Research Article

Estimate the Effect of Propofol and Ketamine on Clinical and Hematological Parameters in Xylazine Pre-Meditated Baladi Egyptian Donkeys

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Abstract | This study aimed to compare the effect of propofol and ketamine on hematological parameters and cardiopulmonary parameters in xylazine pre-medicated Baladi Egyptian donkeys. Eighteen apparently healthy donkeys were divided into two equal groups. All animals were injected with xylazine HCl 2% (1.0mg/Kg) as pre-medication drug intravenously. Then in the first group (G1), was injected by the propofol (2mg/Kg intravenously) while in the second group (G2), was injected with ketamine HCl (2.2mg/Kg intravenously). The onset, duration, and recovery times were recorded for each group. Heart rate, respiratory rates, and rectal temperature were recorded. Blood samples were collected at 0, 20, 40, 80 minutes and 12 hours after administration for detection the hematological changes. Results showed that the onset, duration and total recovery times of anesthesia were 7.33±3.05 min and 3.33±1.53 min, 26.33±3.51 min and 45±3.00 min and 64±4.58 min and 86.67±6.11 min in G1 and G2 respectively. In G1, presence of a significant decrease in RBCs, PCV and Hb values and apnea was recorded. However, non-significant hematological changes were reported in G2. In conclusion, ketamine was produced by rapid induction, long duration, smooth recovery and satisfactory anesthesia without any significant cardio-respiratory changes and produced good and produce efficiently anesthesia in xylazine pre-medicated Baladi Egyptian donkeys in compare with the propofol.

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Introduction

Secure and efficient general anesthesia is applied in donkeys to conduct painless surgical operations using convenient anesthetics with exact dosing (Matthews and Van Dijk, 2004). Ketamine is usually used in donkey anesthesia management (Abakar et al., 2014). However, for induction of maintained short term anesthesia in horse the xylazine-ketamine combination is being frequently used (Young et al., 1993). Propofol is anesthetic agent that characterized by non-irritant rapid action anesthetic agent producing smooth induction and short duration of anesthesia with smooth recovery (Branson and Gross, 1994; Hall et al., 2003). Additionally, the Propofol was reported to has an analgesic effect (Tan and Onsiong, 1998; Jones et al., 1999). A dose-dependent anesthetic effect of propofol was observed in non-premeditated horses; however, pre-medication with detomidine was reported to improve the quality of anesthesia

(Mama et al., 1996; Mathews et al., 1999).

Combinations of propofol with alpha 2-agonist, such as xylazine and detomidine, (Tranquilli et al., 1990; Aguiar et al., 1993; Branson and Gross, 1994), benzodiazepine (Guit, et al., 1990) or ketamine (Hui et al., 1995; Robinson et al., 1997; Lerche et al., 2000; Minoru et al., 2004) has collective anesthetic effects and reduce the propofol doses required to maintain surgical anesthesia in human beings. Drugs commonly used in anesthesia practice may significantly alter the oxidative state of blood cells. This mechanism could contribute to the immune suppression that occurs transiently in the early post-operative period (Costa et al., 2013). The consequent oxidative stress gives rise to cellular damage, including accelerated apoptosis, which is a main contributing factor for post-operative lymphocytopenia and immunological deficit (Delogu et al., 2004).

Additionally, studies showed that the anesthetic drugs inhibit the platelet aggregation in human whole blood in vitro (De La Cruz et al., 1997) in a range of concentrations similar to those found in human plasma after intravenous administration (Gepts et al., 1987). Therefore, hematologic examinations supply valuable information about the metabolic profile during the anesthesia (Kral and Suchy, 2000). Veterinary clinical hematology is a useful diagnostic tool in veterinary practice (Campbell and Coles, 1986; Girardi et al., 2013, 2014).

In Egypt, donkeys are almost used in transportation of the people and goods especially in smallholder farming. Through their prominent role of donkeys in the rural society of the country, research on donkeys has been far behind other domestic species (Nabaa et al., 2015).

The most common anesthetic drug used in donkey was chloral hydrate. Despite its relatively good hypnotic effect, chloral hydrate is poor anesthetic (Reid et al., 1993). The induction of anesthesia after injection of chloral hydrate was rapid with severe nervous manifestation as vigorous struggling, tremors and stiffness in head, neck and limbs (Field, 1993; Silverman and Muir, 1993; El-Sayad, 2006; Ismail et al., 2011).

