EVALUATION OF EFFECTS OF DIFFERENT COMBINATIONS OF SELECTED SEDATIVES ON THE HEMATOLOGICAL PROFILE OF STANDING SEDATED HORSES

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ABSTRACT

Alpha-2 agonists induce changes in the hemogram in equines. The aim of the present study was to examine the magnitude of changes in the selected blood parameters produced by various α.2- agonists combinations. For this purpose, 25 horses were the animals of study during different clinical examinations and minor surgical interventions in standing sedation. Blood samples were collected from the jugular venipuncture of horses before sedation, 15 mins., 30 mins., and 60 mins., after drug administration.The blood parameters evaluated were Packed cell volume (PCV), Haemoglobin concentration (Hb), Red blood cells (RBC), Total leukocytes count (TLC), and Differential leucocytes count (DLC) (neutrophils, eosinophils and monocytes). Analysis of variance (1-way ANOVA) were performed with $p<0.05$. Hb, PCV, TLC and DLC declined gradually in all groups post drug administration. Pre-sedation values for all parameters were significantly different from post-sedation values at 15, 30, and 60 minutes. There was no significant effect of drug groups on Hb, neutrophil and eosinophil values. Group A (Acepromazine + Detomidine combination) produced significant decrease in PCV values compared with group C (Acepromazine + Ketamine) and group D (Acepromazine + Detomidine + Ketamine). RBC values of group B (Detomidine + Ketamine) showed significant difference compared with group C, D, & E (Acepromazine + Xylazine + Ketamine). TLC and monocyte values of group B were significantly different from D & E groups. It was concluded that drug combination with acepromazine, detomidine, xylazine and ketamine cause minimal hematological side effects. Therefore, these drugs could be safely used for inducing standing sedation in horses.

Key words: Horses, Standing sedation, Acepromazine, Detomidine, Ketamine, Xylazine, Hematology.

INTRODUCTION

Restraining and sedation in standing horses is practised in a number of surgical interventions and diagnostic procedures by using chemical drugs in the prescribed doses (DeBowes, 1991; LeBlanc, 1991; Ross, 1991; Ford, 1991; Freeman *et al*., 2000; Valverde, 2010; El Kammar and Gad, 2014). Opiates, α_2-agonists and NSAIDs are the prime categories of medicines utilised in equine practice for pain reduction, though every medicine category has specific side effects (Fielding *et al*., 2004). Various factors like physical status, temperament, size and weight of the patient; surgical intervention to be done; well-being and safety of the patient, surgeon's support staff and patient's owner affect the selection of the chemical agent of the drug. Whether administered singly or mixed with other sedative and/or anaesthetic agents. The α2-agonists can be administered in combinations safely and are effective in producing more favourable restraint and analgesia than by the use of those agents alone (Dart, 1999). Though, the utility of such agents especially analgesics in the horse is not without untoward effects, some of which may turn out to be lethal for the horse's condition. It is, therefore, recommended that analgesics should be used with caution keeping in mind the side effects. In such cases, minimal dose regimens for chemical restraint should be administered as bolus dose (Geiser, 1990). The administration of sedative drugs could result in the physiological changes in blood thereby, disturbing the normal homeostasis of body. The hematological and biochemical changes are due to temporary shift of fluids from extravascular compartment to the intravascular compartment (Wagner *et al*., 1991). The beneficial effect of α_2- agonist drugs are many and include reliable sedation, analgesia, muscle relaxation and anxiolysis, as well as a decrease in the anesthetic requirements of injectable and inhalant agents (anesthetic sparing) (Sinclair, 2003). However, there are several side effects of these drugs including cardiovascular depression, hypertension, reduced cardiac output, recumbency, nausea, vomiting, regurgitation, CNS excitement, ataxia, muscle twitching, tendency to lean forward, head pressing, sweating etc. The practitioners

need to review the general side effects of α_2- agonist, to recognize the clinically lowered dose of these drugs with minimum changes in haematological profile and clinical conditions. The aim of current study was to investigate the magnitude of changes in haemogram produced by various sedative combinations during different clinical examinations and minor surgical exercises which were performed in standing sedation of horses.

MATERIALS AND METHODS

Animals: Horses (n=25) brought to the Indoor Hospital, Department of Clinical Medicine and Surgery (CMS), Faculty of Veterinary Science, University of Veterinary and Animal Sciences (UVAS), Lahore, Pakistan, were enrolled in the study. Weight of the horses ranged from180 – 300 Kilograms, age from 4 – 20 years, and height 13.3 – 16.2 hands. For the sake of safety and ease during examination and treatment, the horses were injected various combinations of sedatives. Out of these twenty-five horses, six were administered these drugs for the sake of examination for thrush (2 horses), exostosis (1 horse), knee hygroma (1 horse) and forelimb tendinitis (2 horses). One of the horses was given the drugs before standing castration. Fifteen horses were given the drugs for antiseptic dressing (ASD) for wounds at various sites and thrush, and three horses were administered sedatives for tooth rasping.

