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TOTAL INTRAVENOUS ANAESTHESIA IN DONKEYS (EQUUS ASINUS): COMPARISON OF ANAESTHETIC AND CARDIORESPIRATORY EFFECTS OF FOUR ANAESTHETIC DRUG COMBINATIONS

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SUMMARY

Twenty eight mature donkeys subjected to elective surgery were randomly assigned to four groups of 7 donkeys. After premedication with 80 µg/kg of romifidine and 0.4 mg/kg of diazepam administered intravenously anesthesia was induced either with 5 mg/kg IV thiopental sodium (group I), 2.2 mg/kg IV ketamine (group II), 3 mg/kg IV propofol (group III) or 5g/50kg IV chloral hydrate (group IV). Anesthesia was maintained with continuous intravenous infusion using a mixture of 1 g thiopental/25 g guaifenesin/30 mg romifidine in 500 ml 5% dextrose (group I), 500 mg ketamine/25 g guaifenesin/30 mg romifidine in 500 ml 5% dextrose (group II), 400 mg propofol/25 g guaifenesin/30 mg romifidine in 500 ml 5% dextrose (group III) or 25g chloral hydrate, 25 g guaifenesin/30 mg romifidine in 500ml 5% dextrose (group IV). The anaesthetic and cardiorespiratory responses to the four injectable anaesthetic combinations are reported . The results indicated that the four anaesthetic combinations could be used as a safe method of total intravenous anesthesia for short and prolonged surgical procedures under field conditions in donkeys.

INTRODUCTION

Total intravenous anesthesia has become a popular technique in human medicine (Ohta et al, 2001), dogs and cats (Ko et al, 1994) and traditionally has been used to provide short- and long-term recumbency and general anesthesia in horses (Taylor et al, 1998; Mama et al, 1998 and Muir et al, 2000).

Such anesthesia has some potential advantages over inhalation anesthesia. Intravenous agents generally cause less myocardial depression and appear to act at specific receptors and have the potential to give a precise effect, in contrast with volatile agents which affect most body systems. On the basis of cardiorespiratory, endocrine and economic data total intravenous anesthesia has been advocated as a potentially superior alternative to inhalation anesthesia in horses (Sear, 1991; Taylor et al, 1998; Muir et al, 2000; Ohta et al, 2001 and Santos et al, 2003).

Numerous advances in equine anesthesia have given the practitioner and clinician a large selection of safe anaesthetic agents for field anesthesia. The clinical experience and investigations have produced various total intravenous anesthetic combinations that fit particular situations and patients. Combinations of sedative-analgesic α2-agonists (xylazine-detomidine-romifidine), muscle relaxant (guaifenesin-diazepam) with a dissociative anesthetic agent (ketamine) or ultra-short acting barbiturates (thiopental sodium) or propofol or chloral hydrate have been described for total intravenous anesthesia in horses (Geiser, 1983; Nolan and Hall, 1985; Taylor and Luna, 1995; Young et al, 1993; Mama, 2000; Bettschart-Wolfensberger et al, 1996/2001; Shehta, 1998; Hubbell et al, 2000; Muir et al, 2002; Bettschart-wolfensberger et al 2003; Frias et al, 2003 and Oku et al, 2003).

The purpose of the present study is to evaluate the anaesthetic and analgesic effects and to monitor the cardiovascular and respiratory changes of four anaesthetic drug combinations used for total intravenous anesthesia in donkeys.

MATERIAL AND METHODS

This study was carried out on 28 mature clinically healthy donkeys with average age of 10 years and average body weight of 100 kg. Food (but not water) was withheld for the 12 hours prior to each anaesthetic exposure. A 14-gauge catheter was placed in the jugular vein for IV administration of all drugs and for blood samples collection.

Anaesthetic Protocol:

In all anaesthetic combinations, donkeys were premedicated with 80 µg/kg of romifidine (SEDIVET® Boehringer Ingelheim, Germany) given intravenously over a period of approximately two minutes. Ten minutes later 0.4 mg/kg of diazepam (NEURIL® Memphis Co for pharm. & chemical Ind., Egypt) was administered intravenously. Donkeys were randomly assigned to four groups each of 7 donkeys and received one of the used four anesthetic combinations.

In group I anesthesia was induced with 5 mg/kg IV thiopental sodium (THIOPENTAL® E.I.P.I.Co., Egypt). Donkeys were then positioned in lateral recumbency and anesthesia was maintained by infusion a freshly prepared mixture of

30 mg romifidine, 1 g thiopental sodium and 25 g guaifenesin (GUAIFENESIN® Elgomhoria Co., Egypt) in 500 ml 5% dextrose.

Anesthesia was induced in group II with 2.2 mg/kg ketamine (KETOLAR® Parke-Davis, USA) IVand then maintained with an infusion of 30 mg romifidine, 500 mg ketamine and 25 g guaifenesin in 500 ml 5% dextrose.

In group III anesthesia was induced with 3 mg/kg propofol (DIPRIVAN® Zeneca limited, Macclesfield cheshire United Kingdom) IV and was maintained with an infusion of 30 mg romifidine, 400 mg propofol and 25 g guaifenesin in 500 ml 5% dextrose.

Anesthesia was induced in group IV with 5 g /50 kg chloral hydrate (CHLORAL HYDRATE®) IVand maintained with an infusion of 30 mg romifidine, 25 g chloral hydrate and 25 g guaifenesin in 500 ml 5% dextrose.