The objective of this study was to compare the effects of injectable anesthetics; propofol and ketamine in xylazine pre-medicated donkeys on clinical and hematological parameters to investigate the best anesthesia practice in donkeys.

Materials and Methods

Pre-medication and anesthetic agents

Commercially available products were used. Xylazine HCL 2% was purchased from ADWIA Co. S.A.E. 10th of Ramadan City, Egypt. The anesthetic agents propofol 1% (Dongkook pharmaceutical, Korea) and ketamine HCL (Ketamine 50mg/ml Sigma-Tec pharmaceutical industry, Egypt) are solutions for intravenous injection in animals.

Experimental animals

All experimental procedures were reviewed and approved by the animal care committee at the faculty of veterinary medicine, Beni-Suef University, Egypt. The present study was conducted using eighteen apparently healthy baladi Egyptian donkeys. Animals were divided into two equal groups. The animals were aged and body weights were determined. The animals aged 3-4 years and body weights ranged between 120 to 150 kg. All animals were fasted for about 12 hours before injection.

Anesthetic regimes in experimental animals

In group-1, animals were injected with xylazine HCL 2% (1.0mg/Kg) as pre-medication drug followed by the propofol (2mg/Kg) as the anesthetic drug. The second group-2 (G2), was injected with xylazine followed by the anesthetic drugs ketamine HCL (2.2mg/Kg). Both anesthetic agents were administered via intravenous routes and the dose was adjusted according to the manufacturer recommendations.

Clinical parameters

The onset, duration and recovery times were recorded for each anesthetic regime. The onset of anesthesia was calculated as the time interval between injection and loss of reflexes (eye, nose and pain 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 loss of reflexes till unassisted standing of the animal (Tiwari et al., 1989). Heart rate, respiratory rate and rectal temperature were detected at 0 min, 20 min, 40 min, 80 min and 12 hours after the anesthetic agent's injection.

Hematological parameters

The blood samples were collected at 0, 20, 40, 80 minutes and 12 hrs. After anesthetic regimes application for determination of any hematological changes,

blood was obtained from each animal by jugular vein puncture. The samples were collected in a commercial sample bottle containing EDTA and analysis was conducted immediately after collection. The percentage PCV were determined using micro-hematocrit method and the red blood cells (R.B.Cs) and white blood cells (W.B.C) counts were determined using the hemocytometer method (Sirois, 1995). Hemoglobin (HB) concentration was determined by the cyano-methaemoglobin method as described by Van kampen and Zijlstra (1961). Platelet count was done by visual count of blood smears from blood specimens. Ten high-power fields were microscopically averaged and then multiplied by 15,000 to determine the platelet count in 1,000 per microliter (Webb et al., 2004).

Statistical analysis

All measurements of the 2 anesthetic regimes were analyzed. Student T test was applied using SPSS software 21 (IMP SPSS Inc, Chicago, IL). Differences were considered statistically significant if the P value was <0.05.

Results and Discussion

The onset, duration and total recovery times of anesthesia

The onset of anesthesia in G1 was faster than using G2 (3.3±1.5 and 7.3±1.5, respectively). In G1 showed significantly shorter duration of anesthesia, and anesthetized animals showed shorter recovery period compared to G2 (Table 1).

Table 1: *Onset, duration and total recovery periods after intravenous injection of propofol and ketamine in xylazine premeditated donkeys.*

Group	Anesthesia		Total recovery period (min)
	Onset (min)	Duration (min)	
Xylazine-propofol	7.3 ± 3.1	26.3±3.5	64.0 ± 4.6
Xylazine-ketamine	3.3 ± 1.5	45.0± 3.0	86.7 ± 6.1

Comparative clinical criteria of xylazine-ketamine versus xylazine-propof anesthetic regimes

The recovery of the G1 was associated with shivering and the animal became in the standing position after 64±4.6 minutes without any signs of nervous manifestation. In contrast, the G2 was characterized by smooth short induction and good muscle relaxation. In G2, Recovery was of smooth quality and total recovery time was significantly prolonged in compared with G1 (86.7±6.1 min).

