Ministry of Higher Education and
Scientific Research
University of Al-Qadisiyah
College of Veterinary Medicine

Injectable general anesthesia In small ruminant

A Research
Submitted to the Department of Veterinary Medicine/ College of Veterinary Medicine-University of Al-Qadisiyah in Partial Fulfillment of the Requirements for the Degree of BVMS in Veterinary Medicine

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2017 HD *1438 AH*

بسم الله الرحمن الرحيم

(وَقُل رَّبِّ زِدْنِي عِلْماً)

صدق الله العلي العظيم

جزء من الآية/١١٤ سورة طه

Supervisor Certification

I certify that this research entitled, (**Injectable general anesthesia in small ruminant**), was prepared under my supervision at the College of Veterinary Medicine/ University of Al-Qadisiyah in partial fulfillment of the requirements for the degree of BVMS in Veterinary Medicine

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/ / 2017

Summary

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

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Literatures Review

2-1 Pain:

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is a complex phenomenon based on pathophysiological and psychological components often difficult to recognize and interpret in the animals (Ott and short, 1998; Leonardi *et al.*, 2006).

In recent years more attention has been paid to the issue of pain in animals, particularly in association with increasing awareness of animal welfare. It is therefore necessary for veterinarians to be able to recognize an confusingly whether an animal suffers from pain or not. In animals we have to recognize the signs of pain according to indirect markers which involve behavioral, physiological and finally clinical responses (Landa, 2012). Current approaches about animal welfare have increased the important of pain management in livestock. Even minor surgical procedures in livestock are now performed using a combination of regional, local, or general anesthesia combined with uninterrupted post-surgical analgesia (George, 2003).

2-2 Analgesia:

Analgesia is a absent of pain in response to stimulation which would normally be painful. Although the animal considered to be unconscious during general anesthesia and, therefore, incapable of gaining pain, there is now evidence that the use of analgesic drugs before and during general anesthesia assists in obtaining a smooth, pain-free recovery. All general anesthetics undoubtedly have an intrinsic analgesic action but further analgesia can be provided by four main methods:

1. Use of local analgesics. 2. Use of α_2-adrenoceptor agonists. 3. Use of non-steroidal anti-inflammatory drugs (NSAIDs) 4. Use of opioid drugs.

With all of these drugs, there is now definite evidence that they are more effective if administered before pain becomes noticeable (Hall, *et al.* 2001).

2-3 Anesthesia in small ruminants:

Ruminants are classically considered farm animals and are often intended for the production of food, these species are used extensively in research and teaching and they are increasingly important as companion animals. Sheep is one of the most widely used reproductive animals and for human's life also for biomedical research. The anesthetic and analgesic drugs and techniques should be used to ensure minimal stress and discomfort during the perioperative period (Taylor, 1991; Lee, 2006).

Rough manipulation of the sheep and when excited may struggle vigorously. This may lead to musculoskeletal trauma, and severe stress. Therefore, anesthesia and analgesia are essential in the management of sheep, and a safe anesthetic method is needed both for surgeon undertaking research and fore practicing veterinarian. Injectable anesthetics also can be used for the induction and maintenance of short term anesthesia. It is preferred inhalant anesthesia, however the inhalational anesthesia should be considered for high-risk animals or prolonged and complicated surgical procedures. Injectable anesthesia is safer, easy and not required highly expensive equipment, therefore, parenteral anesthetic are often preferred in this species. Ketamine, thiopental, and propofol are the most commonly used injectable anesthetic drugs in sheep (Tayler, 1991; Lin,et al., 1997; Galatos, 2011).

