org/10.1111/j.2042-3306.1998.tb04101.x, PMid:9705112

Doherty, T., Redua, M.A., Queiroz-Castro, P., Egger, C., Cox, S.K. & Rohrbach, B.W., 2007, 'Effect of intravenous lidocaine and ketamine on the minimum alveolar concentration of isoflurane in goats', *Veterinary Anaesthesia and Analgesia* 34, 125–131. http://dx.doi.org/10.1111/j.1467-2995.2006.00301.x, PMid:17316393

Dundee, J.W. & McMurray, T.J., 1984, 'Clinical aspects of total intravenous anaesthesia: Discussion paper', *Journal of the Royal Society of Medicine* 77, 669–672. PMid:6148418

Dzikiti, T.B., 2010, 'Total intravenous anaesthesia (TIVA) in goats', PhD thesis, Department of Companion Animal Clinical Studies, University of Pretoria, viewed 12 June 2012, from http://upetd.up.ac.za/thesis/available/etd-05312011-150533/

Dzikiti, T.B., Hellebrekers, L.J. & Van Dijk, P., 2003, 'Effects of intravenous lidocaine on isoflurane concentration, physiological parameters, metabolic parameters and stress-related hormones in horses undergoing surgery', *Journal of Veterinary Medicine A* 50, 190–195. http://dx.doi.org/10.1046/j.1439-0442.2003.00523.x

Dzikiti, T.B., Stegmann, G.F., Dzikiti, L.N. & Hellebrekers, L.J., 2010, 'Total intravenous anaesthesia (TIVA) with propofol-fentanyl and propofol-midazolam combinations in spontaneously breathing goats', *Veterinary Anaesthesia and Analgesia* 37, 519–525. http://dx.doi.org/10.1111/j.1467-2995.2010.00568.x, PMid:21072973

Dzikiti, T.B., Stegmann, G.F., Dzikiti, L.N. & Hellebrekers, L.J., 2011a, 'Effects of fentanyl on isoflurane minimum alveolar concentration and cardiovascular function in mechanically-ventilated goats', *Veterinary Record* 168, 429. http://dx.doi.org/10.1136/vr.d999, PMid:21493442

Dzikiti, T.B., Stegmann, G.F., Dzikiti, L.N. & Hellebrekers, L.J., 2011b, 'Effects of midazolam on isoflurane minimum alveolar concentration and cardiovascular function goats', *Small Ruminant Research* 97, 104–109. http://dx.doi.org/10.1016/j.smallrumres.2011.01.011

Dzikiti, T.B., Stegmann, G.F., Hellebrekers, L.J. & Dzikiti, L.N., 2009, 'Sedative and cardiopulmonary effects of acepromazine, midazolam, butorphanol, acepromazine-butorphanol and midazolam-butorphanol on propofol anaesthesia in goats', *Journal of the South African Veterinary Association* 80, 10–16. PMid:19653513

Dzikiti, T.B., Stegmann, G.F., Cromarty, D., Dzikiti, L.N. & Hellebrekers, L.J., 2011, 'Effects of propofol on isoflurane minimum alveolar concentration and cardiovascular function in mechanically ventilated goats', *Veterinary Anaesthesia and Analgesia* 38, 44–53. http://dx.doi.org/10.1111/j.1467-2995.2010.00585.x, PMid:21214709

Enderle, A.K., Levionnois, O.L., Kuhn, M. & Schatzmann, U., 2008, 'Clinical evaluation of ketamine and lidocaine intravenous infusions to reduce isoflurane requirements in horses under general anaesthesia', *Veterinary Anaesthesia and Analgesia* 35, 297–305. http://dx.doi.org/10.1111/j.1467-2995.2007.00391.x, PMid:19522888

Fajt, V.R., 2011, 'Drug laws and regulations for sheep and goats', *Veterinary Clinics of North America: Food Animals* 27, 1–21. http://dx.doi.org/10.1016/j.cvfa.2010.10.006

Ferré, P.J., Pasloske, K., Whittem, T., Ranasinghe, M., Li, Q. & Lefebvre, H.P., 2006, 'Plasma pharmacokinetics of alfaxalone in dogs after an intravenous bolus of Alfaxan-CD RTU', *Veterinary Anaesthesia and Analgesia* 33, 229–236. http://dx.doi.org/10.1111/j.1467-2995.2005.00264.x, PMid:16764587

Fulton, L.K., Clarke, M.S. & Farris, H.E., 1994, 'The goat as a model for biomedical research and teaching', *Institute for Laboratory Animal Research* 36, 21–29.

