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Research Article

Clinical Evaluation of Xylazine, Ketamine and Guaifenesin as Total Intravenous Anesthesia in Equines

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Abstract | The present study was conducted to evaluate a total intravenous anesthesia (TIVA) protocol in six thoroughbred horses undergoing different surgical and diagnostic procedures using Xylazine, Ketamine and Guaifenesin combination. Sedation of animals was done with intravenous injection of Xylazine hydrochloride 1.1 mg/kg followed by induction of anesthesia with Ketamine @ 2.0 mg/kg and diazepam @ 0.1 mg/kg. The anesthesia was maintained with Triple drip prepared by adding 25 gm of the Guaifenesin powder in 500 ml of 5% Dextrose solution, 500mg of Xylazine and 1 gm of Ketamine. Initially the Triple drip was given @ dose rate of 1 ml/kg/hr and subsequently adjusted depending upon the anesthetic depth of the horses. The mean arterial blood pressure was decreased after induction in comparison to initial pressure, which was subsequently increased after 40 minutes. Xylazine, Ketamine and diazepam combination produced smooth induction, excellent muscle relaxation and stable cardiopulmonary functions in all the horses under the study. The mean time of complete recovery was 85.0± 4.38 minutes indicating the safe use of Xylazine, Ketamine and Guaifenesin combination as short term anesthesia under field conditions.

Keywords | Equine, Guaifenesine, Horse, Ketamine, TIVA, Triple drip, Xylazine

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INTRODUCTION

Equine practitioners frequently anesthetize horses by using general anesthesia for several surgical procedures and diagnostic examinations in order to enhance their accuracy and maximize personal safety. But general anesthesia in horses, especially long term anesthesia carries a risk, which is often higher than that of other domestic species (Bojan et al., 2014). Thus, in the majority of cases like castration, wound examination and treatment, equine surgeons often require a short term anesthesia. At present, Total intravenous anesthesia (TIVA) is a very popular and most commonly used technique to produce short term anesthesia in horses (Kazuto et al., 2007) which has been proven to be safe, simple to perform and does not require any expensive or bulky equipments for its administration. TIVA using combination of a α2 agonist, Xylazine or detomidine with Guaiphenesin and Ketamine which anaesthetize animal by combination of central nervous system (CNS) depression, muscular relaxation and analgesia. The advantages of TIVA compared to using inhalational agents include less cardiopulmonary depression and further it requires less in terms of anesthetic machine and associated equipment.

Generally, the anesthetic protocol should be divided as premedication, induction, maintenance and recovery phases. For all these phase proper drugs or combination of drugs must be used to proper hypnosis, mayorelaxation and analgesia (Bojan et al., 2014). These combinations usually include an injectable anesthetics (ketamine, propofol), an alpha2 agonist, in combination with benzodiazepines

and opioids. Although Ketamine is a good dissociative anaesthetic with less cardiopulmonary depression than the thiopentone, the potential excitement and muscle rigidity when not preceded with a sedative have limited use of this drug alone as anaesthetic in foals and it is unreliable in adult horse. The excellent quality and consistency of sedation by α2 agonist are responsible for their popularity as preanaesthetic in horses. However, intravenous administration of α2 adrenergic receptor agonist at sedative dose is associated with decrease in cardiac output and transient increase in systemic arterial blood pressure (Wagner et al. 1991). Diazepam is good sedative along with muscle relaxant and many clinicians have been reported it's potential to modify the undesirable effects such as cardiovascular changes and/or CNS changes produced by other drugs. Guaifenesin, a centrally acting sedative and muscle relaxant is readily available in field condition and have minimal effect on the diaphragmatic muscles.

Hence TIVA is an only viable alternative for general anesthesia in horses as it has been reported to offer several potential advantages over inhalation anesthesia, including better maintenance of cardiovascular and respiratory function, quite and coordinated recoveries.

Thus, present study was conducted to determine an appropriate combination of Xylazine, Ketamine and Guaifenesinthat would produce safe and satisfactory total intravenous anesthesia in equines for different diagnostic as well as surgical procedures under field conditions.