The IM use of xylazine-ketamine mixture in one injection is used as a general anesthesia in sheep in a dose of 10 mg/k.g B.W of Ketamine and 0.2 mg/k.g B.W of xylazine. It give 31.08±2.8 minutes of anesthesia, with good analgesia, good muscle relaxation, and fast and smooth recovery. While all reflexes are not abolished during anesthesia, bloat also not

developed although the animals not fasted (Abid, 2004). Ketamine xylazine combination can be used as a more suitable anesthetic combination in experimental surgical procedures such as maxillofacial surgery than ketamine diazepam combination in sheep (OzKan *et al.,* 2010). Propofol is characterized by, no analgesia, rapid and smooth induction, short duration of anesthesia, with rapid recovery time (Prassinos, *et al.* 2005)

2-4 Balanced Anesthesia:

Balanced Anesthesia is the technique in which a number of different agents are combined to produce a desired effect. The combination of more than one drug in small doses is used to minimize the dose and subsequently the side-effects of each one of these drugs. It refers to the use of a mixture of these drugs in small amounts of each one to avoid the disadvantages of the large doses of any one. This technique requires a systematic clinical, and pharmacological understanding of the methods of administration, the interaction of these drugs, and the ability to manage the patient before, during, and after the administration of anesthesia. Thus, in a balanced anesthetic technique, anesthesia is produced by using several drugs, often administered by different routes, which can be detoxified and excreted in different ways. In veterinary practice, especially in small animal anesthesia, the inhalant drugs are usually administered alone to maintain anesthesia. Unfortunately, the cardiopulmonary function is reduced in dose-dependent manner by inhalant drugs and deepening the level of anesthesia in order to modify autonomic responses to noxious stimuli may increase morbidity and mortality. For that now the use of balanced anesthesia is increased to minimize the effect of these drugs on the cardiopulmonary systems. Both partial intravenous anesthesia technique (PIVA) (when use the injectable anesthetics and analgesics drugs with the inhalation anesthesia) (Duke, 2013), and total intravenous anesthesia

techniques (TIVA) (when only the injectable drugs are used through the whole time of anesthesia) (Dzikiti, *et al.*, 2010) are used in balanced anesthesia.

2-5 Total Intravenous Anaesthesia (TIVA):

Total intravenous anesthesia (TIVA) is becoming a vital technique for general anesthesia and a stable anesthetic model for some animal species, especially dogs and horses (Doherty and Valverde, 2006; Ortega and Cruz 2011; Valverde, 2013), also in sheep (Vesal and Oloumi, 1998), and recently in goats (Dzikiti, 2013)

when the TIVA might be the only practically possible way to achieve general anesthesia. It is a technique that involves the use of only injectable anesthetics for induction and to maintain an adequate depth of anesthesia for a directed level of central nervous system depression, such as, hypnosis for diagnostic procedures or surgical anesthesia for painful interventions (Dzikiti, 2013).

In veterinary practice, intravenous anesthetic drugs are commonly used as induction agents to facilitate endotracheal intubation, whilst inhalation anesthetic agents form the foundation for maintenance of general anesthesia. Inhalation anesthesia may not be applicable in all situations where anesthesia is required. General anesthesia can then be maintained by intravenous drugs in those situations. Intravenous anesthesia (IVA), instead of inhalation anesthesia, could soon become an conventional means of anesthetic provision for both induction and maintenance of anesthesia in veterinary practice. In goats general anesthesia can be induced 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 5mg/kg-20mg/kg, 3mg/kg-7mg/kg and 4mg/kg-15mg/kg respectively (Hall *et al*., 2001; Dzikiti, 2013). Of these induction agents,

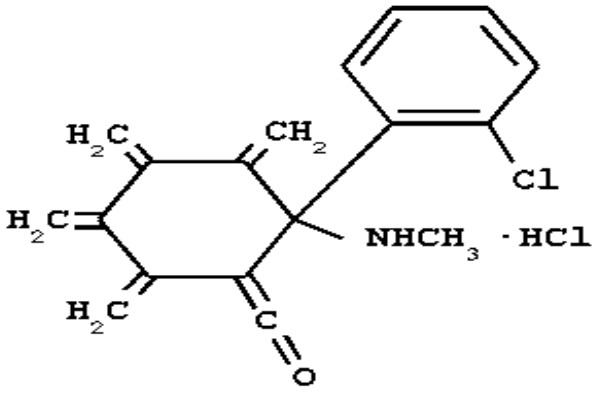
the propofol and possibly ketamine possess pharmacokinetic profiles that make them suitable for TIVA of maintenance of general anesthesia in goats (Dzikiti, 2013).

