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Maintenance of Total Intravenous Anaesthesia in Donkeys Using Continuous Infusion with Detomidine and Ketamine

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ABBREVIATIONS:
TIVA= total intravenous anaesthesia,
K=Ketamine,
D=detomidine,
I= saline drip infusion

ABSTRACT

The objective of the current study was to evaluate the anaesthetic properties, cardio-pulmonary and some biochemical effects following induction of anaesthesia in donkeys using different combinations of detomidine/ketamine. Six donkeys, 3-5 years of age with average body weight of 90±15 kg, were used in the study. Each animal was anaesthetized with one of two different protocols with two weeks interval between each two successive anaesthetic protocols injection as washing out period. In the first protocol, donkeys were premedicated with 50µg/kg detomidine intravenously (IV) and then after 10 minutes donkeys were injected with 4mg/kg ketamine intravenously (IV) for induction of anaesthesia (DK). In the second protocol, anaesthesia was induced as mentioned above and then maintained immediately by intravenous infusion of 6mg/kg ketamine and 50µg/kg detomidine in saline drip (DKI). Physiological parameters: respiratory rate, heart rate and rectal temperature were monitored before, during and following induction of anaesthesia. Induction quality, muscle relaxation, phases of anaesthesia and recovery time and quality were also studied. Some blood biochemical parameters: blood urea, plasma glucose concentration, ALT, and AST activity were measured before and during anaesthesia. Results obtained showed that, respiratory rate and rectal temperature were affected significantly ($p \leq 0.05$) as a result of using each of the two protocols. A significant difference ($p \leq 0.05$) was also observed regarding analgesia, lateral recumbancy, standing and walking time and total recovery time. Muscle relaxation quality ranged between good and poor. Induction quality was found to be smooth to fair in the two protocols. Recovery from DK anaesthesia was smooth to fair and from poor to very poor in case of DKI. Glucose and urea levels were significantly ($p \leq 0.05$) affected in the two protocols used. It is to be concluded that although these protocols induced no cardio-respiratory or metabolic changes, the poor and very poor quality of recovery may limit the usefulness of the intravenous infusion maintenance of anaesthesia with DKI attempted in this study. However, considerable prolongation of anaesthesia was achieved.

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INTRODUCTION

In remote areas, the availability of inhalation anaesthetic accommodations is limited. Hence, no provision is made for the administration of lengthy general anaesthetics. Under field conditions, the use of anaesthetic drugs with minimal side-effects becomes important, as the availability of medical care is also limited. The ideal analgesic provides good analgesia and sedation without any side-effects (Joubert *et al.*, 1999).

Total intravenous anaesthesia (TIVA) has been advocated as alternative and possibly superior method of producing equine anaesthesia in horses on the basis of cardiopulmonary, endocrine and economic data (Taylor *et al.*, 1995, Bettschart-Wolfensberger *et al.*, 1996, and Taylor *et al.*, 1998). Studies investigating the anaesthetic potential of various combinations of α2-adrenocepter agonists (e.g. xylazine, detomidine, romifidine, medetomidine), dissociative anaesthetics (e.g. ketamine, tiletamine) and muscle relaxing drugs (e.g. guaifenesin, diazepam, climazolam, midazolam, zolazepam) for producing TIVA in horses have generally demonstrated less cardiovascular depression compared with inhalation anaesthesia (Taylor *et al.*, 1995, Bettschart-Wolfensberger *et al.*, 1996, Taylor *et al.*, 1998, Muir *et al.*, 2000, and McMurphy *et al.*, 2002).

Detomidine (4-(2.3-dimethylphenyl) ethyl)-1H-imidazole HCl (Vähä-Vahe, 1991), is the most specific agonist for central α2 adrenoceptors, but high doses will activate alpha1 adrenoceptors (Gross and Booth, 1995). Although similar to xylazine, detomidine produces sedation and analgesia of greater magnitude and longer duration (Taylor, 1985, Daunt, 1995). The duration of sedation is dose-dependent, with larger doses resulting in a longer duration of action (Clarke and Taylor, 1986, Daunt, 1995). The use of detomidine in donkeys is not well documented (Whitehead *et al.*, 19991, Mostafa *et al.*, 1995, Joubert *et al.*, 1999). Sedation in donkeys usually occurs within 2–3 minutes following intravenous administration (Mostafa *et al.*, 1995). The recommended dose of detomidine in donkeys is 20 μg/kg and this provides both analgesia and sedation; while lower doses did not produce analgesia (Mostafa *et al.*, 1995). Higher doses of detomidine have been recommended to increase analgesia and prolong sedation in horses (Jöchle, 1989, Daunt, 1995).

