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The Effect of Propofol and Ketamar on Both Clinical and Hematological Parameters in Pre-Medicated Egyptian Donkeys

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Abstract: The present study was designed to differentiate between the effect of propofol and ketamine HCL on both clinical and blood parameters in detomidine pre-medicated Egyptian donkeys. Six apparent healthy donkeys were divided into two equal groups. All animals were pre-medicated by 0.2 mg/kg detomidine intravenously, then the first Group (G1) was injected by the propofol (2 mg/kg intravenously) while the second Group (G2) was injected by ketamine HCL (2.2 mg/kg intravenously). The onset, duration and recovery periods were calculated for each group. Heart rate, respiratory rates and body temperatures were recorded. Blood samples were collected at 0, 15, 30, 60 min and 6 h after the anesthetic drug injected for record any changes were done in blood parameters. Results showed that the onset, duration and total recovery periods of anesthesia were 6.35±3.08 and 4.52±1.23, 29.44±2.51 and 42±1.00 and 62±2.48 and 85.33±3.11 min in G1 and G2, respectively. In G1, marked decrease in RBCs, PCV and Hb values from the zero time and presence of shallow respiration. However, no detectable changes in blood parameters were detected in G2. In conclusion, these findings indicate that ketamine in detomidine pre-medicated donkeys produced rapid induction, long duration, smooth induction, recovery and sufficient anesthesia without any significant changes in all parameters. So, using of ketamine to produce sufficient anesthesia is better in detomidine pre-medicated Egyptian donkeys in compare with the propofol.

Key words: General anesthesia, donkeys, blood parameter, ketamine, propofol, detomidine

INTRODUCTION

Good and sufficient anesthesia was applied in animals to produce painless surgical interference using convenient anesthetics with exact dosing. Ketamine is commonly used in donkey anesthesia (Abakar *et al*., 2014). However, for induction of short term anesthesia in horse, xylazine-ketamine is mostly used (Young *et al*., 1993).

Propofol is an alkyl phenol anesthetic agent intravenously injected. This drug is non-irritant rapid acting anesthetic agent that producing smooth induction and short duration anesthesia (Branson and Gross, 1994; Hall *et al*., 2003). The propofol 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, so, pre-medication with detomidine was reported to improve the quality of anesthesia (Mama *et al*., 1996).

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*., 1991) or ketamine (Hui *et al*., 1995; Robinson *et al*., 1997; Lerche *et al*., 2000; Ohta *et al*., 2004) has collective anesthetic effects and reduce the propofol doses that required to maintain surgical anesthesia in human. Drugs that commonly used in anesthesia may, significantly, interfere in oxidative state of the blood cells. This mechanism due to transient immune suppression that occurs in post-operative period (Costa *et al*., 2013). The consequent stress gives increase to cellular damage, including accelerated apoptosis which is a main factor to post-immunological deficit (Delogu *et al*., 2004).

Additionally, the anesthetic drugs inhibit the platelet aggregation in human whole blood (De La Cruz *et al*., 1997; Gepts *et al*., 1987). Therefore, hematologic examinations give accurate information about the metabolic changes during the anesthesia (Kral and Suchy, 2000). Veterinary clinical hematology is a good diagnostic tool in veterinary practice (Campbell and Coles, 1986; Girardi *et al*., 2014, 2015).

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In Egypt, donkeys are considered as common animals that used in transportation of the people and goods especially in smallholder farming. From this prominent role of donkeys in the rural society of the country, research on donkeys has been far behind other domestic animals (Al Shafei *et al*., 2015). Donkeys were usually anaesthetized by chloralhydrate. Despite its poor anesthetic agent but it is relatively good hypnotic agent (Reid *et al*., 1993). The induction of anesthesia by chloralhydrate was rapid with severe nervous manifestation as vigorous struggling, tremors and stiffness in head, neck and limbs (Field, 1992; Silverman and Muir 1993; El-Sayad, 2006; Ismail *et al*., 2010).