2-6 Ketamine:

Ketamine is a short-acting dissociative anesthetic for chemical restraint and surgical anesthesia in domestic and non-domestic animals
(De Lucas *et al*., 2007). It can be used singly or in combination for pre- and intraoperative sedation, induction, and maintenance of anesthesia, balanced anesthetic applications, regional and spinal anesthesia, and postoperative analgesia (Ozkan *et al.*, 2010; Malik *et al.*, 2011).

2-6-1 Chemical Structure:

Ketamine is 2-(O-chlorophenyl)-2-(methylamine)-cyclohexanone chloride .



(Bergman, 1999).

2-6-2 Mechanism of Action:

Ketamine is noncompetitive antagonist at the NMDA receptor.The NMDA receptor, a member of the glutamate receptor family, as an example of ion channel coupled receptor with excitatory properties which involved in the mechanism of general anesthesia, analgesia, and also in neurotoxicity (Hirota and Lambert, 1996 ; Bergman, 1999). The channel is permeable to $Ca^{2+}$and to a lesser degree to Na^{+} and K^{+}. Ketamine binds to the phencyclidine receptor in the NMDA channel in a noncompetitive

manner. It also interacts with multiple binding sites such as non-NMDA glutamate receptors, nicotinic and muscarinic cholinergic, and monoaminergic and opioid receptors (Kohrs and Durieux, 1998; Bergman, 1999).

2-6-3 Effect of Ketamine on Cardiovascular System:

Ketamine appears to stimulate the cardiovascular system, producing increase in heart rate, cardiac output and blood pressure (Hass and Herper, 1992; Bergman, 1999). It has the ability to increase ciculatary catecholamine concentration by inhibiting neuronal reuptake (Hass and Herper, 1992). There is also some evidance that ketamine has a direct adrenergic effect by binding directly to α – and β adrenergic receptors these observations strongly suggest that sympathomimatic effect of ketamine are due to a combination of centrally mediated increased sympathetic nerves system stimulation, a possible direct effect and the effect of ketamine in blocking the reuptake of catecholamines (Bergman,1999).

In goats, ketamine-xylazin combaintion is responsible for declined ateral blood pressure, bradycardia, increased PaCO2, decreased pH, and hypothermia during anaesthesia (Afshar *et al.*, 2005).

it has contraversial effect on cardiac rhythm, it may increase or decrease the rhythm of the heart. Cardiac dysrhythmias are uncommon following ketamine administration, although some animal studies suggest that ketamine sensitizes the myocardium to the dysrhythmagenic effect of epinephrine (Hass and Herper, 1992; Bergman, 1999). Due to cardiovascular effect ketamine has ability to maintain arterial blood pressure, for that it adviced to use in patient with cyanatic congenital heart disease, hypovolumic patients, and those hsve cardiogenic shock (Hass and Herper, 1992). In sheep the combination of acepromazine-ketamine

caused an inhibition of the cardiovascular system such as decreased of the blood pressure and heart rate (Afsher *et al*., 2005).

2-6-4 Effect of Ketamine on the Respiratory Systeme:

Ketamine is a mild respiratory depressant (Haas and Harper, 1992). It causes a shift of the CO_2 dose-response curve to the right, in a dose-related manner, but does not change the slope of the curve. Respiratory drive to CO_2 may be depressed as much as 15 to 22%. This effect is similar to that of opioids, but dissimilar to the most sedative hypnotics and anesthetics, suggesting that opioid receptors may play a role in the respiratory depressant effect. In clinical studies, the effects were observed only at high doses. Some case reports describe respiratory depression after rapid intravenous injection, but also after routine pediatric use of ketamine administered intramuscularly (Reich and Silvay, 1989; White and Ryan, 1996; Sinner and Graf, 2008). At recreational doses respiratory depression is not likely to occur, but cannot wholly be excluded. Ketamine has a bronchodilatory effect and pharyngeal and laryngeal reflexes are maintained (Hall *et al.*, 2001). In sheep the combination of acepromazine-ketamine caused an inhibition of the respiratary rate at 45 and 60 min., the PaO_2 decreased signficantly at 5,15 and 45 min,and $PaCO_2$ increased at 5 min (Afsher *et al.*, 2005).