Galatos, A.D., 2011, 'Anesthesia and analgesia in sheep and goats', *Veterinary Clinics of North America: Food Animals* 27, 47–59. http://dx.doi.org/10.1016/j.cvfa.2010.10.007, PMid:21215889

Garcia, M., 2012, *Laboratory animal anesthesia and analgesia*, viewed 29 October 2012, from http://www.research.ucsb.edu/compliance/animal-subjects/veterinary-care/laboratory-animal-anesthesia-and-analgesia/

Ghurashi, M.A.H., Seri, H.I., Bakheit, A.H., Ashwag, E.A.M. & Abakar, J.A., 2009, 'Evaluation of ketamine/diazepam anaesthesia for performing surgery in desert goats under field conditions', *Australian Journal of Basic and Applied Sciences* 3, 455–459.

Gibbons, R.W., 1986, 'Anaesthesia of kids with alphaxalone/alphadolone', *Veterinary Record* 119, 339. http://dx.doi.org/10.1136/vr.119.13.339-c, PMid:3776047

Gintant, G.A., Hoffman, B.F. & Naylor, R.E., 1983, 'The influence of molecular form of local anesthetic-type antiarrhythmic agents on reduction of minimum upstroke velocity of canine Purkinje fibers', *Circulation Research* 52, 735–746. http://dx.doi.org/10.1161/01.RES.52.6.735, PMid:6305532

Griffith, H.R., 1934, 'John Snow, pioneer specialist in anesthesia', *Anesthesia and Analgesia* 13, 45. http://dx.doi.org/10.1213/00000539-193401000-00019

Hall, L.W., Clarke, K.W. & Trim, C.M., 2001, *Veterinary anaesthesia*, 10th edn., WB Saunders, London.

Harvinder, S.G. & Prausnitz, M.R., 2007, 'Does size matter?', *Journal of Diabetes Science and Technology* 1, 725–729.

Hasley, M.J., 1991, 'Occupational health and pollution from anaesthetics. A report of a seminar', *Anaesthesia* 46, 486–488. http://dx.doi.org/10.1111/j.1365-2044.1991.tb11692.x

Hatschbach, E., Silva, F.C., Beier, S.L., Lima, A.F. & Massone, F., 2008, 'Comparative study between target-controlled infusion and continuous-infusion anesthesia in dogs treated with methotrimeprazine and treated with propofol and remifentanil', *Acta Cirurgica Brasileira* 23, 65–72. http://dx.doi.org/10.1590/S0102-86502008000100011, PMid:18278395

Hijazi, J. & Boulieu, R., 2002, 'Contribution of CYP3A4, CYP2B6 and CYP2C9 isoforms to N-demethylation of ketamine in human liver microsomes', *Drug Metabolism and Disposition* 30, 853–858. http://dx.doi.org/10.1124/dmd.30.7.853, PMid:12065445

Hikasa, Y., Hokushini, S., Takase, K. & Ogasawara, S., 2002, 'Cardiopulmonary, haematological, serum biochemical and behavioural effects of sevoflurane compared with isofurane or halothane in spontaneously ventilating goats', *Small Ruminant Research* 43, 167–178. http://dx.doi.org/10.1016/S0921-4488(02)00002-0

Hodgkinson, O. & Dawson, L., 2007, 'Practical anaesthesia and analgesia in sheep, goats and calves', *In Practice* 29, 596–603. http://dx.doi.org/10.1136/inpract.29.10.596

Hofer, C.K., Zollinger, A., Büchi, S., Klaghofer, R., Serafino, D., Bühlmann, S. *et al.*, 2003, 'Patient well-being after general anaesthesia: A prospective, randomized, controlled multi-centre trial comparing intravenous and inhalation anaesthesia', *British Journal of Anaesthesia* 91, 631–637. http://dx.doi.org/10.1093/bja/aeg243, PMid:14570783