MATERIALS AND METHODS

Selection of Animals

Study was conducted on six thoroughbred horses aged 2-4 years and weighing 400-500kg admitted at Department of Surgery and Radiology at Mumba Veterinary College and Equine hospital of Royal Western Turf Club of India (RWITC), Mumbai (Table 1). All the horses were healthy and free from clinically important cardiovascular and respiratory tract diseases. The horses used for the study were anaesthetized for different surgical and diagnostic procedure like Arthroscopy, Arthrotomy, Superior check ligament Desmotomy, Tie back etc.

Preparation of Animals Before Surgery

Preparation of animal was done by a thorough bath to the horse a day prior to the operation. Clinical parameter such as rectal temperature, heart rate and respiratory rate were recorded prior to induction of preanaesthetic**.** Horses were fasted for 12 hours and water was withheld for 8 hours prior to administration of anaesthetic. Tetanus toxoid was given to animal one day prior to surgery so as to avoid post operative tetanus. The weights of horses were calculated by weighing on weighing balance.

Table 1: Sex, age and weights of different horses used for study.

Horse no	Sex	Age (Years)	Weight	Surgical procedure
1	Female	3	489	Tie back
2	Male	2	450	Tieback
3	Female	3	400	Pinning of Tibia
4	Male	3	496	Tieback
5	Male	4	490	Tieback
6	Female	3	450	Superior Check ligament desmotomy

Anesthesia and Monitoring

Site of placement of jugular catheter was shaved and scrubbed with alcohol and betadine scrub. A 16 gauge intra jugular catheter was placed and infusion set was attached to the catheter which was further fixed by taking subcutaneous stay sutures. Sedation of animal was done with intravenous injection of Xylazinehydrochloride rate of 1.1 mg/kg (Ilium Xylazine 100: Troy Laboratories Pvt.limited, Australia) followed by induction of anesthesia with Ketamine at rate of 2.0mg/kg ((Aniket (Ketamine 50 mg/kg), Neon laboratories ltd)) and diazepam at rate of 0.1 mg/kg (Calmpose (Diazepam 5mg/ml), Ranbaxy laboratories Ltd., Mumbai). Endotracheal (ET) intubation was done after induction which has cuff at the distal end to produce airtight seal. Size of ET tube was varies depending on size of horse; in thoroughbred horses ET tube of no. 24 or 26 was used after proper sterilization and application of lignocaine jelly. Correct positioning of the ET tube was checked by the chest compression and testing for expired gas coming down the tube. After intubation, the horses were taken on the operating table with the help of winch.

Maintenance of anesthesia was done with Triple drip prepared by adding 25 gm of the Guaiphenesin (Guaiphenesin: Unidrug innovative Pharma technologies Limited, indore, M.P..) powder in 500 ml of 5% Dextrose solution, 500mg of Xylazine and 1 gm of Ketamine. Initially the Triple drip was given @ dose rate of 1 ml/kg/hr and subsequently adjusted depending upon the anaesthetic depth of the horses.

Anaesthetic parameters studied during surgical procedures were signs of sedation, time of induction of anaesthesia, duration of anaesthesia and recovery time. Time of induction of anaesthesia is recorded as the time taken from intravenous injection of induction anaesthetic agent to loss of first painful reflex. The quality of induction (Table 2), maintenance (Table 3) and recovery phase (Table 4) of anaesthesia was assessed.

Intra arterial cannulation was done with 20 gauge catheter (Figure 1), in facial artery or dorsal metatarsal artery to measure the intra arterial pressure 10 minutes after the start of triple drip and at the intervals of 10 minutes during maintenance of anaesthesia. Measurement of Blood oxygen saturation (SpO_2) was done with the help of a patient monitor by placing the sensor on the sublingual artery at an interval of 10 minutes during maintenance of anaesthesia. Quality of anaesthesia during maintenance was judged by muscle relaxation intra arterial pressure and SpO_2 (Table 5).