2-6-5 Effect of ktamine on the central nerveus systeme:

Ketamine produces the so-called dissociative anesthetic state that has been described as functional and electrophysiological dissociation between the thalamo-neocortical and limbic systems. The unique clinical state produced by ketamine is typically a state of catalepsy in which the eyes remain open with a slow nystagmic gaze, whereas the corneal and light reflexes remain intact. Varying degrees of hyper tonus and occasional purposeful movements unrelated to painful stimuli are noted in the

presence of adequate surgical anesthesia. Studies have demonstrated excitatory activity in both the thalamus and limbic systems without clinical evidence of seizure activity after ketamine administration Thus, ketamine would be unlikely to precipitate convulsions in patients with seizure disorders and, in fact, experimental data suggest that ketamine has anticonvulsive and even neuroprotective properties (Himmelseher *et al.*, 1996). The role of ketamine, in particular in lower sub-anesthetic doses, has recently gained increasing interest in pain management (Visser and Schug, 2006).

2-7 Xylazine :

Xylazine (Rampun)® is 2(2,6-dimethyl phenyl amine)-4-H-5,6-dihydro-l,3-thiazine hydrochloride. It is alpha-2 agonist, sedative, analgesic, muscle relaxant drug initially developed in 1962 by Bayer (Leverkusen, Germany) as an antihypertensive drug (Kastner, 2006; Hall et.al, 2001). It finds that the drug has excessive central nervous system depressant effects, and it is subsequently introduced for veterinary use. Alpha-2 agonists are commonly used in large animals' for premedication, sedation and analgesia (Lee, 2006). The sedative effects of alpha-2 agonists are dose dependent with rapid onset and result in mild sedation to recumbency.

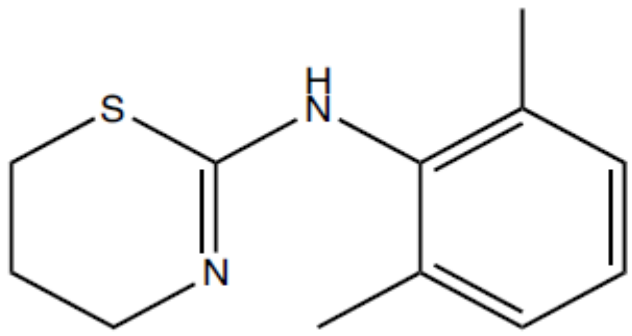
Ruminant are very sensitive to the effect of xylazine (Valverde and Doherty, 2008). Xylazine in sheep, is potent and effective analgesic performances superior to opioid drugs. Whereas goats more sensitive to xylazine than sheep (Mogoa et al., 2000a,b; Galatos, 2011). In sheep, it has a short elimination half-life and is rapidly cleared from plasma after intramuscular (IM) and intravenous (IV) administration (Kastner, 2006). The doses of xylazine range from 0.02 to 0.2 mg/kg, the largest dose produce profound sedation for many hours (Hall, *et al.*, 2001). In small

ruminant, detomidine and xylazine produced similar sedative effects but the analgesia was considerably better with the former (Khan *et al.*, 2004).

it can be given by IV, IM or SC injection although the SC route is not very reliable. Injections are non-irritant although minor temporary swellings have been reported at the site of IM injection of concentrated solutions in horses (Hall *et al.*, 2001).

2-7-1 Chemical structure:

Xylazine is 2- (2,6- dimethyl phenyl amino)- 4H-5,5 dihydro- 4H- 1,3- thiazine



(Hall *et al*., 2001).

2-7-2 Mechanism of action:

The α_2-adrenergic receptors are located in tissues throughout the body, they exist presynaptically and postsynaptically in neuronal and non-neuronal tissues and extrasynaptically in the vasculature as the endogenous ligand for these receptors is norepinephrine in general; sedative and analgesic induced by α_2-adrenergic agents occur by actions in a small group of neuronal in the brain stem the locus coeruleus, the analgesia effects are mediated by the activation of receptors in the spinal cord dorsal horn. The α_2-adrenergic agents appear to have a combined effect of presynaptic inhibition of afferent transmitter release from c fibers and post

synaptic inhibition of spinal cord dorsal horn transmission neurons (Meyer and Fish, 2008).