The selection of the anesthetic drug combinations and dosages was based on the published reports (Muir et al, 2000). The anaesthetic combinations used for maintenance of anesthesia was given through a standard fluid administration set connected to a 14-gauge catheter preplaced in the jugular vein. All combinations were infused dose to effect. Donkeys were intubated and the endotracheal tube was connected to Physiogard monitor (Physiogard TM910, Bruker Medizintechnik GMBH, Germany) to measure respiratory rate and end-tidal carbon dioxide concentration. Donkeys were allowed to breath spontaneously throughout anesthesia.

Cardiovascular (ECG and heart rate) and respiratory monitors (respiratory rate, End-tidal CO2 conecntration and Pulse oximetry) and temperature were recorded by an anaesthetic monitoring system (Physiogard TM910). The Electrocardiogram (ECG) leads were connected using a base apex technique; the left leg lead is placed on the horse's caudal sternum and the right arm lead is placed over the horse's thoracic inlet and the left arm lead is placed somewhere on both sides of the horse's neck (Stanway, 2001) (Fig. 1&2).

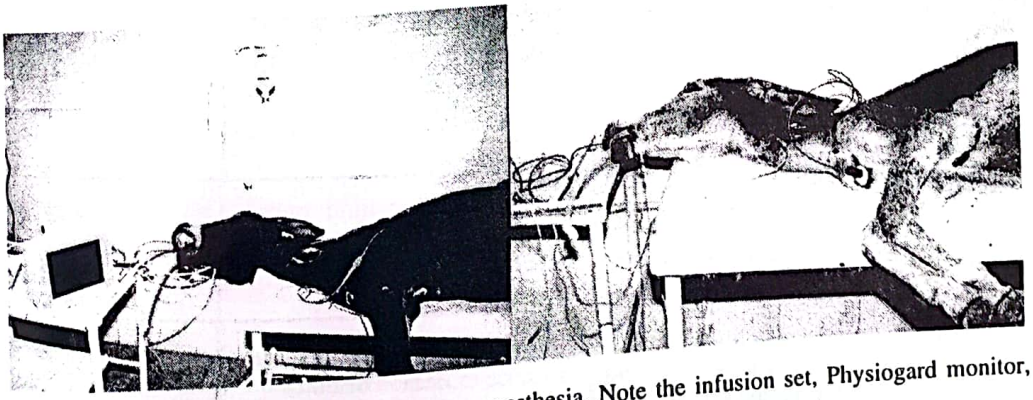

Fig. (1a&b): Donkey under total intravenous anesthesia. Note the infusion set, Physiogard monitor, the Electrodes sites for routine ECG monitoring and SPO2 & etCO2 modules.

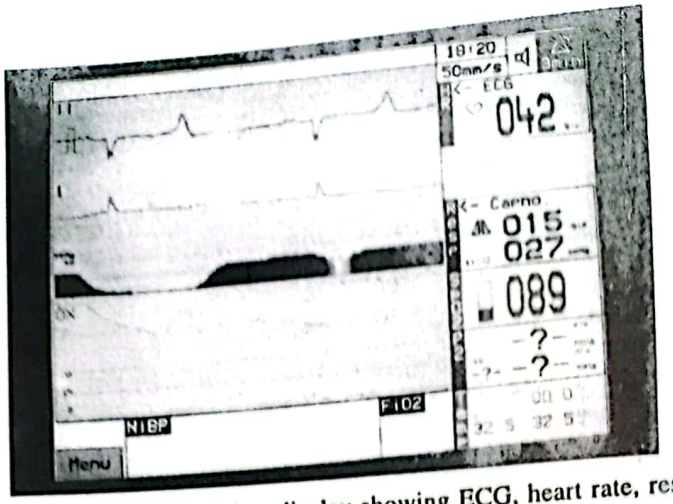

Fig.(2): Physiogard monitor display showing ECG, heart rate, respiratory rate, etCO2, SPO2 and temperature.

Central nervous system function was indirectly monitored by reflex activity by observation and testing the superficial and deep reflexes to determine the depth of anesthesia. The used reflex responses included palpebral, corneal, swallowing and laryngeal reflexes, lacrimation, eyeball position (nystagmus) and muscle relaxation. These reflexes were recorded every five minutes throughout anesthesia.

Quality of sedation, quality of induction, degree of muscle relaxation, quality of analgesia and recovery from anesthesia were scored and the mean values were recorded (Table 1&2) (Mama et al, 1995/1996/1998 and Taylor et al, 2001).

Table (1): Scoring system for the quality of sedation, degree of muscle relaxation and quality of analgesia

Classification score	Quality of sedation	Degree of muscle relaxation	Quality of analgesia
Excellent (4 degree)	Calm, relaxed, no restraint required minimally responsive to environmental stimuli, reluctant to move	No trunk or limb twitching or movement, no resistance to flexion of limbs	No response to surgical stimulation
Good (3 degree)	No restraint required, relaxed, infrequent responses to environmental stimuli, easily walked without problems	Slight trunk or limb muscle twitching, minimal resistance to flexion of limbs	Brief contraction of abdominal or limb muscles, temporary twtiching or spasms
Moderate (2 egree)	Minimal restraint required, interested in environmental stimuli, reactive to noise and sudden movements	Strong trunk or limb muscle twitching, resistance to flexion of limbs	Movement of a forelimb or hind limb
Poor (1 degree)	Unsatisfactory, minimal or no signs of sedation, nervousness or apprehension requiring additional sedative administration.	Muscle rigidity and strong resistance to flexion of limbs	Repeated movement of a forelimb or hind limb requiring additional drug administration.

Table (2): Scoring system for the quality of induction, and quality of recovery from anesthesia.

