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Original Research Article

Comparison of quality of anesthetic effect between intramuscularly administered ketamine, intravenously administered ketamine and intravenously administered propofol in diazepam premedicated goats

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ABSTRACT

This study aimed to evaluate intramuscularly administered ketamine, intravenously administered ketamine and intravenously administered propofol in diazepam premedicated goats. Nine native female goats divided into three groups (each of 3 goats) were premedicated with diazepam 1 mg/kg intramuscularly. Goats of group I were treated with ketamine (8 mg/kg) intravenously, while those of group II treated with ketamine (10 mg/kg) intramuscularly, and group III injected with propofol (5 mg/kg) intravenously. The mean anesthetic onset, anesthetic duration, and total recovery period were calculated. The mean heart rate (HR), respiratory rate (RR), rectal temperature (RT) and biochemical parameters also were recorded. Satisfactory anesthesia and immobilization (smooth induction, and smooth recovery) needed for surgical interventions of short duration were achieved in all groups. The induction was good and smooth in groups I and III. The quality of recovery was good in groups III and I and recovery is longer in group II. In conclusion, this study indicates that the 3 regimens are associated with acceptable anesthetic characteristics; Propofol IV is superior to ketamine because it provides uneventful onset and recovery which are more rapid than ketamine IV or ketamine IM, so reduces anaesthetic risk while administration of ketamine intravenously is superior to its administration intramuscularly.

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1. Introduction

Goats usually accept physical restraint well and that, in conjunction with local or regional analgesia, is often sufficient to enable completion of many procedures. Other diagnostic and surgical procedures that are more complex require general anesthesia **(Lumb and Jones, 2015).**

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 **(Lesley J. Smith 2016)**

Ketamine is an N-methyl-D-aspartate receptor antagonist **(Ersek, 2004**). It induces a state referred to as dissociative anesthesia. Ketamine has a wide range of effects in animals, including analgesia, anesthesia, elevated blood pressure, and bronchodilation. Ketamine is primarily used for the induction and maintenance of general anesthesia, usually in combination with other sedative drugs such as xylazine or butorphanol **(Lin 1996** and **Lin and Pugh, 2002**)

Propofol (2, 6- di isopropylphenol) is a phenolic compound. It is a non - barbiturate, non-dissociative and non-cumulative intravenous anaesthetic agent **(Hall, Clark, and trim 2001**). It has good quality anaesthesia, rapid onset and short duration of action, with rapid recoveries making the drug potentially useful in ruminants, in which these features are particularly desirable **(Nikitas et al, 2005**).The use of propofol for induction and maintenance of anaesthesia have indicated its suitability in goats **(Khan, 2006).**

Diazepam is a benzodiazepine derivative drug. It possesses anxiolytic, anticonvulsant, hypnotic, sedative, skeletal muscle relaxant, and amnestic properties **(Mandrioli et al. 2008).** A combination of diazepam and ketamine with or without xylazine is frequently used to induce general anesthesia in small ruminants **(McEwen *et al.*, 2000)**.

The objective of the current study was to evaluate the clinical and biochemical efficiency of intramuscularly administered ketamine, intravenously administered ketamine and intravenously administered propofol in diazepam pre-medicated goats.

2. Materials and methods

This study was approved in Surgery, Anaesthesiology and Radiology Dept., Faculty of Veterinary Medicine, Beni-Suef University.

Nine healthy female native goats with 2-3 years old and weighting 25-30 kg were used in the study. The animals were kept under uniform diet and management practices during the period of experiment. The animals were administered ivermectin (Iveen Plus® Egyptian company for chemicals and pharmaceuticals, ADWIA) subcutaneously in a dose of 1ml/50kg B. Wt All goats were subjected to thorough clinical examination according to **Radostits et al. (2000)** and parasitological examination according to **Urquhart et al. (1996)** and they were approved healthy and free from internal and external parasites.

The animals were fasted for 12 hours, and water was withheld for 6 hours prior to the start of the experiment. The skin overlying the left jugular vein and area used for intramuscular injection were clipped before each experiment.