The twenty-five horses were randomly divided into 5 groups comprising of 5 horses and sedated with one of the drug combination (Table 1). Drugs were administered following the standard recommended dose.

Table 1. Drug combination used in the study given to different groups.

Group Name	Drug Combinations
Group A	Acepromazine +Detomidine
Group B	Detomidine +Ketamine
Group C	Acepromazine +Ketamine
Group D	Acepromazine+Detomidine +Ketamine
Group E	Acepromazine+Xylazine+Ketamine

Acepromazine (Sedastress; Farvet Laboratories B.V.), Ketamine (Calypsol Gedeon Richter Ltd.) and Xylazine (Xylaz; Eurovet); were acquired from the local market, while Detomodine: (Detogesic; Forte Dodge) was graciously granted by a fellow Veterinarian to be used in the study.

Collection of Samples: The blood samples were collected in 10cc sterilized disposable syringe (BD) from the jugular vein of horses before sedation, 15 mins., 30 mins., and 60 mins. after drug administration. About 3ml of the blood was shifted to vacutainer with anticoagulant [K_3-EDTA (BD)] and the remaining amount in the disposable syringe (BD) was placed in a slant position for the separation of serum in the syringe. After the completion of collection of samples and diagnosis and treatment of the patient, the disposable syringes and the vacutainers were placed in a cool box containing cool packs. The blood samples were then transported and got analyzed in a certified commercial laboratory.

Hematological Observations: Blood samples (both heparinised and non heparinised) were collected via jugular venipuncture of twenty-five horses for Complete Blood Count tests to be performed. The levels of different haematological components were checked to see any change in the values (Higgins and Wright, 1998) before sedation, 15 minutes, 30 minutes, and 60 minutes after drug administration. The parameters evaluated were packed cell volume (PCV), haemoglobin concentration (Hb), red blood cells (RBC) count, total leukocytes count (TLC), and differential leucocytes count (DLC) (neutrophils, eosinophils, and monocytes).

Statistical Analysis: The distribution of outcome variables was assessed by calculating descriptive statistics (mean±S.D), and line graphs were produced. The data acquired in this study was analyzed statistically by ANOVA using Generalized Linear Model and Post hoc Tukey test in Minitab software Release 15 (State College, Pennsylvania, USA). Results were interpreted at 5% level of significance.

Ethical Considerations: The research work was approved by the Advanced Studies and Research Board Committee, UVAS, Lahore, Pakistan. All efforts were taken to minimize the pain and discomfort to the animals during conduct of this study.

RESULTS

Administration of all drug combinations induced a gradual change over time in the PCV, HB, RBC's, TLC and DLC values (Figures 1A, 1B, 1C, 1D, and Figures 2A, 2B, 2C). The result of this study showed that PCV, HB, RBC's and TLC decreased gradually in all groups after administration of the drug combinations at 15 minutes, 30 minutes and 60 minutes interval. However, the fluctuation remained within normal range.

Packed Cell Volume: The results of ANOVA indicated a significant effect ($p \leq 0.05$) of drugs between groups and between measurement times on PCV, while non-significant difference ($p \geq 0.05$) of overall effect of both drug groups & measurement times was seen. Post hoc tukey test showed that PCV values of group A (Acepromazine + Detomidine) were significantly different ($p \leq 0.05$) from group C (Acepromazine + Ketamine) and group D (Acepromazine + Detomidine + Ketamine) but no significant difference ($p \geq 0.05$) was seen with group B (Detomidine + Ketamine) and E (Acepromazine + Xylazine + Ketamine). Pre-sedation

mean values were significantly different from values at 15, 30 and 60 minutes after sedation (Table2).

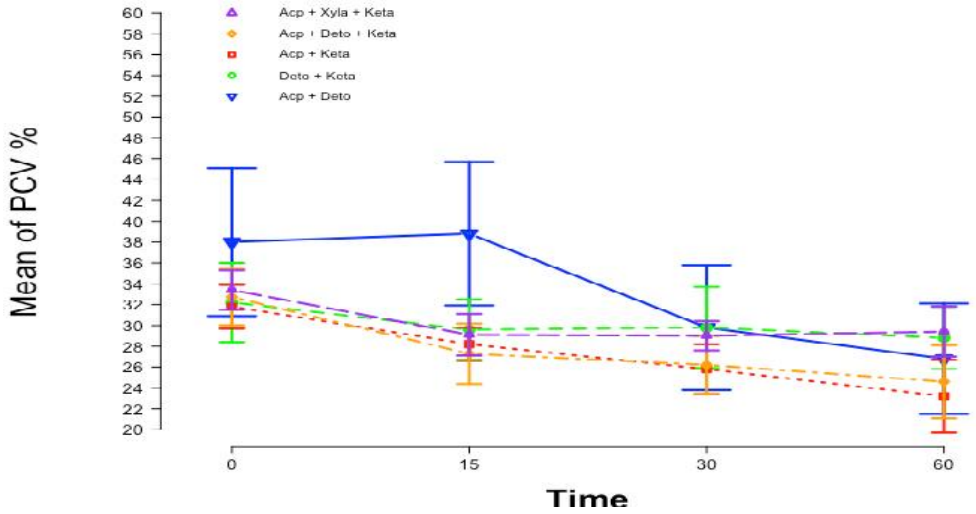

Figure 1A. Mean (± SE) values of PCV of horses over time following administration of Acp + Deto (group A) [blue circle with solid line],Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 2. Effect of various drug combinations on the Packed cell volume (PCV) of horses [mean values].