Joubert, K.E., 2009, 'Computer simulations of propofol infusions for total intravenous anaesthesia in dogs', *Journal of the South African Veterinary Association* 80, 2–9. PMid:19653512

Kanto, J.H., 1985, 'Midazolam: The first water-soluble benzodiazepine. Pharmacology, pharmacokinetics and efficacy in insomnia and anesthesia', *Pharmacotherapy* 5, 138–155. PMid:3161005

Kravetz, R.E., 2005, 'Hypodermic syringe', *American Journal of Gastroenterology* 100, 2614–2615. http://dx.doi.org/10.1111/j.1572-0241.2005.00397.x, PMid:16393208

Kruger, K. & Stegmann, G.F., 2009, 'Partial intravenous anaesthesia in 5 horses using ketamine, lidocaine, medetomidine and halothane', *Journal of the South African Veterinary Association* 80, 233–236. PMid:20458864

Kumar, A. & Thurmon, J.C., 1979, 'Cardiopulmonary, haematocytologic and biochemical effects of xylazine in goats', *Laboratory Animal Science* 29, 486–491. PMid:513619

Lamont, A. & Mathews, K.A., 2007, 'Opioids, non-steroidal anti-inflammatories, and analgesic adjuvants', in W.J. Tranquilli, J.C. Thurmon & K.A. Grimm (eds.), *Lumb and Jones's veterinary anaesthesia and analgesia*, 4th edn., pp. 241–271, Blackwell Publishing, Ames.

Langley, M.S. & Heel, R.C., 1988, 'Propofol: A review of its pharmacodynamics and pharmacokinetic properties and use as an intravenous anaesthetic', *Drugs* 35, 334–372. http://dx.doi.org/10.2165/00003495-198835040-00002, PMid:3292208

Larenza, M.P., Bergadano, A., Iff, I., Doherr, M.G. & Schatzmann, U., 2005, 'Comparison of the cardiopulmonary effects of anaesthesia maintained by continuous infusion of ketamine and propofol with anaesthesia maintained by inhalation of sevoflurane in goats undergoing magnetic resonance imaging', *America Journal of Veterinary Research* 66(12), 2135–2141. http://dx.doi.org/10.2460/ajvr.2005.66.2135, PMid:16379659

Larenza, M.P., Landoni, M.F., Levionnois, O.L., Knobloch, M., Kronen, P.W., Theurillat, R. *et al.*, 2007, 'Stereoselective pharmacokinetics of ketamine and norketamine after racemic ketamine or S-ketamine administration during isoflurane anaesthesia in Shetland ponies', *British Journal of Anaesthesia* 98, 204–212. http://dx.doi.org/10.1093/bja/ael336, PMid:17218377

Lee, D.D., Papich, M.G. & Hardie, E.M., 2000, 'Comparison of pharmacokinetics of fentanyl after intravenous and transdermal administration in cats', *America Journal of Veterinary Research* 61, 672–677. http://dx.doi.org/10.2460/ajvr.2000.61.672, PMid:10850844

Lemke, K.A., 2007, 'Anticholinergics and sedatives', in W.J. Tranquilli, J.C. Thurmon & K.A. Grimm (eds.), *Lumb and Jones's veterinary anaesthesia and analgesia*, 4th edn., pp. 203–239, Blackwell Publishing, Ames.

Mama, K., 2006, 'Clinical application of pharmacokinetics for balanced anaesthesia in small and large animals', *9th World Congress of Veterinary Anaesthesia 2006 proceedings*, Santos SP, Brazil, 12–16 September 2006, pp. 89–91.

Mani, V. & Morton, N.S., 2010, 'Overview of total intravenous anaesthesia in children', *Pediatric Anesthesia* 20, 211–222.