The prepared animals were randomly divided into 3 groups, each has 3 goats;

Group(I):

This group was treated by,

a) Diazepam 0.5% (Neuril®, Memphis for pharmaceuticals and chemical) in dose of 1mg/kg body weight intramuscular

b) After 10min, ketamine 50mg/ml (ketamine ®, Sigma-Tec pharmaceuticals).was injected in dose 8 mg/kg b.wt intravenous.

Group(II):

This group was treated by,

a) Diazepam 0.5% (Neuril®, Memphis for pharmaceuticals and chemical) in dose of 1mg/kg body weight intramuscular

b) After 10min, ketamine 50mg/ml (ketamine®, Sigma-Tec pharmaceuticals).was injected in dose 10mg/kg b.wt intra muscular.

Group(III):

This group was treated by,

a) Diazepam 0.5% (Neuril®, Memphis for pharmaceuticals and chemical) in dose of 1mg/kg body weight intramuscular

b) After 10min, propofol (Diprivan1%®,Corden

pharmaSPA. AstraZeneca group of companies) was injected in dose 5mg/kg b.wt intravenous.

The anesthetized goats were then placed on right lateral recumbency. Their heads were raised to permit free drainage of saliva. All trials were carried out in the absence of any manipulative or surgical procedures. Heart rate, Respiratory rate, and rectal temperature were recorded before administration of the drug(s) (baseline, 0), and then at 5, 10, 15, 20, 30, 60, and 120 minutes after administration of drugs.

According **Farag, et al., 1996**, the onset of anesthesia was calculated as the time interval between injection and loss of reflexes, while duration of anesthesia was measured as the time interval between loss of reflexes and reappearance of reflexes, and the total recovery period was measured as the time interval between the losses of reflexes till unassisted standing of the animal. Onset of anesthesia was judged by presence of muscular relaxation and absence of swallowing reflexes. The depth of anesthesia was checked by pricking the skin and underlying tissues with sterile injection needle and by pinching the skin with hemostatic forceps.

Quality of Induction and Recovery:

The quality of induction and recovery were evaluated using a score system modified by **Prassinos et al. 2005**. Hence, "good", "fair", or "poor" were assigned to the experimental goats in each group according to the criteria depending on the observed signs.

Induction quality scoring:

Good: smooth induction, rapidly assumed recumbency, no signs of excitement.

Fair: slightly prolonged induction, mild excitation, presence of swallowing reflex

Poor: obvious excitement, jumps or attempt to stand after recumbency, full presence of swallowing reflex.

Recovery quality scoring:

Good: smooth, easy transition to alertness, resumption of sternal position, ability to stand within a reasonable amount of time and ability to walk with minimal ataxia.

Fair: transient excitement or whole body movement, some struggle s, hyper- responsiveness that disappears once the goat stands unassisted but with moderate ataxia. Poor: stereotype behaviour, e.g. circling, premature attempts to stand, prolonged struggling.

Blood samples were collected from the jugular vein for biochemical parameters before (0 minute), at 15, 30, 60, 120 minutes, and 4-hour intervals after administration of drugs .Biochemical parameters including blood glucose, blood urea nitrogen (BUN), alanine aminotransferase (ALT), Aspartate Amino Transferase (AST), cholesterol, Creatinine and cortisol level were examined.

1) Estimation of serum total cholesterol level: The blood serum cholesterol was estimated using test kits supplied by Spinreact, according to the method described by **Meiattini et al., (1978**) and its level was expressed in mg/dl.

2) Estimation of serum glucose level: Blood serum glucose was estimated using test kits supplied by Sigma according to the method described by **Trinder (1969),** and its level was expressed in mg/dl.

3) Estimation of serum aspartate aminotransferase activity: Serum aspartate aminotransferase activity (AST) was estimated using test kits supplied by Spinreact, after the method described by **Reitman and Frankel (1957)** and its activity was expressed in IU/L.