2-7-3 Effect of Xylazine on Cardiovascular System:

Xylazine causes dose-dependent cardiovascular depression in IV injection, although this is less after IM and extradural injection. These are attendant with both the central and peripheral effects on alpha$_1$ and alpha$_2$ receptors. Central effects on alpha$_2$ receptors decrease the sympathetic discharge and release of norepinephrine and lead to hypotension and reduced cardiac output. Peripheral effects on alpha$_2$ and alpha1 receptors result in an increase in vascular resistance and blood pressure which provoke a parasympathetic response that result in bradycardia and atrioventricular block. Therefore it is possible to see a biphasic response characterized by initial hypertension from peripheral effects and subsequent hypotension from central and peripheral effects (Valverde and Doherty, 2008).

Small doses of xylazine do not cause appreciated effects on cardiovascular system. Intravenous injection of 0.15 mg kg of xylazine in sheep had only minor effects on cardiovascular appointments
(Kastner, 2006).

Xylazine administered IV significantly decreases heart rate in animals not premedicated with anticholinergic drugs (Hall *et al*., 2001), and severe dose dependent cardiovascular effect like bradycardia, AV dissociation, or AV block, myocardial depression (decreased cardiac output) may occur (Lee, 2008).

Xylazin-ketamine combaintion is responsible for declined ateral blood pressure, bradycardia increased $PaCO_2$ decreased pH and hypothermia in anaestheticed goats (Afshar et al., 2005).

2-7-4 Effect of Xylazine on Respiratory System:

The main adverse effect of xylazine in sheep is on the respiratory system, harvesting hypoxemia, hypercapnia, and pulmonary edema. Even if in other species of animals like dogs the arterial pH, PaO_2, and $PaCO_2$, values are unchanged following 1.1 mg/kg, of IV xylazine administration (Hall *et al*., 2001).

Small ruminants look like more sensitive than cattle to the effects of $alpha_2$ agonists on respiratory system mainly if these drugs are given rapidly intravenously in high dose. In compare with the IM injection of a low doses seen have minimal effect on the cardiorespiratory function. The respiratory effects vary from tachypnea in sheep, to bradypnea in other ruminants, and undesirable effects on gas exchange and blood gases in sheep and to less extent in other ruminants are seen. There is wide variation between breeds and among individuals in the same breed of sheep to the response of alpha2 agonist (Valverde and Doherty, 2008). A range of xylazine doses are alters the respiratory mechanics and gas exchange, causing tachypnea, increased airway pressures and respiratory resistance, decreased lung compliance, pulmonary edema, and hypoxemia with or without hypercapnia (Kastner, 2006).

2-7-5 Effect of Xylazine on the Central Nervous System:

Xylazine induces dose dependent sedation and central nervous depression in ovidae (Kastner, 2006). Also xylazine induced central and peripheral analgesia associated with alpha_2 receptor agonists (alpha_2 mediated) (Valverde and Doherty, 2008), and through a central antinociception effects mediated by endogenous opioids and μ-opioid receptor (Romero, *et al.,* 2013). Alpha_2 adrenergic receptors located peripherally (spinally) in the superficial laminae of the dorsal horn of spinal cord, responsible for the supraspinally and spinally mediated analgesia, and centrally in the periaqueductal gray area of the midbrain, the