Recently, Abakar *et al.*, (2014) evaluated the quality of anaesthesia induced in donkeys using different combinations of diazepam with xylazine-ketamine in an attempt to produce satisfactory anaesthesia under field conditions. Their results indicated that these protocols are safe to be used in donkeys.

Attempts to prolong anaesthesia in horses using triple drip was practiced in the past decades. As well as there are suggestion that higher doses of detomidine are required in donkeys (Whitehead *et al.*, 1991, Gross and Booth 1995, Mostafa *et al.*, 1995).

Recent report (Ghurashi *et al.*, 2016) showed that continous intravenous infusion with Ketamine and Diazepam resulted in significant prolongation of anaesthesia in donkeys. The aim of this study was to evaluate the anaesthetic properties of total intravenous anaesthesia induced using detomidine and ketamine with or without infusion for maintenance of anaesthesia in order to increase the intensity and duration of analgesia in donkeys.

MATERIALS AND METHODS

Place of the study: This study was carried out at the Farm of the College of Veterinary Medicine, Sudan, University of Science and Technology, Khartoum North, Hillat Kuku, Sudan.

Experimental animals: A total of six healthy donkeys of local breed, four males and two females were used in this study. Their age ranged between 3-5 years, with average body weight of 90±15 kg. The animals were kept in closed pens in the College farm, throughout the duration of the study. The animals were fed on green fodder, hay and supplemented with concentrates with free access to water. The animals were kept for two weeks to get acclimatized before starting experiments. Thorough clinical examination was conducted before starting experimental work, after every experiment and routinely throughout the course of the study.

Injection set: Disposable syringes 5, 10 and 20 (Nirma limited health care division Sachana Gujarat 382150, India), and intravenous catheters (18 G) were used for intravenous injection of drugs. Normal saline drips and microdripper 500 ml/hr was used for infusion.

Drugs: Ketamine was used as the major anaesthetic agent in this study together with detomidine as pre-anaethtic medication as follows:

1. Ketamine Hcl 5% (Troika pharmaceuticals Ltd Thol-382728 Gujarat, India).
2. Detomidine 1% (Orion pharma.13483-2).

Pilot study: Six animals were used in the pilot trial. The animals were divided into two groups. Detomidine was injected intravenously at dose rate of 30 and 50µ/kg body weight in the first and second groups, respectively. 10minutes later, each animal in the two groups received ketamine at a dose of 4mg/kg intravenously. The sedative effect of detomidine was studied. The muscle rigidity resulted from injection of ketamine was evaluated.

Anaesthetic protocols: Two different anaesthetic protocols were used as follows:

1- Detomidine 1% 50µg/kg + Ketamine 5% 4mg/kg (DK)

2- Detomidine 1% 50µg/kg + Ketamine 5% 4mg/kg + Infusion (Detomidine 1% 50µg/kg + Ketamine 5% 6mg/kg) in saline solution (DKI).

Induction of anaesthesia with ketamine was carried out 10 minutes after injection of detomidine.

Maintenance of anaesthesia was carried out by continuous drip infusion for 20±2 minutes.

Signs and observations following injection of the premedication and/or anaesthetic

Following injection of detomidine animals were monitored for 10 minutes to describe the signs and observations of per-anaesthetic medication injection.

Maintenance of anaesthesia: Maintenance of anaesthesia with detomidine/ketamine infusion was done using saline drip with calibrated microdripper immediately and as soon as possible after induction of anaesthesia with ketamine. The drip was calibrated to come to an end at 20±2 minutes.