4) Estimation of serum alanine aminotransferase activity: Serum alanine aminotransferase activity was estimated using test kits supplied by Spinreact, after the method described by **Reitman and Frankel (1957)** and its activity was expressed in IU/L.

5) Estimation of cortisol concentration. The cortisol concentration in plasma was determined using the Coat-A-Count Assay kit, after the method described by **Kannan et al., (2001)** its level was expressed in nmol/L.

Statistical Analyses: All data were presented as mean ± SD. The data for time of onset and duration of analgesia, HR, RR, rectal temperature, and biochemical parameters were analyzed by ANOVA (analysis of variance) and Duncan's test as a post hoc. Statistical analysis was undertaken using Graph pad Prism version

5 software program. A value of< 0.05 was considered significant.

Results

The anesthetic effects of intra-venous diazepam and ketamine combination (group I) after injection of ketamine IV, revealed that the mean time of onset was (35) seconds, the mean time for duration of anesthesia was (20) minutes, while the mean time for total recovery period was (24) minutes. The anesthetic effects of intramuscular injection of diazepam and ketamine combination (group II) after injection of ketamine I.M., revealed that the mean time of onset was (4) minutes, the mean time for duration of anesthesia was (30) minutes, while the mean time for total recovery period was (35) minute. The anesthetic effects of intramuscular injection of diazepam and propofol combination (group III) after injection of propofol I.V., revealed that the mean time of onset was (15) second, the mean time for duration of anaesthesia was (28) minutes, while the mean time for total recovery period was (10) minutes**(Table 1)**. Marked lack of jaw tone, absence of swallowing reflex, slight salivation, complete muscular relaxation and absence of pedal reflex were observed at the end of the onset period in all groups (I , II and III) . Duration of induction period and recovery was significantly longer in goats that received ketamine intramuscularly than in goats that received intravenously administered ketamine or propofol.

Results of respiration rate, pulse rate, temperature and of biochemical parameters were tabulated in **Tables (2)** and **(3)**. There were no significant difference in heart rates and respiratory rates between the 3 groups, but there were some differences within groups across the time points.

The respiratory rate decreased significantly ($P <$ 0.05) in all groups at 15 min after induction then, it increased in group I, II, and III at 60 min after induction.

The heart rate significantly ($P < 0.05$) increased in groups I and II at 15 min after induction when compared to group III. Then the heart rate decreased in all groups from 20 min to 60 min after induction.

Blood glucose Indicates a significant ($P<0.05$) difference between the pre-anesthetic blood glucose and that measured at recovery.

Following the administration of anaesthetics, smooth induction was observed in all the goats in groups I and III. The goats in groups I and III rapidly assumed lateral recumbent position and no forms of excitement were observed. However, all goats in groups II exhibited slight excitement, slight prolonged induction and the presence of swallowing reflex was observed **(Table 4).**

Recovery was also smooth and the goats stood some minutes after assuming sternal recumbency. These were observed in all the goats in group III and two goats in groups I. However, transient excitement, struggle to stand, and moderate ataxia were observed in all the goats in group II, one goat in group I (Table 4).

Table (1): Onset, duration and total recovery period of the Group (I) (ketamine 10 mg/kg intramuscularly), Group (II) (ketamine 8 mg/kg intravenously) and the Group (III) (propofol 5 mg/kg intravenously) in diazepam premedicated goats.

Item Group		Onset of anesthesia	Duration of anesthesia	Total recovery period
Group (I)	Minimum-Maximum	30 -40 seconds	19-22 minutes	20-28 minutes
	Mean	35 seconds	20 minutes	24 minutes
Group (II)	Minimum-Maximum	3-5 minutes	25-35 minutes	30-40 minutes
	Mean	4 minutes	30 minutes	35 minutes
Group (III)	Minimum-Maximum	10-15 seconds	25-29 minutes	8-12 minutes
	Mean	12 seconds	27 minutes	10 minutes

Table (2): Heart rate respiratory rate and temperature readings (mean ± standard deviation) obtained immediately after injection for the Group (I) (ketamine 10 mg/kg intramuscularly), Group (II) (ketamine 8 mg/kg intravenously)and the Group (III) (propofol 5 mg/kg intravenously) in diazepam premedicated goats.