Mannarino, R., Luna, S.P.L., Monteiro, E.R., Beier, S.L. & Castro, V.B., 2012, 'Minimum infusion rate and haemodynamic effects of propofol, propofol-lidocaine and propofol-lidocaine-ketamine in dogs', *Veterinary Anaesthesia and Analgesia* 39, 160–173. http://dx.doi.org/10.1111/j.1467-2995.2011.00679.x, PMid:22248386

McKenzi, G., 2008, 'Total intravenous anesthesia – TIVA', *Iranian Journal of Veterinary Surgery* suppl. 2 (2nd ISVS and 7th ISVSAR), 108–117.

Moens, Y., 2004, 'Syringe pumps for anaesthesia/analgesia: Toy or tool?', *29th World Congress of the World Small Animal Veterinary Association proceedings*, Rhodes, Greece, 06–09 October 2004, viewed 12 June 2012, from http://www.vin.com/proceedings/Proceedings.plx?CID=WSAVA2004&PID=8565&Print=1&O=Generic

Mogoa, E.G.M., Stegmann, G.F. & Guthrie, A.J., 2000, 'Effects of xylazine on acid-base balance and arterial blood-gas tensions in goats under different environmental temperature and humidity conditions', *Journal of the South African Veterinary Association* 71, 229–231. PMid:11212933

Muir, W., Lerche, P., Wiese, A., Nelson, L., Pasloske, K. & Whittem, T., 2008, 'Cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in dogs', *Veterinary Anaesthesia and Analgesia* 35, 451–462. http://dx.doi.org/10.1111/j.1467-2995.2008.00406.x, PMid:18793290

Pablo, L.S., Bailey, J.E. & Ko, J.C.H., 1997, 'Median effective dose of propofol required for induction of anaesthesia in goats', *Journal of the American Veterinary Medical Association* 211, 86–88. PMid:9324507

Plumb, D.C., 2005, *Plumb's veterinary drug book*, 5th edn., PharmaVet Inc., Stockholm.

Posner, L.P., 2007, 'Midazolam or diazepam – Which should I choose in my practice?', viewed 14 February 2008, from http://www.ivis.org/proceedings/navc/2007/SAE/031.asp?LA=1

Prassinos, N.N., Galatos, A.D. & Raptopoulos, D., 2005, 'A comparison of propofol, thiopental or ketamine as induction agents in goats', *Veterinary Anaesthesia and Analgesia* 32, 289–296. http://dx.doi.org/10.1111/j.1467-2995.2005.00204.x, PMid:16135210

Pypendop, B.H. & Ilkiw, J.E., 2005, 'The effects of intravenous lidocaine administration on the minimum alveolar concentration of isoflurane in cats', *Anesthesia and Analgesia* 100, 97–101. http://dx.doi.org/10.1213/01.ANE.0000139350.88158.38, PMid:15616060

Rademaker, C.M.A. & De Vries, L.S., 2008, 'Pharmacology review: Lidocaine for neonatal seizure management', *Neoreviews* 9, e585–e589, viewed 22 June 2012, from http://neoreviews.aappublications.org/content/9/12/e585.full.pdf

Rees, G.J. & Gray, T.C., 1950, 'Methyl-n-propyl ether', *British Journal of Anaesthesia* 22, 83–91. http://dx.doi.org/10.1093/bja/22.2.83, PMid:15411475

Reid, J., Nolan, A.M. & Welsh, E., 1993, 'Propofol as an induction agent in the goat: A pharmacokinetic study', *Journal of Veterinary Pharmacology and Therapeutics* 16, 488–493. http://dx.doi.org/10.1111/j.1365-2885.1993.tb00215.x, PMid:8126766

Riebold, T.W., 2007, 'Ruminants', in W.J. Tranquilli, J.C. Thurmon & K.A. Grimm (eds.), *Lumb and Jones's veterinary anaesthesia and analgesia*, 4th edn., pp. 731–746, Blackwell Publishing, Ames.