			PCV				
	Group		**A[a]**	**B[ab]**	**C[b]**	**D[b]**	**E[ab]**
Time (Mins.)	**0***	**Mean±S.D**	38.0±7	32.2±3	31.8±2	32.7±2	33.5±2
	15¶	**Mean±S.D**	32.8±7	29.6±3	28.2±2	27.3±3	29.1±2
	30¶	**Mean±S.D**	29.8±6	29.8±4	25.8±2	26.2±3	29.0±1
	60¶	**Mean±S.D**	26.8±5	28.8±3	23.2±3	24.6±3	29.4±2
Normal Values *Parry, 2009*			**29 to 53 (%)**				

Each value is the mean of 5 horses.

[a, b]Drug groups with different alphabets in superscript were statistically different from each other at p≤0.05based on Post Hoc Tukey's test.

*, ¶Measurement time effect with different symbols in superscript was statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.

Hemoglobin: The results of ANOVA exhibited a significant effect (p≤0.05) of measurement times on Hb concentration, while a non-significant difference (p≥0.05) of drug groups and overall effect of drug groups and measurement times was seen. The results of post hoc statistical analysis revealed that pre-sedation mean values were significantly different from values at 15, 30 and 60 minutes post-sedation (Table 3).

Red Blood Cells: The effect of drug groups & measurement times on RBC's was significant (p≤0.05), while there was no significant difference (p≥0.05) of the overall effect of drug groups and measurement times. The results of post hoc statistical analysis showed a significant difference between group B (Detomidine + Ketamine), groups C (Acepromazine + Ketamine), group D (Acepromazine + Detomidine + Ketamine) and E (Acepromazine + Xylazine + Ketamine), but there was no significant difference with group A (Acepromazine + Detomidine). The results further revealed that pre-sedation mean values were significantly different from values at 15, 30 and 60 minutes post-sedation (Table 4).

Total Leucocyte Count: A significant effect (p≤0.05) of drug groups & measurement times was seen on TLC, while there was no significant difference (p≥0.05) of the overall effect of drug groups and measurement times. The results of post hoc statistical analysis showed that there was no significant difference between group A, groups B, C, D and E. However, TLC values of group B (Detomidine + Ketamine) were significantly different from group D (Acepromazine + Detomidine + Ketamine) and group E (Acepromazine + Xylazine + Ketamine). Furthermore, pre-sedation mean values were significantly

different from values at 15, 30 and 60 minutes post- sedation (Table 5).

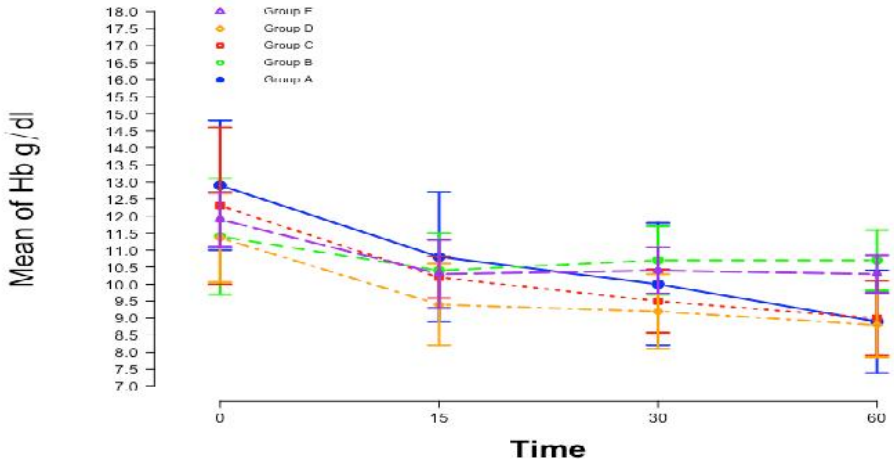

Figure 1B. Mean (± SE) values of HB of horses over time following administration of Acp + Deto (group A) [blue circle with solid line],Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 3.Effect of various drug combinations on Hemoglobin (Hb) concentration of horses [Mean Values]

			Hb				
Group			**A**	**B**	**C**	**D**	**E**
Time (Mins.)	**0***	**Mean± S. D.**	12.9±2	11.4±2	12.3±2	11.3±1	11.9±0.8
	15¶	**Mean± S. D.**	10.8±2	10.4±1	10.2±0.6	9.4±1	10.2±1
	30¶	**Mean± S. D.**	10±2	10.7±1	9.5±1	9.2±1	10.4±0.7
	60¶	**Mean± S. D.**	8.9±2	10.7±1	8.9±1	8.8±1	10.2±0.5
Normal Values *Parry, 2009*			**10 to 19 (g/dl)**				

Each value is the mean of 5 horses.
*, ¶Measurement time effect with different symbols in superscript was statistically different from each other atp≤0.05 based on Post Hoc Tukey's test.