Classification score	Quality of induction	Quality of analgesia
Excellent (5 degree)	Smooth, timely transition to lateral recumbency, good muscular relaxation	Quliet, coordinated efforts efforts (1 to 2) to sternal and standing posture
Good (4 degree)	Smooth, transition to lateral recumbency,minor facial or limb movements	Quiet, slightly uncoordinated efforts (1to2), to sternal and standing postures
Moderate (3 egree)	Slight delay in transition to lateral recumbency with increased (compared with good) muscular rigidity or limb improvement	Multiple (>2) quiet attempts to sternal and standonng postures, mild to moderate ataxia when standing.
Poor (2 degree)	Increased muscular activity before and during transition from standing to lateral recumbency	Uncoordinated attempts to sternal and standing postures with or without minor injury
Very poor (1 degree)	Vigorous struggling, paddling limb motions, increased coordinated muscular activity	Multiple attempts to sternal or standing posture resulting in major or life-threatening injury

The induction time (i.e time from initial anaesthetic drug administration until lateral recumbency) anaesthetic time (i.e. time from anaesthetic induction to the end of anaesthetic drug combination), surgery time (i.e. time from initial skin incision to placement of the last suture), and recovery time (i.e time from the end of anaesthetic drug administration to standing) were recorded (Muir et al., 2000).

Surgical conditions were scored by the surgeon on a scale of 1 (very poor: moves in response to incision, little relaxation) to 5 (excellent: no movement, good relaxation) based on relaxation and access to the site in each case (Taylor et al, 2001).

Venous blood samples were collected from all donkeys before induction, 15 and 45 min. after the beginning of anaesthetic infusion and after recovery for hematological investigations (hemoglobin, red blood cell counts, total leucocytic counts, and proportion of segmented neutrophils, lymphocytes, basophils, eosinophils, monocytes and immature neutrophils) (Coles, 1986). Serum was collected for total protein (Weichselbaum, 1946) and glucose (Trinder, 1969) analysis.

The data were analyzed by one-way ANOVA using SPSS (Statistical Product & Service Solutions) (Kuehl, 1994). A least significant difference comparison test was used to detect significant differences from baseline values with-

in combinations and to detect significant differences at specific times among combination groups. Data were presented as mean ± standard error. For all analysis, a value of $p<0.05$ was considered significant.

RESULTS

Intravenous administration of romifidine was followed by obvious signs of sedation, which developed within one to two minutes. In general the donkey lowered its head, and exhibited ptosis and lower lip droop. Donkeys showed marked reluctance to move, hanging its head, adopt a wide-base stance with mild ataxia (Fig. 3). Protrusion of the penis was observed in all male donkeys. Quality of sedation induced by romifidine was judged to be fair to good in all donkeys and was not significantly different among groups.

The mean induction time in group 4 was significantly longer than the other tested three anesthetic combinations. Mean quality of induction was not significantly different among the groups. All anesthetic inductions were smooth and excitement free and received a classification score of good to excellent. Minimal restraint by two assistants was applied during the induction. When the donkeys reached sternal recumbency it was gently rolled into lateral recumbency. Rigidity and slight muscle tremor persisted for a variable period. The time to relaxation after administration of anesthetic combinations ranged from 60 to 80 seconds. It was difficult to open the mouth of 10 donkeys owing to the persistence of jaw tone immediately after anesthesia was induced, but once the jaws were open, it was usually easy to intubate the donkeys. Intubation was easily accomplished on the second or third attempt in all donkeys (Fig. 4). Swallowing reflex was observed in 8 donkeys.

Fig.(3): Signs of romifidine sedation

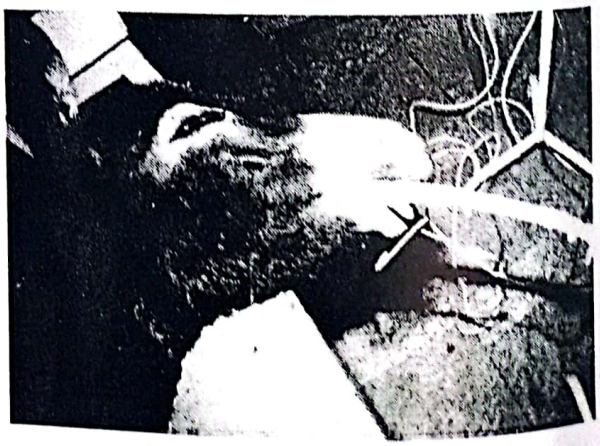

Fig.(4): Endotracheal intubation and signs of anesthesia

Anesthesia was maintained for an average of one hour in all combinations. It was characterized by brisk palpebral reflexes, variable degrees of nystagmus frequently accompanied by strong corneal reflex, reduced tearing, occasional swallowing and ear movement.

All combinations were infused dose to effect. The median infusion rate was 1 ml/kg/hr with a range of 0.8 to 1.2 ml/kg/hr in group I; 1.1 ml/kg/hr with a range of 0.8 to 1.4 ml/kg/hr in group II; 1.5 ml/kg/hr with a range of 1.2 to 1.8 ml/kg/hr in combination group III and 0.5 ml/kg/hr with a range of 0.4 to 0.6 ml/kg/hr in group IV.

The four anesthetic drug combinations were evaluated through different surgical interferences on 16 donkeys; 4 donkeys in each group (castration, small intestinal resection and anastomosis, wound repair, herniorraphy, skin tumor resection and laparotomy). Surgical conditions were adequate in all donkeys. Purposeful responses to surgical stimulation took place in 5 donkeys. Quality of analgesia was judged to be moderate in all donkeys and was not significantly different among the tested combination groups. Muscle relaxation in the majority of donkeys was judged to be good, but significant differences among groups were not detected.