		Respiration rate	Heart rate	Temperature ◦C
0	**Group I**	28.00±1.00	81.00±3.61	39.07±0.31
	Group II	27.33±2.08	80.33±1.53	38.970.15±
	Group(III)	28.00±2.00	75.67±1.15	39.27±0.35
5 minutes	**Group I**	18.00±1.00	87.33±2.08	38.50±0.10
	Group II	18.67±0.58	85.00±0.00	38.53±0.06
	Group(III)	20.33±0.58	75.67±4.04	38.57±0.25
10 minutes	**Group I**	17.00±0.00	93.67±3.21	38.30±0.26
	Group II	17.00±0.00	89.00±0.00	38.43±0.06
	Group(III)	18.33±0.58	82.33±4.62	38.47±0.06
15 minutes	**Group I**	16.00*±0.02	105.00*±5.00	38.33±0.06
	Group II	16.00*±0.00	105.33*±4.62	38.33±0.06
	Group(III)	16.02*±0.01	92.67±6.66	38.43±0.12
30 minutes	**Group I**	22.33±2.52	89.67±0.58	38.77±0.06
	Group II	22.00±0.00	89.67±0.58	38.60±0.17
	Group(III)	20.00±0.00	90.67±1.15	38.80±0.01
60 minutes	**Group I**	24.00±1.73	85.00±0.00	39.00±0.00
	Group II	24.00±0.00	86.00±0.00	39.27±0.46
	Group(III)	23.00±0.00	85.00±0.00	39.00±0.57
120 minutes	**Group I**	25.00±2.00	81.33±2.31	39.13±0.23
	Group II	27.00±1.00	80.00±0.00	39.07±0.31
	Group(III)	23.33±0.58	79.00±1.73	39.20±0.20

* significant ($p < 0.05$)

Table (3): Biochemical parameters of animals injected with Group(I) (ketamine 10 mg/kg intramuscularly), Group(II) (ketamine 8 mg/kg intravenously)and the Group(III) (propofol 5 mg/kg intravenously) in diazepam premedicated goats. mean ± standard deviation

Parameter	Group	0 min	15 min	30 min	60 min	120 min	240 min
Blood Glucose (mg/dL)	Group I	60.67±4.04	65.00±5.00	81.33*±7.09	67.67±1.53	64.33±1.15	61.67±2.31
	Group II	62.67±5.03	65.00±5.00	81.33*±7.09	67.67±1.53	64.33±1.15	61.67±2.31
	Group III	65.00±5.00	73.33±5.86	88.67*±1.53	81.33±4.73	71.67±2.89	68.33±5.51
BUN (mg/dL)	Group I	16.40±2.42	16.83±2.35	17.50±2.43	16.67±2.25	16.43±2.20	16.33±2.36
	Group II	15.97±2.85	16.67±2.37	17.43±2.40	16.63±2.26	16.40±2.21	16.30±2.36
	Group III	13.73±1.10	14.20±0.92	15.73±1.42	14.63±0.85	14.50±0.79	14.20±0.82
ALT (Unit/mL)	Group I	34.33±4.04	35.67±3.51	38.67±3.06	35.67±3.79	34.00±3.46	33.33±4.16
	Group II	33.67±4.51	35.67±4.51	38.67±3.06	35.67±3.79	34.00±3.46	33.33±4.16
	GroupIII	31.33±3.21	33.67±2.08	38.33±0.58	35.00±0.00	35.00±1.00	32.33±3.21
AST (Unit/mL)	Group I	98.67±2.31	104.33±2.08	114.33±3.51	108.00±5.00	103.00±3.00	97.67±8.08
	Group II	100.67±10.07	107.00±7.55	115.00±9.54	113.67±12.22	104.00±4.58	97.33±8.62
	GroupIII	148.33±12.58	154.00±12.77	163.00±6.93	156.00±9.64	153.67±10.12	151.00±10.58
Creatinine mg/dl	Group I	0.80±0.10	0.87± 0.12	0.97±0.12	0.87±0.12	0.80±0.10	0.83±0.06
	Group II	0.77±0.15	0.83±0.15	0.93±0.15	0.83±0.15	0.77±0.12	0.80±0.10
	Group III	1.02±0.10	1.00±0.10	1.10±0.17	1.04±0.05	0.97±0.06	0.97±0.06
Cholesterol (mg/dl)	Group I	84.33±4.51	85.33±4.51	85.53±4.32	84.67±5.03	84.00±5.00	84.00±4.58
	Group II	83.67±4.51	85.33±4.04	85.50±4.27	84.67±5.03	84.00±5.00	84.00±4.58
	Group III	86.33±4.73	86.70±4.20	87.33±3.79	86.33±4.73	86.00±4.36	85.33±4.73
Cortisol (nmoL)	Group I	1.90±0.36	1.73±0.15	1.50±0.20	2.20±0.17	2.27±0.15	2.33±0.12
	Group II	1.83±0.31	1.77±0.21	1.53±0.21	2.13±0.15	2.30±0.17	2.37±0.15
	Group III	1.67±0.29	1.80±0.10	1.67±0.15	2.03±0.59	2.30±0.61	2.63±0.42