The aim of this study is to compare the effects of propofol and ketamine in detomidine pre-medicated donkeys on clinical and hematological parameters to detect the best anesthetic protocol for donkeys.

MATERIALS AND METHODS

Pre-medication and anesthetic agents: Dormosedan (Detomidine HCL 10 mg/mL, pfizer) was used as pre-medicated drug. The anesthetic agents propofol 1% (Propofol, 200 mg/20 mL, Mepha pharmaceutical group, hungary) and ketamine HCL (Ketamine 50 mg/mL Sigma-Tec pharmaceutical industry, Egypt) are solutions for intravenous injection in animals.

Animals: The present study was conducted using 6 apparently health donkeys. Animals were divided into two equal groups. The animals aged 3-4 years and body weights ranged between 120-150 kg. All animals were fasted for about 12 h before injection.

Anesthetic protocols in experimental animals: In group-1, animals were injected with detomidine HCL 1% (0.2 mg/kg) as pre-medication drug followed by the propofol (2 mg/kg) as the anesthetic drug. The second Group-2 (G2) was injected with detomidine HCL 1% (0. 2 mg/kg) followed by the anesthetic drugs ketamine HCL (2.2 mg/kg). All anesthetic agents were injected via. intravenously and the dose was adjusted according to, the manufacturer recommendations.

The onset, duration and recovery periods were listed for each anesthetic protocol. The onset period of anesthesia was measured as the time interval between injection and loss of reflexes while duration period of anesthesia was measured as a time interval between loss of reflexes and reappearance of reflexes and the total recovery period is the time interval between the losses of reflexes till unassisted standing of the animal (Tiwari *et al*., 1989). Heart rate, respiratory rate and body temperature were recorded at 0, 15, 30, 60 min and 6 h after the anesthetic agent's injection.

The blood samples were collected at 0, 15, 30, 60 min and 6 h. After anesthetic agent's application for detection any changes will do. 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 Bood 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. About 10 high-power fields were microscopically averaged and then multiplied by 15,000 to determine the platelet count in 1,000 μL (Webb *et al*., 2004).

Statistical analysis: All measurements of the 2 anesthetic regimes were analyzed. Student t test was applied using using SPSS Software 21 (IMP SPSS Inc, Chicago, IL). Differences were considered statistically significant if the ($p<0.05$).

RESULTS AND DISCUSSION

The onset of anesthesia in G2 was faster than present in G1 (4.52±1.23 and 6.35±3.08, respectively). The G1 protocol has a significantly shorter duration of anesthesia and anesthetized animals showed shorter recovery period compared to G2 protocol (Table 1).

The total recovery period in G1 was associated with shaking and the animal became in the standing position after 62±2.48 min without any signs of nervous manifestation. In contrast in G2 was characterized by smooth short induction and good muscle relaxation. Recovery was of smooth quality and total recovery time was significantly prolonged when compared with G1 (85.33±3.11 min).

In G1, the heart rate began to increase at 15 min. The significant rising was noticed by 30 min after injection. In the same time, the respiratory rate showed considerable decrease by 60 min. All parameters returned to normal

Table 1: Onset, duration and total recovery periods after intravenous injection of propofol and ketamine in detomidine pre-medicated donkeys

Items	Onset of anesthesia (min)	Duration of anesthesia(min)	Total recovery period (min)
Group (1)	6.35±3.08	29.44±2.51	62±2.48
Group (2)	4.52±1.23	42±1.00	85.33±3.11

Table 2: Heart rate, respiratory rate and body temperature after intravenous injection of propofol and ketamine in detomidine pre-medicated donkeys