The recovery period required for the donkeys to return to standing position in combination groups 1, 2 and 3 were significantly shorter than that in combination group 4. Quality of recovery was subjectively judged to be good to excellent for combination group 1, 2 and 3 and to be poor to moderate in combination group 4 (Table 4). The number of attempts to stand in group 1, 2 and 3 was almost lower than that in group 4. Donkeys stood up without spending long time in sternal recumbency. Some donkeys stood at the first attempt, with no observed ataxia. Several attempts to stand were observed in 5 donkeys. Donkeys did not become excited and there were no risk of self-inflicted injury. Signs of residual sedation (head droop, lower lip droop, dragging toes) were apparent in many cases.

The mean value of the induction, anesthetic and the recovery period and the mean scoring value of sedation, induction, analgesia, degree of muscle relaxation and recovery quality in the four anesthetic combinations were summarized in table 3.

Preanaesthetic values for heart rate, respiratory rates and temperature were within normal limits in all groups. HR did not change significantly throughout anesthesia in group 2 and 3 and tended to significantly decrease at 5 min. in group 1

Table (3): Characteristics of anesthesia in donkeys received the four anesthetic combinations

Characteristics	Group I	Group II	Group III	Group IV
Sedation quality score	3.6 ± 0.22	3.7 ± 0.19	3.5 ± 0.3	3.4 ± 0.28
Induction time (min.)	2.2 ± 0.2	2.6 ± 0.3	2.0 ± 0.4	5.2 ± 0.3*
Induction quality score	4.29 ± 0.18	4.71± 0.18	4.57± 0.20	4.14± 0.34
Anaesthetic time (min.)	56.5 ± 6.7	54.6 ± 12.7	43.3 ± 8.3	63.0 ± 8.8
Analgesia Quality score	2.57 ± 0.2	2.29 ± 0.26	2.14 ± 0.34	2.14 ± 0.34
Muscle relaxation score	3.86 ± 0.14	3.43 ± 0.30	3.14 ± 0.40	3.43 ± 0.30
Recovery time (min)	30.8 ± 4.2	29.3 ± 5.6	26.3 ± 1.8	102 ± 11.6*
Recovery quality score	4.43 ± 0.20	4.14 ± 0.26	4.29 ± 0.29	2.86 ± 0.34

and at 20 min. in group 4 (Table 4). HR was significantly lower in group 3 and 4 compared with values in group 1 and 2 (Table 5).

Regarding ECG the statistical analysis revealed a significant decrease in R-R interval at 30 min. in group 1. P-R interval was significantly increased at 50 and 55 min., R-R interval was significantly decreased at 50 min., Q-T interval was significantly increased at 5 and up to 60 min. and T wave was significantly increased at 25 and up to 60 min. after induction of anesthesia in group 2. In group 3, R- R interval was significantly decreased at 10 min. In group 4, it was significantly increased at 25, 30, 40 and 45 min. and the Q-T interval was significantly increased at 45 min. after induction of anesthesia (Table 4).

Comparing ECG among the evaluated anesthetic combinations, the results revealed that P-R and R-R intervals were significantly higher in group 3 and Q-T interval and T wave were significantly higher in group 4 compared with values for the other evaluated combinations (Table 5). Atrial fibrillation was noticed in donkeys anaesthetized with thiopental combination whereas; ventricular premature depolarization and tachycardia were noticed in one donkey at 30 min. after beginning of infusion. Atrial fibrillation and ventricular premature depolarization were recorded at 20 min. after chloral hydrate infusion (Figs. 5-8).

Respiratory rate was significantly decreased at 15 and 50 min. in group 1.; at 5 min in group 2 and at 5 and 60 min. in group 4 (Table 4). RR

was significantly lower in group 3 compared with the other three groups. Intermittent apnea (1-2 min.) was observed in some donkeys of group 2 and 3 during the infusion (Table 5).

ETCO2 was maintained at between 18 and 30 mmHg in group 1; 25 and 38 mmHg in group 2; 21 and 30 mmHg in group 3 and 26 and 41 mmHg in group 4 during the anesthetic period (Table 4). In group 1 the ETCO2 was significantly lower than that in the other groups (Table 5).

PaO2 was significantly decreased in group 1 at 15, 30, 35 and 60 min. and in group 4 at 20, 25, 35, 40, 55 and 60 min. after induction of anesthesia. In the other group it did not show significant changes (Table 4). It was significantly greater in donkeys of group 1 and 4 than in donkeys in the other groups (Table 5).

Regarding rectal temperature it was significantly decreased at 15 and up to 60 min. in group 1 and at 40, 45, 50 and 55 min. in group 4 and insignificant decrease was shown in group 2 and 3 (Table 4). It was significantly lower in donkeys of group 1, 3 and 4 than in donkeys of group 2 (Table 5).

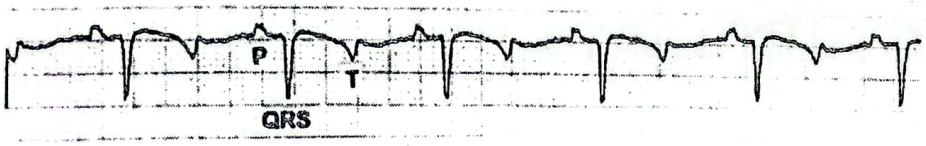

Fig.(5): ECG from a normal donkey illustrating P wave, QRS complex and T wave morphology

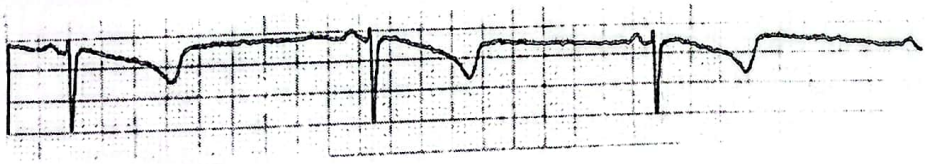

Fig. (6): ECG showing atrial fibrillation with fibrillatory P waves between normal QRS complexes.