Anaesthesia Phases and scales:

Quality of anaesthesia: induction quality, muscle relaxation and recovery quality were scored as illustrated in Table (1)

Table 1: Criteria of scoring the quality of induction, muscle relaxation and recovery in donkeys anaesthetized with DK or anaesthetized and maintained with DKI

Score	Quality	Character
Induction quality:		
1	Smooth	Gradual falling to the ground with no paddling and no stiffness of limbs
2	Fair	Gradual falling to the ground with mild paddling and no stiffness of limbs
3	Rough	Gradual falling with vigorous paddling and strong stiffness of limbs
Muscle relaxation:		
1	Excellent	Complete relaxation (jaws, neck, abdomen and limbs)
2	Good	Relaxation of neck, abdomen and limbs
3	Poor	Rigidity in muscles of jaws, neck, abdomen and limbs
Recovery :		
1	Smooth	Donkey capable of standing at first attempt - mild ataxia
2	Fair	Donkey remained calm and needed two- three attempts to stand - clear ataxia
3	Poor	Donkey remained calm but assisted to stand
4	Very poor	Donkeys excitement during recovery - assisted and supported

Induction of anaesthesia: was considered subjectively as the period taken by the animal to fall to the ground, showed signs of unconsciousness, respond negatively to painful stimuli and paddling and stiffness of limbs stopped if it is present.

Analgesia phase: was assessed subjectively as the period during which the animal shows signs of unconsciousness and responds negatively to noxious or painful stimuli (pinprick in the perineal and scrotal region).

Lateral recumbency: was considered subjectively as the duration at which the animal responds positively to painful stimuli, muscles regained their tonicity and the animal is incapable of adopting sternal position.

Sternal recumbency: It was considered as the duration of time during which the animal was able to adopt sternal recumbancy without falling to lateral recumbancy and without adopting standing position (Ghurashi *et al*., 2008).

Standing phase: It is the stage at which the animal stood but unable to walk ten steps (Ghurashi *et al.,* 2007).

Recovery: The animal was considered to be recovered from anaesthesia when it was able to support itself in standing position and walk for ten steps without falling down (Ghurashi *et al.*, 2008).

Total recovery: Total recovery time was considered as the total time calculated from the time of induction of anaesthesia until recovery was attained (Nuha, 2004).

Physiological parameters: Respiratory rate, heart rate and rectal temperature were monitored before injection of detomidine, 10 minutes after injection of detomidine, immediately after induction of anaesthesia, and at 10 minutes interval until full recovery was attained following induction of anaesthesia, using standard methods (Kelly, 1984).

Blood samples collection and Biochemical analyses: Blood samples were collected before injection of the

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pre-anaesthetic medication and at 30, 60 and 90 minutes following injection of the anaesthetic. Whenever blood sample was collected it was delivered immediately to the laboratory to separate plasma in eppendorf container and kept at -20°C until analysis. Urea, Glucose, AST and ALT were measured using commercial kit (Vitro Scient-Egypt) according to colorimetric methods described by Fawcett and Scott (1960), Barham and Trinder, (1972), and Reitman and Frankel (1957).

Statistical analysis

T- Test was used to compare the results obtained concerning the different anaesthetic phases, while ANOVA was used to compare results for physiological parameters. GraphPad Prism 5.0 (GraphPad Software) was used to perform these analytical operations. A descriptive statistics value (percentage) was used to compare subjective data i.e. Induction, analgesia, muscle relaxation and recovery.

RESULTS

The results obtained from the first pilot study revealed that injection of detomidine at dose rate of 30 µg/kg resulted in mild muscle relaxation, lowering of head, mild ataxia and partial relaxation of penis.

Induction of anaesthesia with ketamine 4mg/kg after premedication with detomidine 30 µg/kg resulted in rough induction of anaesthesia together with exaggerated muscle rigidity and limb movements and laboured respiratory movements. Injection of detomidine at dose rate of 50µg/kg resulted in good muscle relaxation, obvious ataxia and complete protrusion of penis. Induction of anaesthesia with ketamine at dose e rate of 4mg/kg after premediaction with detomidine at dose rate of 50 µ/kg resulted in good induction with no muscle rigidity, no limb movement and no respiratory distress.

The study revealed that the dose of 30 µg/kg of detomidine is not enough to tolerate the muscle rigidity caused by ketamine. The dose of 50 µg/kg of detomidine was chosen for the study.