Time	0 (min)		15 (min)		30 (min)		60 (min)		160 (min)	
Parameter	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2
Heart rate	63±1.3	63±1.4	66±2.6	62±1.1	70±3.04	62±1.6	67±2.43	63±1.9	64±2.1	63±1.8
Respiratory rate	19±1.80	19±2.06	14±1.05	18±1.79	13±1.31	17±2.15	16±2.87	18±2.11	17±1.04	18±1.39
Body temperature	37±0.7	37±0.5	36±0.12	36±0.23	36±0.27	36±0.53	36±0.39	36±0.38	37±0.43	37±0.32

Table 3: Effect of intravenous anesthesia of propofol and ketamine on haematological parameters in detomidine pre-medicated donkeys

Time	0 (min)		15 (min)		30 (min)		60 (min)		6 (h)	
parameters	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2
RBCs (×106/μL)	5.17±0.34	5.5±0.41	4.96±0.15	5.6±0.22	4.63±0.32	5.4±0.17	4.55±0.22	5.3±0.17	5.05±0.26	5.4±0.21
PCV (%)	25.23±2.32	26.35±1.8	24.53±2.31	25.29±1.4	22.23±1.45	24.24±2.4	20.06±1.05	23.49±1.5	24.47±3.16	25.83±2.1
WBCs (×103/μL)	8632± 255.39	8856±259.2	8384±302.38	8733±244.2	8218±210.07	8622±236.1	8107±208.33	8569±242.3	8565±231.66	8787±133.2
Hb (g/dL)	8.73±0.25	8.85±0.12	8.53±0.21	8.79±0.21	8.33±0.17	8.68±0.27	7.85± 0.14	8.4±0.18	8.7±0.3	8.79±0.17
Platelets (/μL)	106343±10253.2	108636±9263.3	103676±9261.6	106363±9153.2	103070±8737.8	105654±8943.1	101646±8376.5	104553±9116.2	105080±9858.9	10736±9133.2

rates by 160 min. On the other hand, G2 showed non- worthy decreases of both heart and respiratory rates. In both groups, no important changes of body temperature were noticed (Table 2).

The RBCs counts G1 were expressive decreased when compared with the base line values starting at 15 min after injection. Meanwhile the WBCs counts showed gradual decrease overtime. The Hb contents and PCV also showed gradual decreases which become observed by 60 min (7.86±0.25) compared to the base line values (8.73±0.25). The blood platelets count did not show any important changes at any time during the experiment. The same pattern of hematological changes was observed in G2 with the exception of the RBCs counts that showed non-observed changes. In both groups all blood parameters returned to normal base line values by 6 h after anesthesia (Table 3).

Anesthetic drugs used in donkey such as chloral hydrate are of poor anesthetic power with severe nervous manifestation as vigorous struggling, tremors and stiffness in head, neck and limbs (El-Sayad, 2006; Ismail *et al*., 2010). But propofol is 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; GholipourKanani and Ahadizadeh, 2013).

To investigate the best anesthetic protocol in donkeys, propofol was compared to ketamine in detomidine 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 detomidine was previously described by (Jones, 2001) who reported that the epidural administration of ketamine with thiazine derivative 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 detomidine 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 G1, 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 and dogs (Field, 1992). However, all measurements had returned to normal baseline values similar to those before propofol administration.

Compared to G1, the intravenous injection of detomidine 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).

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). Moreover, the WBC decrease for short is a result of acute stress and corticosteroid induced changes following administration of the ketamine and detomidine (Carroll *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'Brien *et al*., 2004; Wilson *et al*., 2004; Costa *et al*., 2013).

The transient decreased in platelets count in both anesthetic protocols 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.

CONCLUSION

In conclusion, compared to the propofol, the ketamine in detomidine pre-medicated donkeys produced rapid induction, long duration smooth recovery and satisfactory anesthesia in donkeys. Additionally, the combination does not significantly alter the cardio-respiratory and hematological parameters in anesthetized donkeys. Therefore, the detomidine-ketamine combination can be considered a good anesthetic regime for induction of satisfactory general anesthesia in donkeys.

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