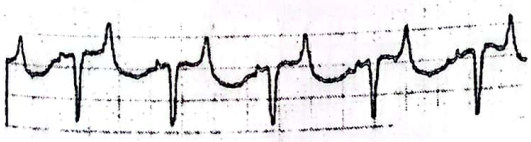

Fig.(7): ECG demonstrating ventricular premature depolarization

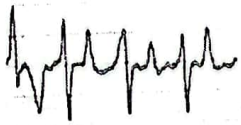

Fig. (8): ECG illustrating ventricular tachycardia

Table (4): Cardiorespiratory effects of four anaesthetic combinations used for total intravenous anesthesia in donkeys

Groups	Examined variables	Baseline values	Time during maintenance of anesthesia															
			5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min
Group I	HR (beat/min)	59.2	37.5*	49	47.5	45.5	51.3	56.2	50.3	50.2	50.6	49	51	49.4	46.7	53.3	58.3	56.3
	P wave	0.02	002	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	P-R interval	0.05	0.05	0.05	0.04	0.06	0.05	0.04	0.05	0.05	0.04	0.05	0.05	0.04	0.05	0.04	0.05	0.04
	QRS duration	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	R-R interval	0.28	0.23	0.31	0.30	0.31	0.25	0.21*	0.22	0.22	0.24	0.31	0.24	0.26	0.30	0.25	0.24	0.26
	Q-T interval	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
	T wave	0.03	0.04	0.03	0.03	0.03	0.03	0.04	0.03	0.03	0.04	0.03	0.03	0.03	0.04	0.03	0.03	0.03
	RR (breath/min)	20.8	18	17	14.2*	20	20	17.5	19.5	18	23.5	15*	22.5	23	22.3	27	16	18
	ETCO2 (mmHg)	NA	18.6*	30.5*	24*	27.5*	27*	29*	19*	27*	24.3*	18*	19.5*	21.2*	23*	23.5*	23*	24*
	PaO2 (%)	98.3	89.8	90.8	85.7*	90.5	92.7	86.8*	81.5*	87.3	88.1	88.5	89.3	84.8*	89.2	87	84*	97
	Temp. (°C)	37	34.7	34.4	33.8*	33.6*	33.1*	33.4*	32.4*	32.5*	33.1*	33.2*	32.7*	32.8*	32.6*	32.7*	32.3*	33.5*
Group II	HR (beat/min)	64.3	50	53	52	45	52	42.5	49	45	44.5	50.6	54.6	73.5				
	P wave	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02				
	P-R interval	0.4	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.4	0.04	0.06*	0.06*	0.04				
	QRS duration	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02				
	R-R interval	0.27	0.24	0.24	0.28	0.28	0.24	0.26	0.28	0.25	0.24	0.17*	0.26	0.24				
	Q-T interval	0.06	0.08*	0.08*	0.06	0.08*	0.08*	0.08*	0.08*	0.06	0.08*	0.08*	0.08*	0.08*				
	T wave	0.03	0.03	0.03	0.02	0.02	0.04*	0.03	0.04*	0.04*	0.04*	0.04*	0.04*	0.04*				
	RR (breath/min)	22	2.5	26.5	18	17	18.5	19	20	18	22	22	20	20				
	ETCO2 (mmHg)	NA	28.5	25.5	36.5	37.5	36.5	32.2	34.1	36.2	28.9	30.3	36.2	34.4				
	PaO2 (%)	98.8	84.8	83.6	83.6	98	89.6	95.6	96.3	94.8	96.3	96.6	96.3	95.5				
	Temp. (°C)	38.1	37.2	36.8	36.3	36.1	36.4	36.2	36.1	36	36	35.6	35	35				
Group III	HR (beat/min)	47.3	48	42.3	40.3	43	43.3	40	46	47	46	45	47	43				
	P wave	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02				
	P-R interval	0.04	0.04	0.05	0.04	0.05	0.04	0.06	0.06	0.06	0.06	0.06	0.06	0.06				
	QRS duration	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0..02	0.02	0.02				
	R-R interval	0.28	0.28	0.24*	0.28	0.31	0.29	0.33	0.26	0.30	0.28	0.32	0.30	0.28				
	Q-T interval	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08				
	T wave	0.03	0.04	0.03	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04				
	RR (breath/min)	18.6	4.8	12	18.6	16.5	17	18	16	17	14	16	18	18				
	ETCO2 (mmHg)	NA	21.5	28.5	27.5	28.5	28	27.5	26.6	28.2	29.1	26.4	27.5	27.3				
	PaO2 (%)	98.8	85.8	98.5	97	91.6	87	90.6	95	95	94	90	92	92				
	Temp. (°C)	36.8	35.7	35.1	34.6	34.4	33.9	33.8	34.1	34.1	34.2	34.3	34.1	34.1				
Group IV	HR (beat/min)	53.6	46.6	43	40	33*	40	39	45.7	38.2	45.8	43.2	55	51.5	46	55.3	43	47.3
	P wave	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	P-R interval	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	QRS duration	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	R-R interval	0.28	0.20	0.28	0.24	0.30	0.32*	0.32*	0.26	0.36*	0.32*	0.28	0.23	0.21	0.35*	0.18	0.29	0.23
	Q-T interval	0.09	0.09	0.09	0.09	0.09	0.10	0.08	0.11	0.09	0.13*	0.09	0.10	0.11	0.10	0.10	0.07	0.08
	T wave	0.05	0.05	0.06	0.04	0.03	0.06	0.03	0.04	0.05	0.04	0.05	0.04	0.04	0.04	0.04	0.05	0.04
	RR (breath/min)	20	13.4*	17.5	16.8	21.3	19	16.7	20	23	27.6	24.6	22.7	9.5*	18	20	20	18
	ETCO2 (mmHg)	NA	30.5*	32.2	41	44.5	39.3	35.6	39.5	33	28.3*	36	26*	26*	31.6*	29.3*	28*	26*
	PaO2 (%)	98.4	82.4	82.7	87	89.5	81*	84*	87.6	84.3*	82.5*	87.5	86*	87.6*	88.5	92	83.3*	90.5
	Temp. (°C)	37.4	36	35	36.6	35.3	34.6	34.8	34.6	33.9*	33.8*	33.7*	32.3*	34	33.4*	33.7*	33*	33.3*