Signs and observations following injection of Detomidine:

Following intravenous injection of detomidine 50µg/kg in donkeys, the main signs observed were dropping of the head, lowering the lip, abduction of the legs, protruding of the penis, profound ataxia and continuous snoring and rubbing of the upper lip and gum with the foot or even the ground .

Salivation was observed to occur in all animals subjected to anaesthesia with the above mentioned protocols, and it started usually following induction of anaesthesia until at least the end of analgesia phase. A frequent urination was also observed in animals under investigation. Each animal did urinate at least three times during anaesthesia starting from induction of anaesthesia until full recovery was attained.

Quality of induction, muscle relaxation and recovery:

Results obtained in the current study indicated that smooth and fair induction were occurred at equal percentages namely 50% for each in the total number of animals used, following induction of anaesthesia using DK protocol; while in the other protocol DKI smooth and fair induction were observed to occur in 66.7% and 33.3% in the animals used in the study respectively (Table 2).

Table 2: Induction quality following induction and maintenance of anaesthesia using DK or DKI

Protocol	Smooth		Fair		Rough		Total No. of animals
	No.	%	No.	%	No.	%	
DK	3	50%	3	50%	0	0	6
DKI	4	66.7%	2	33.3%	0	0	6

DK= Detomidine 50µg/kg + Ketamine 4mg/kg (DK)
DKI= Detomidine 50µg/kg + Ketamine 4mg/kg + Infusion (Detomidine 50µg/kg + Ketamine 6mg/kg) in saline solution (DKI).

Muscle relaxation was found to occur at different scales and for different duration of time following induction of anaesthesia using DK or DKI. Induction of anaesthesia DK resulted in muscle relaxation for 10 minutes while induction and maintenance anaesthesia with DKI resulted in muscle relaxation for more than 40 minutes. Muscle relaxation observed to occur ranged between poor and good in both protocols, none of the animals used in the study showed excellent muscle relaxation (Table, 3).

Table 3: Muscle relaxation quality of muscle relaxation following induction and maintenance of anaesthesia with DK or DKI

Time	0			10			20			30			40			50		
	No. of animals																	
Scale	P	G	E	P	G	E	P	G	E	P	G	E	P	G	E	P	G	E
DK	3	3	0	2	4	0	6	0	0	6	0	0	6	0	0	6	0	0
DKI	2	4	0	0	6	0	0	6	0	0	6	0	0	6	0	6	0	0

P= poor, G =good, E= excellent
DK= Detomidine 50µg/kg + Ketamine 4mg/kg (DK)
DKI= Detomidine 50µg/kg + Ketamine 4mg/kg + Infusion (Detomidine 50µg/kg + Ketamine 6mg/kg) in saline solution (DKI).

Recovery from anaesthesia induced using DK was observed to be of fair quality in 50% and of smooth quality in the other 50% of the animals used in the study. While recovery from anaesthesia induced using DKI was graded to be of poor and very poor in quality in 50% of the animals, respectively (Table, 4).

Table 4: Recovery quality following induction and maintenance of anaesthesia using DK or DKI

Scale	Smooth		Fair		Poor		Very poor		Total No. of Animals
Protocols	No.	%	No.	%	No.	%	No.	%	
DK	3	50%	3	50%	0	-	0	-	6
DKI	0	-	0	-	3	50%	3	50%	6

DK= Detomidine 50µg/kg + Ketamine 4mg/kg (DK)
DKI= Detomidine 50µg/kg + Ketamine 4mg/kg + Infusion (Detomidine 50µg/kg + Ketamine 6mg/kg) in saline solution (DKI).

Studying and comparing the different anaesthetic phases between DK and DKI showed significant difference ($p \leq 0.05$) in the duration of analgesia duration,

lateral recumbancy phase, standing and walking time and total recovery time. The duration of sternal recumbancy phase was found to be of non significant difference between the two protocols used in the study.

Table 5: Duration (min.) of anaesthetic phases in donkeys following induction and maintenance of anaesthesia with DK or DKI

Protocols	Anaesthetic phases (min.)				
	Analgesia	Lateral recumbancy	Sternal recumbancy	Standing and walking	Total recovery
DK	11.50±3.78 a	22.00±4.71 a	11.6±2.50a	3.83±1.72a	37.67±6.47a
DKI	41.17±4.91 b	79.67±3.40 b	18.17±6.40a	16.33±4.68b	114.2±10.21b

- Different letters in the same raw indicate significant difference ($p \leq 0.05$).
DK= Detomidine 50µg/kg + Ketamine 4mg/kg (DK)
DKI= Detomidine 50µg/kg + Ketamine 4mg/kg + Infusion (Detomidine 50µg/kg + Ketamine 6mg/kg) in saline solution (DKI).