* significant ($p < 0.05$).

Table (4): quality of induction and recovery of the Group (I)

(ketamine 10 mg/kg intramuscularly), Group(II) (ketamine 8 mg/kg intravenously)and the Group(III) (propofol 5 mg/kg intravenously) in diazepam premedicated goats using score system.

	Group I	Group II	Group III
Quality of induction	**3good**	**3 fair**	**3 good**
Quality of recovery	**2 good** **1 fair**	**3 fair**	**3 good**

*

Number of animals that show respective signs in each goat group.

Discussion

The relatively longer duration of intramuscularly treated group in comparison to intravenously treated group probably reflects local tissue fixation of the drug and slow lymphatic and hematogenous absorption **(Braid *et al.*, 1965).**

The body temperature in all groups reduced significantly after injection at 15 min. These results agree with that of **Tiwari *et al.*, (1994)**, who recorded that xylazine-ketamine-diazepam injection in dogs reduced body temperature at 60 minutes after injection.

The profound decrease in respiratory rate in all groups at 15 min may be attributed to the respiratory depression effect of ketamine and propofol **(Hodgkinson and Dawson 2007)**

The increase in heart rate in group I and II may be as a result of light anaesthesia or as a result of cardiac stimulatory effect of ketamine, this was agreed by (**Hall, Clark and Trim, 2001)**

serum glucose levels in all groups remained significantly high ($P < 0.05$) at 1, 3, and 6 hrs post injection then declined to normal level 24 hours after injection. The obtained results were in consistent with those obtained by (**Vibha and Pandey, 1988; Sarkate 1989 and Tiwari *et al.*, 1994).**

Increase in blood glucose levels might be due to an increase in adrenocortical hormone during general anesthesia and mobilization of liver glycogen under the influence of increased adrenaline level **(Tiwari *et al.*, 1994).**

The synergistic effect of propofol and other drugs used in the therapy might have resulted in the short onset of analgesia in groups B, C, and D. Propofol causes rapid induction (within 10 to 20 sec) which results in unconsciousness **(Prassinos *et al.*, 2005)** .

The smooth induction recorded in most of the groups may also be attributed to the combined anesthetic and sedative actions of the drugs used. However, rapid recovery may be attributed to non-cumulative effect of propofol **(Dzikiti *et al.*, 2010).**

The results of AST, ALT, creatinine, cholesterol, cortisol and BUN in both groups, remained within normal ranges, suggesting absence of hepatic or renal insufficiency; this was in agreement with (**Benjamin, 1984 and Kaneko, et al., 1997).**

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