Table (5): Comparison of the cardiorespiratory effects among the evaluated four anesthetic combinations.

Variables	Group I	Group II	Group III	Group IV
Heart rate (beat/min)	50.6 ± 1.2	52.0 ± 2.5	43.9 ± 0.9*	45 ± 1.5*
P wave (seconds)	0.02 ± 0	0.02 ± 0	0.02 ± 0	0.02 ± 0
P-R interval (seconds)	0.04 ± 0	0.04 ± 0	0.05± 0*	0.04 ± 0
QRS duration (seconds)	0.02 ± 0	0.02± 0	0.02 ± 0	0.02 ± 0
R-R interval (seconds)	0.25 ± 0	0.25 ± 0.008	0.28 ± 0.007*	0.27 ± 0.01
Q-T interval (seconds)	0.08 ± 0	0.07 ± 0.002	0.08 ± 0.005	0.09 ± 0.003*
T wave (seconds)	0.03 ± 0	17.4 ± 3.3	0.03 ± 0	0.04 ± 0.001*
Respiratory rate (breath/min)	19.6 ± 0.8	34.8 ± 2.7	14.5 ± 2.2*	19.3 ± 1.3
Carbon dioxide tension (ETCO2 mmHg)	24.9 ± 1*	94.4 ± 1.1	29 ± 2.2	33.1 ± 1.3
Pulse oximetry (PaO2 %)	88.9 ± 1*	36.3 ± 0.2	94.3 ± 1.3	87.9 ± 1*
Temperature	33.4 ± 0.2*	36.3 ± 0.2	34.7 ± 0.3*	34.3 ± 0.2*

Hematological findings included a significant decrease in total leucocytic counts and proportion of monocytes. Insignificant changes in the hematological parameters were observed in donkeys in group 2 and a significant decrease in the proportion of immature neutrophils was noticed in group 3. A significant decrease in total leucocytic count, proportion of immature neutrophils and a significant increase in proportion of monocytes was noticed in group 4. Serum glucose level was significantly increased in group 1 and 4 and insignificantly increased in group 2 and 3 (Table 6).

Comparison of the hematological parameters among the evaluated total intravenous anesthetic combinations the statistical analysis revealed that hemoglobin values were significantly lower in group 1 and 3. Total leucocytic counts were significantly higher in group 1, 2 and 4. The proportion of segmented neutrophils was significantly higher in group 3. The proportion of lymphocytes was significantly higher in group 1 and 2. The proportion of eosinophils was significantly higher in group 3 and 4. The proportion of immature neutrophils was significantly higher in group 2 and 3 and the total protein was significantly higher in group 1 (Table 7).

Regarding the cost of anesthetic drug combinations used for induction and maintenance of anesthesia for each 100 kg body weight in the examined donkeys, it was 21.8, 52, 38 and 15.6 Egyptian pound for the four groups respectively

Table (6): Mean values (± SE) for various hematological variables measured in donkeys received the four anesthetic combinations.