Generally the two anaesthetic protocols used had a depressive effect on the respiratory rate. Injection of detomidine resulted in significant ($p \leq 0.05$) drop in respiratory rate in one group and the drop in respiratory rate was found to be of no significant value in the other group. Both protocols caused a significant drop ($p \leq 0.05$) in respiratory rate immediately after induction of anaesthesia and it remained significantly dropped ($p \leq 0.05$) for 10 minutes in case of DK and for 30 minutes in case of DKI anaesthesia. Forty minutes after induction of anaesthesia with DKI a significant ($p \leq 0.05$) increase in the respiratory rate was observed to occur and it remained at high level until full recovery was attained.

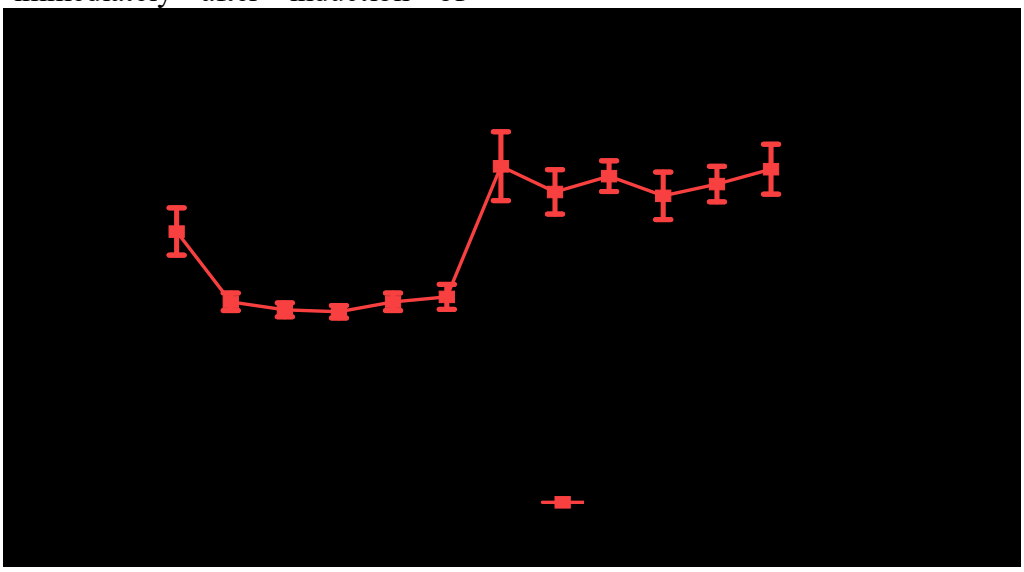

Figure 1: Effect of induction of anaesthesia with DK and induction and maintenance of anaesthesia with DKI on respiratory rate

Non- significant change in the heart rate was observed to occur as a result of induction of anaesthesia with DK and induction and maintenance of anaesthesia with DKI as illustrated in Figure (2).