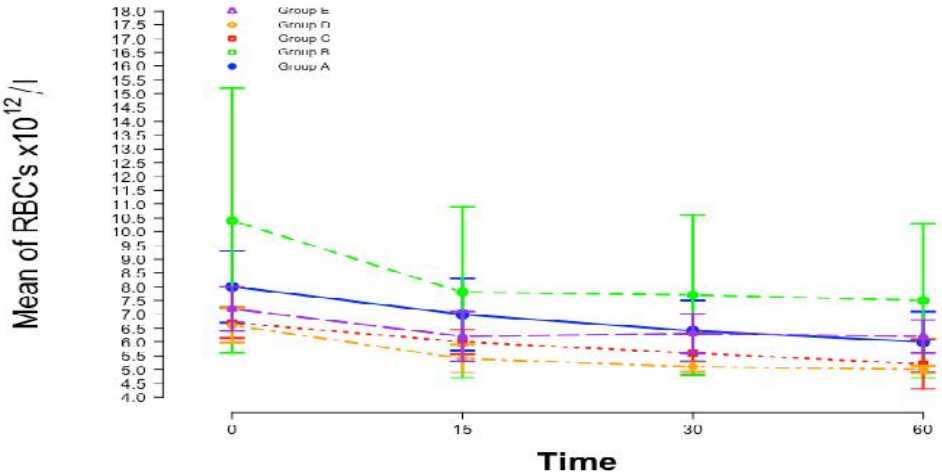

Figure 1C. Mean (± SE) values of RBC's of horses over time following administration of Acp + Deto (group A) [blue circle with solid line],Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 4.Effect of various drug combinations on the Red blood cells (RBC'S) count of horses [Mean Values]

			RBC's				
	Group		**A^{ab}**	**B^{a}**	**C^{b}**	**D^{b}**	**E^{b}**
Time (Mins.)	**0***	**Mean ±S. D.**	7.9±1	10.4±5	6.7±0.6	6.6±0.6	7.2±0.8
	15¶	**Mean± S. D.**	6.9±1	7.7±3	5.9±0.4	5.4±0.5	6.2±0.9
	30¶	**Mean±S. D.**	6.4±1	7.7±3	5.6±0.7	5.1±0.2	6.3±0.7
	60¶	**Mean±S. D.**	5.9±1	7.5±3	5.2±0.9	4.9±0.1	6.2±0.6
Normal Values			**6.5 to 12 (x 10^12/l)**				
Parry, 2009							

Each value is the mean of 5 horses.
[a, b]Drug groups with different alphabetic in superscript were statistically different from each other at p≤0.05based on Post Hoc Tukey's test.
*, ¶Measurement time with different symbols in superscript were statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.

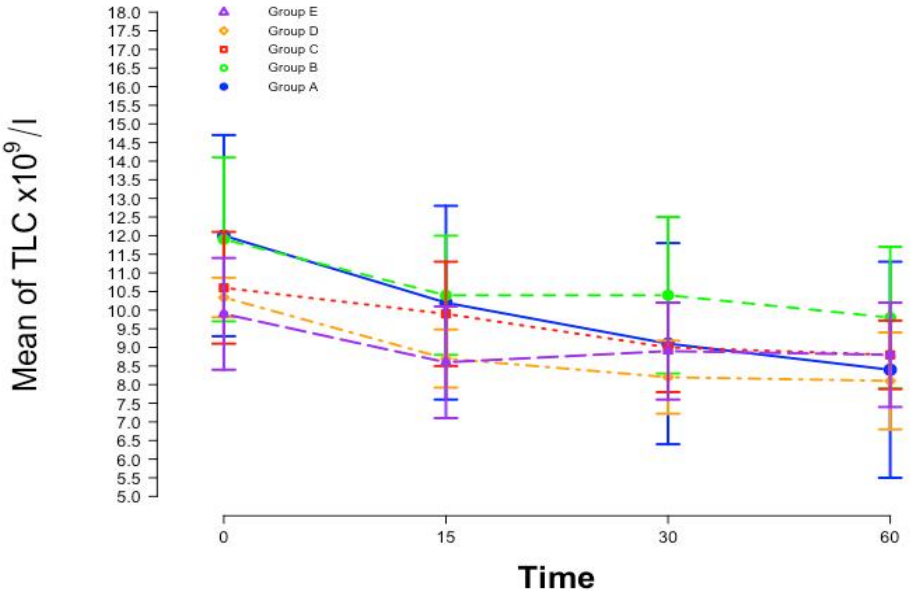

Figure 1D. Mean (± SE) values of total leukocytes count (x10^9/l) of horses over time following administration of Acp + Deto (group A) [blue circle with solid line], Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 5. Effect of various drug combinations on the Total leukocyte count (TLC) of horses [Mean values]