Hematological variables	Sample time	Group I	Group II	Group III	Group IV
Hemoglobin (gm%)	Baseline	12.0 ± 0.6	13.4 ± 1.3	12 ± 1.9	11.7 ± 0.9
	15 min.	11.6 ± 1.1	11.6 ± 1.7	10.4 ± 1.1	12 ± 1.5
	45 min.	12.0 ± 1	13.4 ± 1.2	12.2± 1.2	12.5± 1.6
	After recovery	11.6 ± 2.2	13.6 ± 1.3	NA	11.4 ± 1
Red blood cell counts ($X10^6$/µl)	Baseline	11.6 ± 6.7	2.6 ± 0.4	5.6 ± 0.9	4.5 ± 0.2
	15 min.	4.6 ± 0.4	4.5 ± 0.6	4.3 ± 1.1	3.5 ± 0.6
	45 min.	4.7 ± 0.4	5.1 ± 0.6	3.6 ± 0.3	3.4 ± 0.1
	After recovery	5 ± 0	5 ± 0.3	NA	4.1 ± 0.5
Total leucocytic counts ($X10^3$/µl)	Baseline	12.2 ± 1.3	12.1 ± 3.4	8.8 ± 0.5	14.3 ± 0.9
	15 min.	8.8 ± 1.4*	19.1 ± 3.6	8.8 ± 2.2	8.8 ± 1.6*
	45 min.	13.4 ± 1.5	17.2 ± 2.5	8.4 ± 1.4	9.8 ± 1.1
	After recovery	10.6 ± 1.7	18.8 ± 2.7	NA	13.7 ± 2.1
Segmented neutrophils (%)	Baseline	21.4 ± 4.5	22.0 ± 3	39.3 ± 1.7	29.2 ± 3.9
	15 min.	19.2 ± 6	35.3 ± 15.8	48 ± 9	22 ± 10.3
	45 min.	23.8 ± 3.2	28.3 ± 18.3	30 ± 4.1	39.5 ± 4.5
	After recovery	NA	NA	NA	27 ± 23
Lymphocytes (%)	Baseline	68.2±4.9	66.5 ± 9.5	45.6 ± 5.2	54.4 ± 4.9
	15 min.	70.1 ± 8.6	71 ± 13	42 ± 6	69 ± 13.5
	45 min.	67.2 ± 6.4	85.5 ± 5.5	56.6 ± 2.9	58 ± 7
	After recovery	88.0 ± 12	NA	NA	NA
Basophils (%)	Baseline	0	0.5 ± 0.5	0	0
	15 min.	2 ± 0.2	0	0	0
	45 min.	0	1.3 ± 1.3	0	0
	After recovery	0	NA	NA	0
Eosinophils (%)	Baseline	2.8 ± 1.2	1.5 ± 1.5	6.3 ± 3.1	3 ± 1.5
	15 min.	2.8 ± 1	2 ± 1.5	5.3 ± 2.6	3.5 ± 1.5
	45 min.	1.5 ± 0.9	0	2.3 ± 0.8	2.5 ± 1.5
	After recovery	4 ± 4	NA	NA	7 ± 1
Monocytes (%)	Baseline	3.5 ± 1.3	1.5 ± 1.5	1 ± 1.5	0.6 ± 0.4
	15 min.	2.5 ± 1.1	1 ± 0.5	1.3 ± 1.3	2 ± 0.8*
	45 min.	0.4 ± 0.2*	2 ± 1.1	1.6 ± 0.8	0
	After recovery	0	NA	NA	0
Immature neutrophil (%)	Baseline	4.1 ± 2.3	9.5 ± 5.5	7.6 ± 0.8	13.8 ± 2.7
	15 min.	5± 3.5	6.5± 3.5	3.3± 0.6*	3.5± 2.3*
	45 min.	7.4 ± 3.2	2.5 ± 1.5	9.3 ± 1.3	6.6 ± 2.6
	After recovery	6.0 ± 6	NA	NA	NA
Glucose (mg/dl)	Baseline	83.5 ± 16.9	104 ± 16	81 ± 20.1	76 ± 9.6
	15 min.	191.3±37.7*	136.5 ± 1.5	104 ± 20.9	133.8 ±18.5*
	45 min.	141.2 ± 9.7	127.5 ± 7.5	70.3 ± 3.7	102.6 ±10.5
	After recovery	NA	NA	NA	NA
Total protein (g/dl)	Baseline	5.8 ± 0.3	5 ± 0.75	5.2 ± 0.1	5.2 ± 0.4
	15 min.	5.8 ± 0.6	5.4 ± 0.6	5.1± 0.2	5.2± 0.2
	45 min.	5.7 ± 0.3	5.4 ± 0.6	5.5 ± 0.7	5.5 ± 0.7
	After recovery	NA	NA	NA	NA

NA: not analyzed

Table (7): Comparison of the hematological parameters among the evaluated four anesthetic combinations.

Hematological variables	Group I	Group II	Group III	Group IV
Hemoglobin (gm%)	11.6 ± 0.2*	13 ± 0.4	11.5 ± 0.5*	11.9 ± 0.2
Red blood cell counts ($X10^6/\mu l$)	6.4 ± 1.7	4.3 ± 0.5	4.5 ± 0.5	3.8 ± 0.2
Total leucocytic counts ($X10^3/\mu l$)	11.2 ± 0.9*	16.8 ± 1.6*	8.6 ± 1.3	11.6 ± 0.9*
Segmented neutrophils (%)	21.4 ± 1.3	28.5 ± 3.8	39.1 ± 5.1*	29.4 ± 3.6
Lymphocytes (%)	73.3 ± 4.9*	74.3 ± 5.7*	48.0 ± 4.3	60.4 ± 4.3
Basophils (%)	0.6 ± 0.6	0.6 ± 0.3	0	0
Eosinophils (%)	2.7 ± 0.5	1.16 ± 0.6	4.6 ± 1.2*	4 ± 1*
Moncytres (%)	1.6 ± 0.8	1.5 ± 0.2	1.3 ± 0.1	0.8 ± 0.5
Immature neutrophil (%)	2.1 ± 0.9	6.1 ± 2*	6.7 ± 1.7*	0.8 ± 0.5
Glucose (mg/dl)	138.6 ± 31.1	122.6 ± 9.6	85.1 ± 9.9	104.1± 16.7
Total protein (g/d)	5.7 ± 0.03*	5.2 ± 0.1	5.0 ± 0.08	5.3 ± 0.1

DISCUSSION

Total anesthesia is applied to get the maximum privileges of its components and to minimize their negative effects. However, it is still limitedly used in equine. In the present study, Romifidine premedication was successfully achieved at a dose rate of 80 µg / kg as it did not interact with the used anesthetics. The drug was previously used in combination with ketamine and thiopental in horses by Gomez- Villamandos et al (1994/ 1995); Keller and Genzow (1994) and Kerr et al (1996). In the meantime, the addition of diazepam improved muscle relaxation, sedation and resulted together with romifidine in smooth induction and recovery (Marntell and Nyman, 1996). Moreover, it reduced anxiety and corrected some clinical adverse effects as respiratory depression and low heart rate (England et al, 1992 and Diamond et al, 1993).