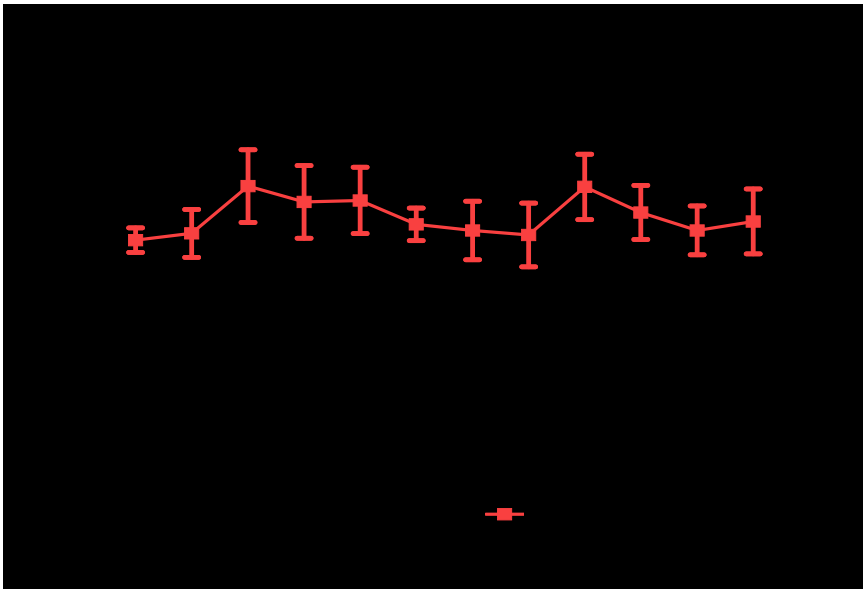

Figure 2: Effects of induction of anaesthesia with DK and induction and maintenance of anaesthesia with DKI on heart rate

Figure (3) shows the effect of induction of anaesthesia with DK and induction and maintenance of anaesthesia with DKI on rectal temperature. Both DK and DKI were observed to cause a significant drop ($p \leq 0.05$) in rectal temperature, this drop was observed to occur 10 minutes after injection of detomidine and the significant hypothermia was found to last for 10 minutes and 30 minutes in case of using DK and DKI respectively.

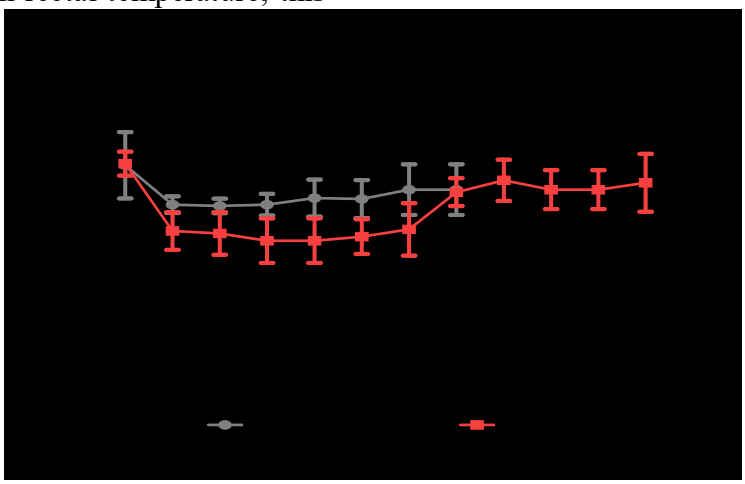

Figure 3: Effect of induction of anaesthesia with DK and induction and maintenance of anaesthesia with DKI on rectal temperature

No significant change in the concentration of blood urea was observed as a result of using DK for induction of anaesthesia, while induction and maintenance of anaesthesia with DKI caused significant ($p \leq 0.05$) increase in blood urea level at 30, 60 and 90 minutes following induction of anaesthesia. Both protocols caused significant ($p \leq 0.05$) increase in blood glucose which was observed to occur at 90 minutes and at 30, 60 and 90 minutes

after induction of anaesthesia with DK and DKI, respectively. Both protocols evaluated induced no significant change in ALT and AST activity.

Table 6: Changes observed in some blood biochemical constituents in donkeys following induction and maintenance of anaesthesia using DK or DKI

Parameters (unit)	Protocols	Time (min.)			
		Base	30	60	90
Urea (mmol/l)	DK	2.93 ±0.48a	3.62±0.82a	3.98±0.97a	4.49±1.17a
	DKI	3.16 ±0.69a	5.36±0.47b	5.32±0.35b	5.54±0.48b
Glucose (mmol/l)	DK	4.49±0.08a	4.72±0.44ab	5.33±1.20ab	7.12±1.65b
	DKI	3.16±0.56a	5.89±1.91ab	5.99±2.56ab	7.24±2.64b
ALT(UI)	DK	3.84±1.40 a	5.35±1.61 a	4.37±1.39 a	5.49±2.05 a
	DKI	7.68±2.45 a	7.10±3.82 a	8.25±3.20 a	7.79±2.49 a
AST(UI)	DK	87.95±35.67a	84.04±18.26a	103.5±31.09a	101.5±29.57a
	DKI	91.14±18.60a	110.7±33.96a	117.6±36.65a	129.1±39.60a

- Different letters in the same raw indicate significant difference ($p \leq 0.05$).
DK= Detomidine 50µg/kg + Ketamine 4mg/kg (DK)
DKI= Detomidine 50µg/kg + Ketamine 4mg/kg + Infusion (Detomidine 50µg/kg + Ketamine 6mg/kg) in saline solution (DKI).