			TLC				
	Group		**A^{ab}**	**B^{a}**	**C^{ab}**	**D^{b}**	**E^{b}**
Time (Mins.)	**0***	**Mean±S. D.**	12±3	11.9±2	10.6±2	10.3±0.5	9.9±2
	15¶	**Mean±S. D.**	10.2±2	10.4±2	9.9±1	8.7±1	8.7±1
	30¶	**Mean±S. D.**	9.1±3	10.4±2	9.0±1	8.2±1	8.9±1
	60¶	**Mean±S. D.**	8.4±3	9.8±2	8.8±1	8.1±1	8.8±1
Normal Values			**3.4 to 12.7 (x 10^9/l)**				
Parry, 2009.							

Each value is the mean of 5 horses.
[a, b]Drug groups with different alphabetic in superscript were statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.
*, ¶Measurement time with different symbols in superscript were statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.

Differential leukocyte count: Significant difference ($p \leq 0.05$) was recorded in the mean values of neutrophils from pre-sedation values and values at 60 minutes post-sedation. Similarly, for monocytes and eosinophils, the mean values were significantly different ($p \leq 0.05$) at 30 and 60 minutes post-sedation from pre-sedation values. The numbers of all types of cells (neutrophils, monocytes and eosinophils) fluctuated within the normal physiological standard limits and therefore have no clinical significance as far as the effect of different drugs on the hematopoietic system is concerned. The results of ANOVA showed a non-significant difference ($p \geq 0.05$) of drug groups and the overall effect of drug groups and measurement times on absolute count (neutrophils) (Table 6). For absolute count (monocytes) values, a significant effect ($p \leq 0.05$) of drug groups was seen, while a non-significant difference ($p \geq 0.05$) of combined effect of drug groups and measurement times was recorded. The results of post hoc statistical analysis showed that group B exhibited significant difference with groups D & E (Table 7). For absolute count (eosinophils), no significant difference ($p \geq 0.05$) of drug groups and overall effect of drug groups and measurement times were seen (Table 8).

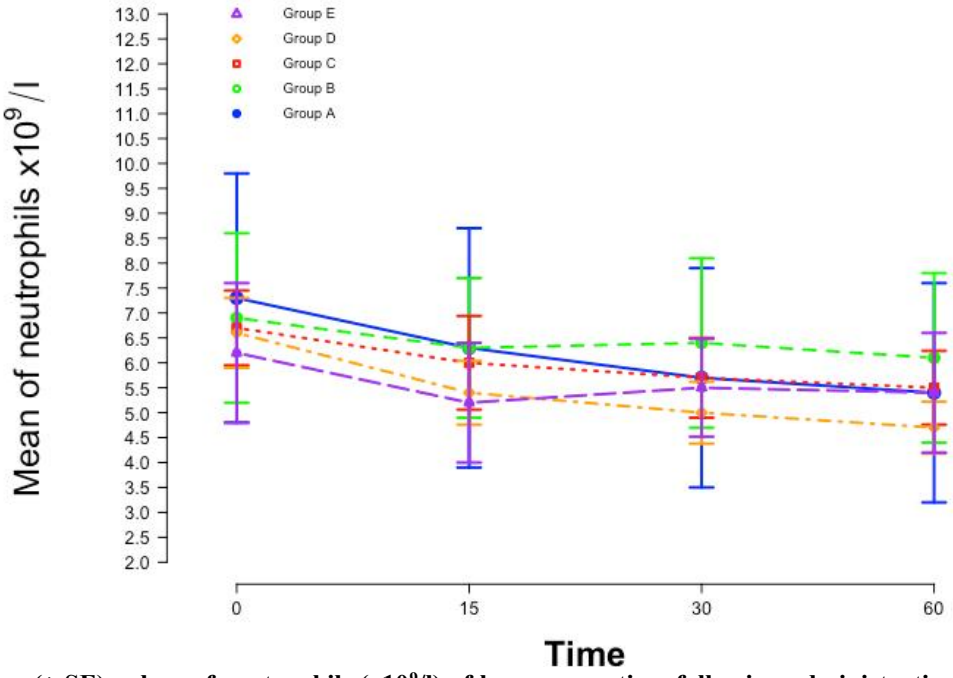

Figure 2A. Mean (± SE) values of neutrophils (x10^9/l) of horses over time following administration of Acp + Deto (group A) [blue circle with solid line],Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 6. Effect of various drug combinations on the Neutrophils (absolute count) of horses [Mean values]

Absolute Count (Neutrophils)							
Group			A	B	C	D	E
Time (Mins.)	0*	Mean±S. D.	7.3±2	6.9±2	6.7±0.7	6.6±0.7	6.2±1
	15*¶	Mean±S. D.	6.3±2	6.3±1	5.9±1	5.4±0.6	5.2±1
	30*¶	Mean±S. D.	5.7±2	6.4±2	5.7±1	5.0±0.6	5.5±1
	60¶	Mean±S. D.	5.4±2	6.1±2	5.5±0.7	4.7±0.5	5.4±
Normal Values			**2 to 8.6 (x 10^9/l)**				
Parry, 2009							

Each value is the mean of 5 horses.