Roberts, F. & Freshwater-Turner, D., 2007, 'Pharmacokinetics and anaesthesia', *Continuing Education in Anaesthesia, Critical Care and Pain* 7, 25–29. http://dx.doi.org/10.1093/bjaceaccp/mkl058

Sear, J.W., Phillips, K.C., Andrews, C.J.H. & Prys-Roberts, C., 1983, 'Dose-response relationships of infusions of althesin or methohexitone', *Anesthesia* 38, 931. http://dx.doi.org/10.1111/j.1365-2044.1983.tb12021.x

Sneyd, J.R., 2004, 'Recent advances in intravenous anaesthesia', *British Journal of Anaesthesia* 93, 725–736. http://dx.doi.org/10.1093/bja/aeh253, PMid:15347606

Stanski, D.R., 2000, 'Monitoring depth of anaesthesia', in R.D. Miller, *Anaesthesia*, 5th edn., pp. 1087–1113, Churchill Livingstone, New York.

Stegmann, G.F. & Bester, L., 2001, 'Sedative-hypnotic effects of midazolam in goats after intravenous and intramuscular administration', *Veterinary Anaesthesia and Analgesia* 28, 49–55. http://dx.doi.org/10.1046/j.1467-2987.2000.00034.x

Suarez, M.A., Dzikiti, B.T., Stegman, F.G. & Hartman, M., 2012, 'Comparison of alfaxalone and propofol administered as total intravenous anaesthesia for ovariohysterectomy in dogs', *Veterinary Anaesthesia and Analgesia* 39, 236–244. http://dx.doi.org/10.1111/j.1467-2995.2011.00700.x, PMid:22405473

Taylor, P.M., 1991, 'Anaesthesia in sheep and goats', *In Practice* 13, 31–36. http://dx.doi.org/10.1136/inpract.13.1.31

Toner, P.H., 2005, 'Balanced anaesthesia today', *Best Practice and Research: Clinical Anaesthesiology* 19, 475–484. http://dx.doi.org/10.1016/j.bpa.2005.02.005

Vallaba, M., Santiago, I. & Gómez de Segura, I.A., 2011, 'Effects of constant rate infusion of lidocaine and ketamine, with or without morphine on isoflurane minimum alveolar concentration in horses', *Equine Veterinary Journal* 43, 721–726. http://dx.doi.org/10.1111/j.2042-3306.2010.00355.x, PMid:21668490

Valverde, A. & Doherty, T.J., 2008, 'Anesthesia and analgesia in ruminants', in R. Fish, P.J. Danneman, M. Brown & A. Karas (eds.), *Anesthesia and analgesia in laboratory animals*, 2nd edn., pp. 385–411, Academic Press, London. http://dx.doi.org/10.1016/B978-012373898-1.50018-8

Valverde, A., Doherty, T.J., Hernández, J. & Davies, W., 2004, 'Effect of lidocaine on halothane minimum alveolar concentration in dogs', *Veterinary Anaesthesia and Analgesia* 31, 264–271. http://dx.doi.org/10.1111/j.1467-2995.2004.00165.x, PMid:15509291

Valverde, A. & Gunkel, C.I., 2005, 'Pain management in horses and farm animals', *Journal of Emergency and Critical Care* 15, 295–307. http://dx.doi.org/10.1111/j.1476-4431.2005.00168.x

Vesal, N., Spadavecchia, C., Steiner, A., Kirscher, F. & Levionnois, O.L., 2011, 'Evaluation of the isoflurane-sparing effects of lidocaine infusion during umbilical surgery in calves', *Veterinary Anaesthesia and Analgesia* 38, 451–460. http://dx.doi.org/10.1111/j.1467-2995.2011.00636.x, PMid:21831050

Waelbers, T., Vermoere, P. & Polis, I., 2009, 'Total intravenous anaesthesia in dogs. A review', *Vlaams Diergeneeskundie Tijdschrift* 78, 160–169.

White, P.F., Way, W.L. & Trevor, A.J., 1982, 'Ketamine – Its pharmacology and therapeutic uses', *Anesthesiology* 56, 119–136. http://dx.doi.org/10.1097/00000542-198202000-00007, PMid:6892475

Wilson, J., Doherty, T.J., Egger, C.M., Fidler, A., Cox, S. & Rohrbach, B., 2008, 'Effects of intravenous lidocaine, ketamine, and the combination on the minimum alveolar concentration of sevoflurane in dogs', *Veterinary Anaesthesia and Analgesia* 35, 289–296. http://dx.doi.org/10.1111/j.1467-2995.2007.00389.x, PMid:18363578