Cardio-respiratory parameters of anesthetized animals

In G1, the heart rate started to increase at 20 minutes. The significant increase was noticed by 40 minutes after injection. Meanwhile, the respiratory rate showed significant decrease by 40 minutes. All parameters returned to normal rates by 160 minutes. On the other hand, xylazine-ketamine anesthetized animals showed non-significant decreases of both heart and respiratory rates. In both groups, no significant changes of rectal temperature were observed (Table 2).

Table 2: *Heart rate, respiratory rate and body temperature after intravenous injection of propofol or ketamine in xylazine premeditated donkeys.*

Time	Anesthetic regime	Cardiorespiratory parameter		
		Heart rate	Respiratory rate	Rectal temperature
0 min	Xylazine-propofol	63 ± 2.30	19 ± 1.85	37 ± 0.8
	Xylazine-ketamine	63 ± 1.90	19 ± 2.09	37 ± 0.6
20 min	Xylazine-propofol	65 ± 2.06	14 ± 2.05	36 ± 0.2
	Xylazine-ketamine	62 ± 1.40	17± 1.79	36 ± 0.3
40 min	Xylazine-propofol	69 ± 3.04	12 ± 1.41	36 ± 0.2
	Xylazine-ketamine	61 ± 1.24	16 ± 2.35	36 ± 0.4
80 min	Xylazine-propofol	67 ± 2.53	15 ± 2.80	36 ± 0.3
	Xylazine-ketamine	63 ± 1.90	18 ± 3.11	36± 0.5
12 h	Xylazine-propofol	64 ± 2.94	17 ± 1.09	37 ± 0.3
	Xylazine-ketamine	63 ± 1.90	18 ± 1.69	37 ± 0.4

Hematological changes in anesthetized animals

The RBCs counts in G1 were significantly decreased as compared to the baseline values starting at 20 minutes after injection. Meanwhile, the WBCs counts showed gradual decrease overtime. The Hb contents and PCV also showed gradual decreases which become significant by 80 minutes after xylazine-propofol injection (7.96± 0.15) compared to the baseline values (8.83±0.21). The blood platelets count showed significant decrease at 80 min of testing in G1. The same pattern of hematological changes was observed in xylazine-ketamine anesthetized animals with the exception of the RBCs counts that showed non-significant changes. In both groups all blood parameters returned to normal baseline values by 12 hrs after anesthesia (Table 3).

Table 3: *Effect of intravenous anesthesia of propofol and ketamine on hematological parameters in xylazine*

premeditated donkeys.

Time	Anesthetic regime	Hematologic parameter				
		RBCs (×10⁶/µL)	PCV (%)	WBCs (×10³/µL)	Hb (g/dL)	Platelets (/µl)
0 min	Xylazine-propofol	5.14± 0.33	25.33±2.52	8633± 275.39	8.83±0.21	106333±10263.2
	Xylazine-ketamine	5.6 ± 0.44	26.25±2.1	8836± 289.2	8.9±0.18	108666±9273.3
20 min	Xylazine-propofol	4.93±0.25	24.33±2.51	8383±301.38	8.63±0.22	103666±9291.6
	Xylazine-ketamine	5.5±0.21	25.21±2.4	8739±245.2	8.8±0.11	106333±9143.2
40 min	Xylazine-propofol	4.83±0.31	22.33±1.53	8216±202.07	8.43±0.16	100000±8717.8
	Xylazine-ketamine	5.3±0.11	24.34±2.1	8621±235.1	8.7±0.15	105354±8943.1
80 min	Xylazine-propofol	4.53±0.21	20.00±1.00	8106±200.33	7.96± 0.15	99666±8386.5
	Xylazine-ketamine	5.2±0.19	23.89±1.7	8579±232.3	8.5±0.17	104563±9113.2
12 h	Xylazine-propofol	5.03±0.25	24.67±3.06	8566±251.66	8.7±0.2	105000±9848.9
	Xylazine-ketamine	5.3±0.22	25.88±2.3	8788±143.2	8.8±0.19	107363±9143.2

Compared to chloral hydrate, propofol, an alkyl phenol hypnotic, is a vastly used intravenous anesthetic in veterinary practice. Following intravenous administration, the onset of anesthesia may be expected within several minutes **(**Bennett et al., 1998**).** However, propofol could not be used as a sole anesthetic for general anesthesia in different domestic animals (Bayan et al., 2002; Zama et al., 2005; Gholipour-Kanani and Samaneh, 2013).