DISCUSSION

Clinical signs and observations induced following injection of detomidine in donkeys was similar to those obtained following injection of xylazine (α2-adrenocetor agonist in donkeys (Abakar *et al.*, 2014). McCrackin *et al.,* (1994), who reported initial apprehension followed by lowering of the head, drooping of the eyelids and lower lip and the horse becomes rapidly ataxic. In goats, intramuscular injection of xylazine, resulted in lowering of head and neck, partial drooping of eyelids, muscular in-coordination and staggering gait (Saleh, 1993).

The diuresis induced by detomidine in the current study was suggested to be associated with increased glomerular filtration rates, inhibition of anti-diuretic hormone release, and inhibition of antidiuretic hormone effect on the renal tubules as well as increased release of atrial natriuretic factor (Duthie and Nimmo, 1987, England and Clarke, 1996). Voiding of urine observed in donkeys in the current study may be attributed to the sympathomimetic effect of detomidine and that is in agreement with observations of Joubert *et al.*, (1999). The mechanisms responsible for this are similar to those described for alpha2 adrenergic agonists.

The smooth to fair quality of induction observed in both anaesthetic protocol, is acceptable quality and may be due to the muscle relaxing effect of detomidine reported by Matthews *et al*., (2008)and Amin and Najim, (2011) , as ketamine is expected to cause rough induction due to its effect on muscles (Hall *et al*., 2001). Ketamine produces no muscle relaxation and tonic clonic spasms of limb muscles may occur even in the absence of surgical or other stimulation (Hall *et al*., 2001). Muscles relaxation observed in this study is in agreement with previous results obtained by Matthews *et al*., (2008) and Amin and Najim, (2011), who reported occurrence of good muscle relaxation in horses and donkeys, respectively following induction of anaesthesia using detomidine/ketamine combination.

Alpha 2 adrenoceptor agonists improve the quality of recovery in horses Santos *et al*., (2003). This finding is in line with recovery quality observed following induction of anaesthesia using the first protocol (DK) where recovery was found to be smooth and fair in quality. In this study recovery from anaesthesia with DKI was found to be of poor or very poor quality and this may be attributed to the effect of high dose of ketamine and high dose of detomidine where they are reported to have a dose depent effect (Short *et al.,*1984.and Hall *et a.,* 200l)

Induction and maintenance of anaesthesia DKI resulted in a significant ($p \leq 0.05$) prolongation in the duration of analgesia, lateral recumbancy, standing and walking time and total recovery time compared with the same phases resulted from anaesthesia with DK. The significant difference in the duration of the phases observed in this study between the two protocols may be attributed to the difference in the dose where in the second protocol the dose is almost double the dose in the first protocol. Ketamine and detomidine were reported to have a dose dependent effect (Short *et al.*, 1984 and Hall *et al.*, 200l).

A significant depression in respiratory rate was observed following the use of DK and DKI at 10 minutes and 20 minutes respectively. Ketamine is reported to have no depressive effect or even stimulatory effect on the respiratory system (Morse *et al.*, 2004; and Von Ungern- Sternberg *et al.,* 2007). The depressive effect on the respiratory rate may be attributed to the muscle relaxing effect of Detomidine (El-Kammar and Gad, 2014 and El-Kammar *et al.,* 2014). Although, opioids and alpha2 adrenergic agonists are known to depress ventilation and alter arterial partial pressures of carbon dioxide and oxygen, none of the donkeys in the current study showed any symptoms of respiratory failure a result that is in agreement with previous observation of Joubert *et al.*, (1999).