*, ¶Measurement time with different symbols in superscript were statistically different from each other at $p \leq 0.05$ based on Post Hoc Tukey's test.

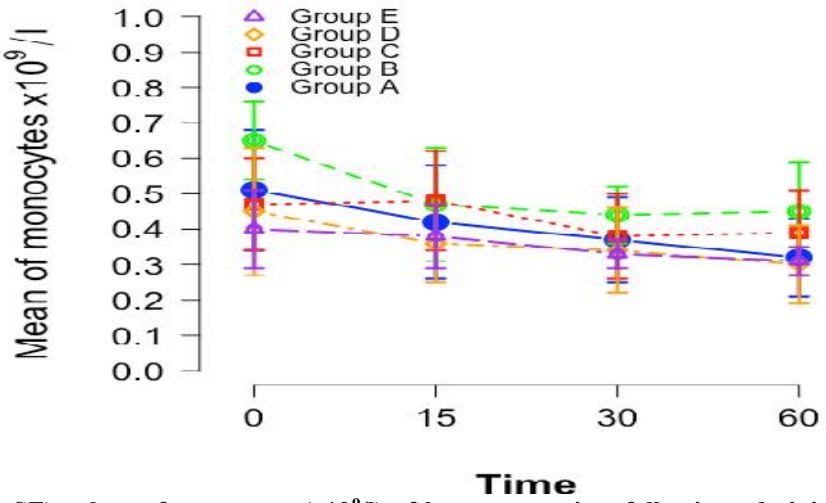

Figure 2B.Mean (± SE) values of monocytes (x10^9/l) of horses over time following administration of Acp + Deto (group A) [blue circle with solid line],Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 7.Effect of various drug combinations on the Monocytes (absolute count) of horses [Mean values]

Absolute Count (Monocytes)							
Group			A^{ab}	B^{a}	C^{ab}	D^{b}	E^{b}
Time (Mins.)	0*	Mean± S. D.	0.5±0.2	0.6±0.1	0.5±0.1	0.5±0.2	0.4±0.1
	15*¶	Mean±S. D.	0.4±0.2	0.5±0.2	0.5±0.1	0.4±0.1	0.4±0.2
	30¶	Mean± S. D.	0.4±0.1	0.4±0.1	0.4±0.1	0.3±0.1	0.3±0.04
	60¶	Mean± S. D.	0.3±0.1	0.5±0.1	0.4±0.1	0.3±0.1	0.3±0.04
Normal Values			**0 to 1.0 (x 10^9/l)**				

Parry, 2009

Each value is the mean of 5 horses.

[a, b]Drug groups with different alphabetic in superscript were statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.

[*, ¶]Measurement time with different symbols in superscript were statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.

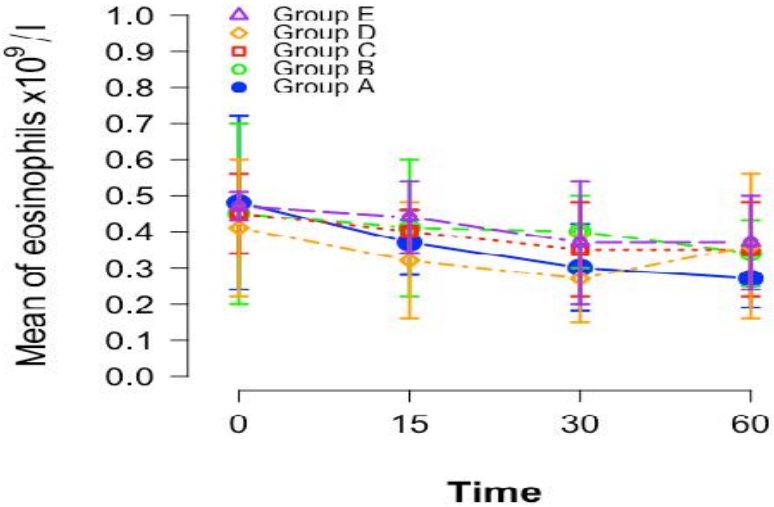

Figure 2C. Mean (± SE) values of eosinophils (x10^9/l) of horses over time following administration of Acp + Deto (group A) [blue circle with solid line],Deto + Keta (group B) [green hollow circle with short dashed line], Acp + Keta (group C) [red square with dotted line], Acp + Deto + Keta (group D) [yellow diamond with short dashed and dot line], and Acp + Xyla + Keta (group E) [purple triangle with long dashed line].