To investigate the best anesthetic regime in draught donkeys, propofol was compared to ketamine in xylazine pre-medicated donkeys in terms of anesthetic effect, alterations of clinical and hematological parameters. Propofol created a relatively longer onset and short duration and recovery compared to ketamine (Aguiar et al., 1993; Abd-Almaseeh, 2008). This finding can be explained by the lipophilic nature of propofol, its rapid uptake by vessels rich organs (e.g. brain, liver, kidney), and quickly redistribution and metabolism in liver (Bettschart-Wolfensberger et al., 2005; Muir et al., 2007).

The longer duration obtained by ketamine in combination with xylazine was previously described by (Jones, 2001) who reported that, the epidural administration of ketamine with xylazine in dogs created longer duration of analgesia than ketamine alone. The variable duration of analgesia is usually dependent on lipid solubility, physiochemical properties, and protein binding capacity of the drugs combinations (Singh et al., 2005). The longer duration and depth of anesthesia was suggested as a good additive interaction between ketamine and xylazine in donkeys (Sarrafzadeh-Rezaei et al., 2007). Similarly, the ketamine- lignocaine combination produced longer duration of analgesia in caudal epidural analgesia using dromedary camel (Azari et al., 2014).

In the xylazine-propofol injected animals, the significant increase of heart rate and the marked decrease of respiratory rate were previously reported with using propofol as a general anesthetic in equine (El-Sayad, 2006), buffalo calves (Ratnesh et al., 2014) and dogs (Field, 1992). However, all measurements had returned to normal baseline values similar to those before propofol administration.

Compared to xylazine-propfol combination, the intravenous injection of xylazine and ketamine combination generated unnoticeable transient decreases in RBC, PCV and Hb with insignificant transitory decreases in WBC and platelets in donkeys. Considerable decrease in blood parameters for a short time after using detomidine-midazolam-ketamine or ketamine-xylazine anesthesia were previously reported in calves (Kilic, 2008), rhesus macaques (Lugo-Roman et al., 2010) and dogs (Gulanber et al., 2001; Atalan et al., 2002; Demirkan et al., 2002). Species difference may also have a role in the differences in hematological changes after xylazine-ketamine anesthesia.

The transitional decreasing in PCV, Hb and WBC was also attributed to the circulating blood cells collection in spleen and the changing of fluid from extra-vascular to intra-vascular for maintaining the normal cardiac output in animals (Kinjavdekar et al., 2007; Kilic, 2008; Mion and Villevieille, 2013; Umar and Wakil, 2013; Ratnesh et al., 2014). Moreover, the WBC decrease for short is a result of acute stress and corticosteroid induced changes following administration of the ketamine and xylazine **(**Carrol et al., 1997).

The decrease in Hb content after propofol exposure and potential apnea compared with control animals was previously reported in dogs (Wilson et al., 2004) and human (Volti et al., 2006). However, the decrease in RBCs and Hb was attributed to the reservation of red blood cells in non-splenic sites considering the lack of correlation between hematocrit and spleen size following the anesthetic protocols with propofol (Tsuchiya et al., 2002; O'Brein et al., 2004; Wilson et al., 2004; Costa et al., 2013).

The significant decreased in platelets count in G1 may be a result of acute direct myelo-suppression or splenic sequestration due to pooling of circulating blood cells. Our finding is consistent with that of Lemke et al. (2002) and Aydilek et al. (2007), where decreased platelet counts were observed in dogs and horses.

In conclusion, compared to the propofol, the ketamine in xylazine premidicated donkeys produced rapid induction, long duration, smooth recovery and satisfactory anesthesia in donkeys. Additionally, the combination does not significantly alter the cardiorespiratory and hematological parameters in anesthetized donkeys. Therefore, the xylazine-ketamine combination can be considered a good anesthetic protocol for induction of general anesthesia donkeys in compare with propofol.

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Authors Contribution

Animal handling, data collection and manuscript preparation.

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