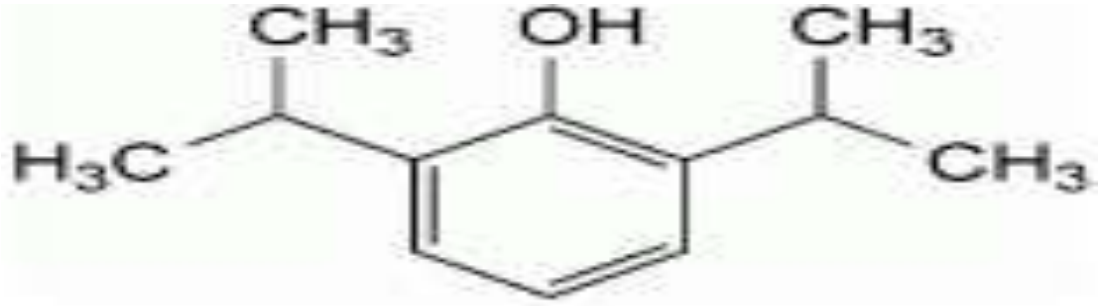
site of origin of the descending inhibitory pathways of pain modulate the release of norepinephrine. In large and small ruminants sedation with it causes nervous depression which leads to postural changes (recumbancy), in addition to unconsciousness and a state close to general anesthesia (Hall *et.al*.2001;Kastner, 2006).

2-8 Propofol :

Propofol is a non – barbiturate sedative hypnotic developed in Europe in the 1970 and was gradually utilized by anesthesiologists in the United State over the next two decades (Arora, *et.al.* , 2007) .

In 1983 and 1984 in Europe and United States it was evaluated in clinical trials . After its launch in 1986 , propofol rapidly become the most commonly used intravenously anesthetic drug . It the first introduced into clinical practice in 1986 by Astra Zeneca under trade name diprivan (a shortened version of DI – isopropyl IV Anesthetic) . (Kulling, *et.al.* , 2003) , The active ingredient is 2 , 6 – diisopropylphenol which exists as an oil at room temperatures . it was initially introduced in a preparation containing the surface active agent Cremophor EL but it is now presented in an emulsion form .its anesthetic is white or slightly yellowish lipid – based emulsion . its rountinely used for short – term sedation of human and small animal patients for the induction , maintenance of general anesthesia as intensive care unit (ICU) (Thurmon, *et.al.* , 1996 ; Baker and Naguib , 2005)

2-8-1 Chemical structure:



2-8-2 Mechanism of Action and effect on body:

Is the most commonly used induction agent and acts by enhancing transmission at the GABA-A receptor. Because of its rapid onset, titrat-ability and short duration of action, propofol is also frequently utilized as an IV infusion to provide sedation for MAC or sedation cases, or as part of a balanced general anesthetic. Propofol is a water insoluble agent that can only be administered intravenously. It is prepared as 1% emulsion with egg lecithin, glycerol, and soybean oil.

Propofol's initial distribution half-life is 2–8 min, and it undergoes rapid hepatic metabolism to water soluble metabolites which are excreted by the kidneys. Remarkably, few pharmacokinetic changes are noted in the elimination of propofol for patients with liver or renal disease.

Propofol is a potent cardiovascular and respiratory depressant, and it should only be used by persons qualified and prepared to maintain the patient's airway and hemodynamic stability. Propofol is often avoided in cases where **(** Alexs,et.al.2011 **)**

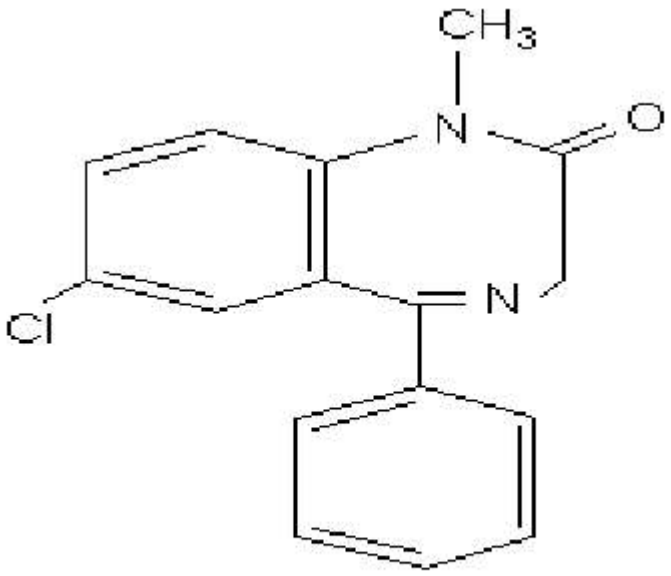
2-9 Diazepam:

Is a benzodiazepine drug has calming, muscle relaxant and anti convulsant effects. It is used as a preanaesthetic for releave of skeletal muscle spasm and as an anti-convulsant. It is indicated in animals with history of seizure disorders, so it is frequently administrated

prior to Ketamine to prevent seizures and muscle hypertonus (Thurmon et al., 1996).