Table 8. Effect of various drug combinations on the Eosinophils (absolute count) of horses [Mean Values]

Absolute Count (Eosinophils)							
Group			A	B	C	D	E
Time (Mins.)	0*	Mean ±S. D.	0.5±0.2	0.4±0.2	0.4±0.1	0.4±0.2	0.5±0.04
	15*¶	Mean ±S. D.	0.4±0.1	0.4±0.2	0.4±0.1	0.3±0.2	0.4±0.1
	30¶	Mean ±S. D.	0.3±0.1	0.4±0.1	0.3±0.1	0.3±0.1	0.4±0.2
	60¶	Mean ±S. D.	0.3±0.1	0.3±0.1	0.4±0.1	0.4±0.2	0.4±0.1
Normal Values *Parry, 2009*			**0 to 1.0 (x 10^9/l)**				

Each value is the mean of 5 horses.

*, ¶Measurement time with different symbols in superscript were statistically different from each other at p≤0.05 based on Post Hoc Tukey's test.

DISCUSSION

The objective of current investigation was to assess and measure the effect of five i/v drug combinations on haematological parameters in horses. Acepromazine, detomidine, ketamine, and xylazine are amongst various drugs used regularly in equine practice. To exploit the potentiation of their sedative effects while keeping side effects as low as possible, different combinations of these different agents were used. Drug combinations were selected on the basis of previous clinical experience.

Hb, PCV and TLC declined gradually in all groups post drug administration. Hawkey, (1985) explained the phenomenon that decrease in the Hb, PCV and TLC may be due to pooling of the circulating blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity. Similar findings have been stated by Kullmann *et al* (2014), reporting significant decrease over time in PCV and RBC's values after administration of alph-2 agonist. Decrease in PCV have been reported in adult horses after administration (IV or IM) xylazine and detomidine (Gasthuys and Parmentier, 1990; Wagner *et al*. 1991). Jean *et al*. (1990) and Singh *et al*. (2007) conducted studies in cattle and goats respectively, while the current study was conducted in horses. Similarly, Kinjavdekar *et al*. (2007) also stated about decrease in Hb, PCV, and TLC after injection of different drug combinations in goats. El-Kammar and Gad, (2014) also demonstrated that Hb and PCV values significantly decreased post detomidine injection. Akbar *et al*. (2014) also reported a decrease in the Hb values post-sedation in dogs while TLC values increased gradually. However, Gasthuys *et al*. (1987) detected a rise in PCV at 30 minutes post drug administration, while investigating detomidine effects in horses, which is in contrast with the current study. The increase in PCV value could either be produced by increased urine production of activation of capillary fluid shift mechanism or by the release of the splenic red blood cells reservoir (Kumar and Thurmon, 1978).

In current study, there was a gradual decrease in the mean values of RBCs. Gasthuys*et al*. (1987) reported initial rise in RBCs followed by decreased values.

Statistically, the PCV values of group A (Acepromazine + Detomidine) were significantly different (p≤0.05) from group C (Acepromazine + Ketamine) and group D (Acepromazine + Detomidine + Ketamine). For the TLC values, group B (Detomidine + Ketamine) were significantly different from group D (Acepromazine + Detomidine + Ketamine) and group E (Acepromazine + Xylazine + Ketamine). While Hb and RBC's values indicated a non-significant difference (p≥0.05) between distinctive groups. Akbar *et al*. (2015) also reported non-significant difference for TLC, Hb and ESR values among different drug groups in cats.

The differential leukocyte count (DLC) showed gradual decrease in mean values of neutrophils, monocytes, and eosinophils in all groups. Significant difference (p≤0.05) was recorded in mean values of neutrophils from pre-sedation values & values at 60 minutes post-sedation. Similarly, for monocytes and eosinophils, the mean values were significantly different (p≤0.05) at 30 & 60 minutes post-sedation from pre-sedation values. The numbers of various cells varied within the standard physiological limits and therefore, have no clinical significance as far as the effect of different drugs on the haematopoietic system is concerned. Singh *et al*. (2007) reported the findings of their studies with epidural ketamine-xylazine combinations in goats. They reported that there is no effect on monocytes and eosinophils while there was rise in neutrophil count. These findings differ from the current study, which could be due to the reason that they used different species of animal, route of administration and drug combinations. In another study on cats by Akbar *et al*. (2015), the hematological profile depicted only a significant increase in eosinophils in group C (Medetomidine+Ketamine) as compared with the control (Placebo). Their results differ from the current study and the reason could be that they used these drugs in different animal species i.e. cats.

Conclusion: The results of this study showed that numbers of different cells varied within the standard physiological limits and therefore have no clinical significance as far as the effect of different drugs on the haematopoietic system is concerned. It is concluded that drug combination with acepromazine, detomidine, xylazine and ketamine cause minimal haematological side effects. Therefore, these drugs can be safely used for inducing standing sedation in horses.

Acknowledgments

Authors Contributions: Each author contributed significantly in the design of the study, conduct, data collection and analysis of results and compilation of manuscript.

Conflict of Interest: The author(s) declare (s) that there is no conflict of interests regarding the publication of this article.