The first used combination romifidine/thiopental/ guaifenesin induced smooth induction of deep anesthesia, good muscle relaxation, moderate analgesia and smooth good recovery. In horses, other investigators concluded that the better quality of the induced anesthesia was due to the synergistic effect of the used drugs (Muir et al, 1979; Shehata, 1998 and Bennett et al, 1998). In the meantime, combining these drugs together decreased the solely used doses of each of them thus decreasing their adverse clinical effects known to accompany barbiturates anesthesia as hypotension and apnea or respiratory depression. However, such effects were not completely overcome throughout the obtained anesthesia as both respiratory and heart rates were reduced for minutes af-

ter induction. Monitoring PaO2 and etCO2 reflected the insignificance of respiratory changes that took place. Moreover, ECG revealed decreased R-R interval, atrial fibrillation, ventricular premature depolarization and tachycardia. It is widely accepted that the use of barbiturates and chloral hydrate could predispose to such cardiac arrhythmiafs (Azab, 1991; Reef and Meguirk, 2000 and Menzies-Gow, 2001). Hypothermia was observed throughout the anaesthetic period which was attributed to the depressant effect of the used drugs on the thermoregulatory center (Karam and Youssef, 1991 and Tomasic, 1999). This combination resulted in leukocytosis and hyperglycemia. It is worthy to mention that the duration of the induced anesthesia made it possible to carry on different operations under its effect.

The second used combination (ketamine/ guaifenesin/romifidine) induced smooth induction, moderate analgesia, good muscle relaxation and smooth good quality recovery in donkeys. However, animals showed brisk palpebral reflex, variable degree of nystagmus and occasion swallowing during this anesthesia. Some or all of these criteria were also noted in horses and zebras (Klein, 1995; Mama, 2000 and Stanway, 2001). In spite the smooth good quality recovery, it was very difficult to make animals to get up before they were ready so some donkeys may need a "boost" on the tail to stand (Matthews et al, 1994/1997). As the elimination half-life in donkeys is short, this might be the cause of comparatively shorter induced anesthesia thus it could be applicable minor surgical operations. Comparing clinical changes and ECG findings with those previously recorded by other authors in horses and ponies showed that they were within acceptable limits (Rezakhani and Yazdanmehr, 1977; Luna et al, 1992 and Taylor et al, 1998). Monitoring PaO2 and etCO2 reflected the impairment of pulmonary function that took place also in horses anesthetized by the same combination (Greene et al, 1986 and Marntell and Nyman, 1996). The combination has the advantage of inducing good muscle relaxation that is missed if ketamine is used alone, thus it could be attributed to the addition of guaifenesin.

The third used combination (propofol/ guaifenesin/romifidine) induced smooth good quality induction and recovery, moderate analgesia and good muscle relaxation. However, the use of propofol alone induced variable induction scores ranging from excellent to poor (Nolan et al, 1996 and Ohta et al, 2001). This combination did not result in significant change in heart rate, however, propofol alone showed variable, dose dependent and time related effect on heart rate. Mama et al (1995/1996) recorded tachycardia in

horses after propofol infusion. Monitoring PaO2, etCO2 and ECG revealed that such combination seemed fascinating as its pulmonary and cardiac effects were within normal during anesthetic period.

The fourth combination (chloral hydrate/ guaifenesin/romifdine) induced moderate smooth induction, moderate analgesia, good muscle relaxation and fair long recovery. Animals showed brisk palpebral reflex and variable degrees of nystagmus. Chloral hydrate is known to have poor analgesic effects thus it needs to be combined with α2-agonists to improve analgesia (Muir and Hubbell, 1991 and Ez-Eldien, 1996). Adding guaifenesin to Chloral hydrate cause induction to be smooth and muscle relaxation to be satisfactory in donkeys (Roberts, 1968 and Shehata, 1998). In the mean time, chloral hydrate was found to cross slowly the brain barrier that is why the recovery period was long (Wright, 1958 and Dahiya et al, 1985). Regarding cardiopulmonary effects of the combination, there was a clear depression in both heart and respiratory rates. Moreover, ECG revealed decreased R-R interval, increased Q-T interval, atrial fibrillation, ventricular premature depolarization. Muir and Hubbell (1991) got the opinion that chloral hydrate was of such clinical effect as it has a depressing action on medullary centers. In the meantime, Lumb and Jones (1973) suggested that the release of adrenaline after chloral hydrate injection was the cause of cardiac fibrillation and aterioventricular block during recovery. This combination resulted in leucopenia and hyperglycemia which was also recorded by Shehata (1998) in donkeys and horses.

Comparing the used four combinations in donkeys, it could be concluded that group IV showed the longest induction period whereas the induction quality was similar in the four groups. The used four combinations resulted in similar sedation, analgesia and muscle relaxation quality. The longest recovery time and the poor recovery quality were met with the combination used in group IV. Regarding the cardiac and pulmonary effects group I & II showed the least changes in both heart beats and ECG, meanwhile, group II & III resulted in minimum pulmonary effects. Concerning the blood parameters group II & III showed insignificant changes; meanwhile group I & II showed hyperglycemia. Thiopental and chloral hydrate anaesthetic combinations were significantly cheaper then ketamine and propofol anaesthetic combinations. In the meantime, ketamine and propofol anaesthetic combinations were excellent for debilitated animals whereas chloral hydrate should not be used in animals with liver damage or debilitated animals. These results indicate that continuous intravenous infusion of thio-

pental / guaifenesin / romifidine, ketamine / guaifenesin / romifidine, propofol / guaifenesin / romifidine and chloral hydrate / guaifenesin / romifidine anaesthetic combinations can be used as a safe method of total intravenous anesthesia for short and prolonged surgical procedures under field conditions in donkeys.

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