Anaesthesia with either DK or DKI resulted in no significant change in heart rate, a finding that is in line with the findings of Ali, (2013) who reported the non-significant effect of Detomidine/ diazepam or detomidine/ medazolam ketamine bearing in mind that diazepam or zolazepam have no effect on heart rate (Hall *et al.,* 200l). Vainio, (1982) reported the suppressive effect of detomidine on heart rate , this effect did not appear in during this study and it might be antagonised by the stimulatory effect of ketamine on heart rate reported by Haskins *et al*., (1985). The cardiovascular actions of ketamine include increases in heart rate and cardiac output which are attributed to increase in centrally mediated tone, release of catecholamines from peripheral storage sites, inhibition of neural, extra-neural uptake of catecholamines and inhibition of barorecptor reflex activity (Muir, 1991, and Muir *et al.*, 2000). Ketamine also produces direct vasodilation of vascular smooth muscle and an inotropic effect on the myocardium (Lin, 1996). The cardiovascular stimulating effects induced by ketamine are blunted or prevented by prior administration of benzodiazepines and α2-agonists (Lin, 1996).

After intravenous injection of alpha2 adrenergic agonists, the following cardiovascular effects have been described; blood pressure initially increases rapidly due to direct

stimulation of peripheral alpha1 receptors, which increases systemic vascular resistance, usually within 2–5 minutes of administration. This is accompanied by a significant fall in heart rate due to a baroreceptor response (Vähä-Vahe, 1991, and Daunt, 1995). The heart rate usually returns to normal within a few minutes (Duthie and Nimmo, 1987). The cardiovascular side effects are dose-dependent and reach their maximum effect 15–30 min after intravenous injection (Duthie and Nimmo, 1987).

Duthie and Nimmo, (1987), Daunt, (1995), and England and Clarke, (1996), reported that, heart rates decreased significantly over the first minute. This correlates well with what has been reported in equines treated with detomidine with or without butorphanol, and with the single account of the use of detomidine in donkeys. After the initial drop, the heart rate tended to return to baseline values. It is well-known that after administration of alpha2 adrenergic agonists the heart rate tends to return to normal, usually within 20–30 min.

Therefore, we considered that the cardiovascular changes observed in the current study in donkeys anaesthetized with DK or DKI were a result of the additive and synergistic effects of detomidine and ketamine. DK and DKI caused a significant drop in rectal temperature after injection of detomidine and after induction of anaesthesia for 10 minutes and 30 minutes respectively. The significant hypothermia observed in this study may be attributed to the suppressive effect of detomidine on rectal temperature as reported by (England and Clark, 1996, El-Kammar and Gad.2014, and El-Kammar *et al.,* 2014)

In this study DK was found to have no significant effect on blood urea concentration this finding is in agreement with previous results obtained by El-Kammar and Gad, (2014), who reported the no significant effect of the same protocol on urea in donkeys. DKI was found to cause a significant increase in urea level this finding is in line with the finding of Ali, (2013) who reported significant increase in urea level as a result of using detomidine /ketamine combinations in equines.

In this study DK and DKI caused significant increase in blood glucose level during the whole course of anaesthesia this finding is supported by the findings of Amin *et al*., (2012) and Ambrosio *et al.,* (2012) who reported the same results in donkeys and horses, respectively.

Both DK and DKI were found to cause no significant effect on ALT and AST activity, this finding is supported by the results obtained in donkeys by El-Kammar and Gad, (2014) who used ketamine detomidine combination and it is partially supported by Amin *et al.*, (2012) who used ketamine combinations in she donkeys. Khan and his colleagues (2003), evaluated the effects of detomidine (a novel veterinary sedative and analgesic) on blood chemistry and electrolyte profile in buffalo calves, injected intravenously at the dosage rate of 50 μg/kg body weight.

CONCLUSION AND RECOMMENDATIONS

Our results indicate that the DKI-TIVA can provide general anaesthesia in donkeys for approximately 35-40 minutes with minimum cardiopulmonary depression. We elected not to administer supplemental oxygen in order to more closely mimic field anaesthesia

where oxygen is not routinely administered. During DKI-TIVA, all donkeys breathed fresh air spontaneously and respiratory as well as heart rate remained in safe levels. In this study, the infusion of DKI can be expected to provide a substitute anaesthetic protocol for TIVA induced using guaifenesin-ketamine-detomidine.

The quality of recovery in this study ranged from poor to very poor primarily because of the presence of ataxia. The tendency to display ataxia after standing is relatively common in horses pre-medicated with detomidine.

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