REFERENCES

Akbar, H., M. A. Khan, M. A. Khan, M. S. Khan, S. Aslam, A. Nasir and A. A. Anjum (2014). Effects of different doses of medetomidine on clinical hematological parameters in dogs. The J. Anim. Plant. Sci., 24 (3): 730-737.

Akbar, H., M. A. Khan, S. G. Bokhari, M. D. Ahmad, M. Nawaz, A. A.Anjum, H. M. Khan (2015). Efficacy of Medetomidine hydrochloride alone and in combination with Ketamine hydrochloride for surgical anesthesia in Cats. Pakistan Vet. J., 35 (2): 151-154.

Dart, C. M. (1999). Advantages and disadvantages of using alpha$_2$ agonists in Veterinary practice. Aust. Vet. J., 77(11):720-721.

DeBowes, R. M. (1991). Standing rectal and tail surgery. Vet. Clin. North Am. Equine Pract., 7(3):649-667.

El-Kammar, M. H. and S. B.Gad (2014).Evaluation of the sedative, analgesic, clinicophysiological, haematological effects of intravenous detomidine, detomidine-butorphanol, romifidine, and romifidine-butorphanol in standing donkeys. Equine. Vet. Educ., 26(4): 202-207

Fielding, C. L., G. W. Brumbaugh, N. S. Matthews,K. E. Peck, A. J. Roussel (2004). Clinical effects of ketamine infusions in awake horses. J. Vet. Emerg. Crit. Care, 14(S1); S14.

Ford, T. S. (1991). Standing surgery and procedures of the head. Vet. Clin. North Am. Equine Pract. 7(3):583:602.

Freeman, S. L. andG. C.England (2000). Investigation of romifidine anddetomidine for the clinical sedation of horses. Vet. Rec., 147:507-11.

Gasthuys, F., P. Terpstra, C. V. Hende and A. De Moor (1987). Hyperglycemia and diuresis during sedation with detomidine in the horses. J. Vet. Med. (Series A)., 39:641-648.

Gasthuys, F., A.Moor and D. Parmentier (1990).Haemodynamic changes during sedation in ponies. Vet Res Comm., 14:309–327.

Geiser, D. R. (1990).Chemical restraint and analgesia in the horse. Vet. Clin. North Am. Equine Pract., 6(3):495-512.

Hawkey, C. M. (1985).Changes in blood count during sedation and anesthesia.Brit. Vet. Zoolog. Soc. Newsletters., 19: 27-31.

Higgins, A. J. and I. M.Wright, (Eds.) (1995). The Equine Manual, W. B. Saunders, Philadelphia.

Jean, G. St., R. T. Skarda, W. W. Muir andG. F.Hoofsis (1990). Caudal epidural analgesia induced by xylazine administration in calves. Am. J. Vet. Res., 51: 1232-1236.

Kinjavdekar, P., G. R. Singh, H. P.Amarpal, Aithal and A. M. Pawde (2007). Clinico-physiological effects of spinally administered ketamine and its combinations with xylazine and medetomidine in healthy goats. Vet. Res. Comm., 31: 847-861.

Kullmann, A., M. Sanz, G. T. Fosgate, M. N. Saulez, P. C. Page and E. Rioja (2014). Effects of xylazine, romifidine, or detomidine on hematology, biochemistry, and splenic thickness in healthy horses.Canad. Vet. J., 55:334-340.

Kumar, A. and J. C. Thurmon (1978). Physiologic, Haemocytologic and Biochemical effects of Acetylpromazine with and without pre-medication in goats. Ind. Vet. J., 55:199-201.

LeBlanc, P. H. (1991). Chemical restraint for surgery in the standing horse. Vet. Clin. North Am. Equine Pract., 7(3):521-533.

Parry, B. W. (2009). Clinical Pathology Reference Data. In: Current Therapy in Equine Medicine. Eds. N. E. Robinson and K. A. Sprayberry. 6thEdn. Saunders Elsevier, Missouri, USA. pp. 956-980.

Ross, M. W. (1991). Standing abdominal surgery. Vet. Clin. North Am. Equine Pract. 7(3):627-639.

Sinclair, M. D. (2003). A review of the physiological effects of α_2-agonists related to the clinical use of medetomidine in small animal practice. The Canad. Vet. J.,44 (11), 885–897.

Singh, K., P. Kinjavdekar, H. P. Amerpal Aithal, A. Gopinathan, G. R. Singh, A. M. Pawde and K. Pratap (2007). Effects of epideual ketamine-xylazine combinations on the clinico-physiological and hemato-biological parameters of uremic and healthy goats. Vet. Res. Comm., 31: 133-142.

Valverde, A. (2010). Alpha-2 agonists in pain therapy in horses. Vet Clin Equine. 26: 515-532.

Wagner, A.E.,W.W. Muir and K.W. Hinchcliff (1991). Cardiovascular effects of xylazine and detomidine in horses. Am. J. Vet. Res., 52, 651–657.