Diazepam is insoluble in water and, therefore, prepared in an oily solvent that is locally irritant and can cause tissue damage and skin sloughing if administrated peri-vascularly. Parental solution for IV injection include propylene glycol and ethanol and may cause thrombophlebitis (Hall et al.,2001; Kohn *et al.*, 1997)

2-9-1 **Chemical Structure**



Diazepam
(Valium)

2-9-2 Mechanism of Action:

Diazepam acts on specific benzodiazepine receptors sites located on post synaptic nerve endings located within C.N.S. The greatest concentration of these receptors is located in the cerebral cortex. These receptor sites are found in decreasing density in the hypothalamus cerebrum, midbrain hippocampus, medulla and spinal cord (Thurmon *et al.,* 1996). The effects of Diazepam occurs at neural pathway in which gammaaminobutyric acid (GABA) is primary neurotransmitters (Thurmon *et al.,* 1996). GABA acts on the chloride channel and it

increases the flow of chloride ions into the cell causing hyperpolarization and make the cell more refractory to other stimuli (Hall et al.,2001).

2-9-3 Effect of Diazepam on the Central Nervous System:

Diazepam exerts its main sedative auxiolytic effects by the depression of the limbic system, thalamus and hypothalamus and it produces calming or taming effects in animals (Paddle Ford, 1995). Also it produces muscle relaxation properties by inhibition of intranuncial neurons of spinal levels (Hall et al.,2001). Tranquilizer effects of benzodiazepines are species variable, overdose causes depression of C.N.S. ranging from drowsiness to coma. In mild cases, it causes drowsiness and confusion. In serious cases. It causes ataxia hypotonia and coma which may lead to death. Excitation may follow administration in dogs and cats (Khon *et al.*, 1997). It has a stimulation effect on appetite. For that, it is used in anorexic cats (Hall et al.,2001; Mckelvey and Holling Shead, 1994).

2-9-4 Effect of Diazepam on Cardiovascular System:

Diazepam, in general, has minimal cardiovascular disorder due to its less depressant effect on heart rate and peripheral blood vessels than most other tranquilizer (Hall *et al.*2001). It causes depression of myocardial contraction. These depressant effects have been to be less than many other tranquilizers or sedatives. Also it has antidysrhythmic action, it is useful in treating certain kinds of myocardial hyperexcitability. Coronary blood flow also increases after benzodiazepines administration. This may prove beneficial if Diazepam, for instance, is used as anesthetic adjunct for cases with myocardial ischemia (Short, 1987).

Diazepam solution should be injected slowly to decrease the incidence of venous thrombosis. Clinical doses cause only minimal cardiac depression (Thurmon *et al.*, 1996) and rapid iv administration may cause hypotension and bradycardia (Paddle Ford, 1995).

2-9-5 Effect of Diazepam on Respiratory System:

Diazepam, in general has mild respiratory effects. In large doses or when given during anaesthesia, it may cause decreased alveolar ventilation, PaO_2 and it increases $PaCo_2$ (Short, 1987; Thurmon *et al.*, 1996). Because Diazepam is not water soluble and is dissolved in Propylene which is a cardiopulmonary depressant, rapid iv injection may cause hypotension bradycardia and apnea (Paddl ford, 1995).

Conclusions

1-In veterinary anesthesia the economic considerations and the limited number of anesthetic and analgesic drugs authorized to use in small ruminants may directive the use of the drug and the technique.

2-General anesthesia 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.

3-Balanced anesthesia, 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 anesthetic agents at high dosages to maintain general anesthesia.

4-In sheep and goat ketamine xylazine combination can be used as a more suitable anesthetic combination in experimental surgical operation.

5-The propofol can be used as a more suitable anesthetic drug for induction anesthesia in sheep and goats.

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