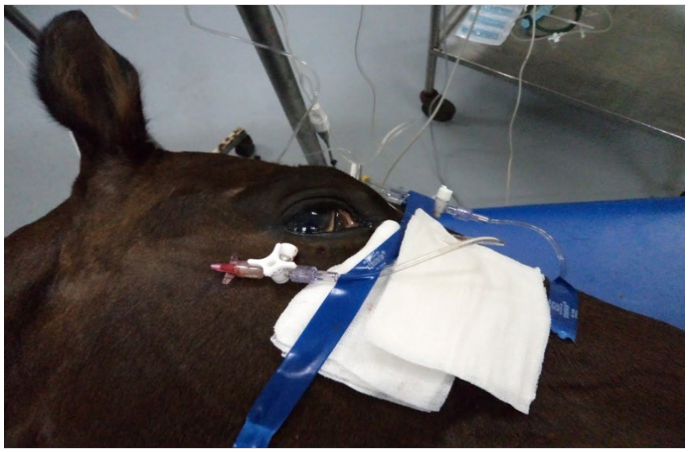

Figure 1: Placement of Intra arterial catheter.

Table 2: Score card for quality of induction

Score	Quality	Character
Grade A	Excellent	Presence of all characteristic sign without any complication.
Grade B	Satisfactory	Presence of all characteristic signs along with slight complication which did not interfere with the course of anaesthesia.
Grade C	Partially satisfactory	Presence of only few of the characteristic signs along with complication, which interferes with course of anaesthesia
Grade D	Unsatisfactory	Absence of the chacteristic signs of anaesthesia and thus totally unsatisfactory anaesthesia

Table 3: Score card for quality of maintenance

Score	Quality	Character
Grade A	Excellent	Smooth and require 1 or 2 drug increments
Grade B	Satisfactory	Require 3 or 4 drug increments
Grade C	Partially satisfactory	Require multiple drug increments
Grade D	Unsatisfactory	Unable to maintain surgical anesthesia

Table 4: Score card for quality of recovery

Score	Quality	Character
Grade A	Excellent	Smooth and Fast Recovery
Grade B	Satisfactory	Smooth and Prolonged recovery
Grade C	Partially satisfactory	Struggling and Fast Recovery
Grade D	Unsatisfactory	Struggling and Prolonged Recovery

Clinical Parameter like Rectal temperature (°F), heart rate (beats/minute), pulse rate (beats/min) and respiration rate (breaths /min) were studied before induction of anaesthesia as well as at 15, 30, 45 and 60 minutes during anaesthesia and after complete recovery.

Blood was collected aseptically from the jugular vein of all the horses for the study of haematological and biochemical parameters before induction of anaesthesia, during anaesthesia and after complete recovery from anaesthesia.

Table 5: Score card for quality of muscle relaxation.

Score	Quality	Character
Grade A	Excellent	Complete relaxation
Grade B	Good	Adequate muscle relaxation for surgicalProcedure
Grade C	Moderate	Partial relaxation of head, neck, and limbMuscles
Grade D	Poor	Rigidity in muscles of neck, head, and limbs

Statistical Analysis

The results were tabulated and statistically analysed by Randomised Block Design (RBD) as described Snedecor and Cochrasn (1994).

RESULTS

Quality of Sedation and Induction of Anaesthesia

All the horses used for the study were healthy and free from clinically important cardiovascular and respiratory tract diseases. After premedication with Xylazine hydrochloride horses were observed for the signs of sedation. Quality of sedation was good in five horses with Xylazine (1.1 mg/kg) and showed signs of sedation like prolapse of penis, anal sphincter relaxation, shifting of weight, lowering of neck, drooling of lips and behavioural alteration.With Xylazine, Ketamine and diazepam combination the mean time of induction was 2.33± 0.43 minutes and there was no significant variations observed. No limb movement was noticed after induction of anesthesia with Ketamine and diazepam

indicating excellent quality induction of anesthesia. Mean time for loss of gag reflex was 3.25± 0.445 minutes.

The quality of induction was judged on the basis of presence or absence of pain after induction of anaesthesia. Quality of induction was excellent in all the horses with presence of all characteristic signs of anaesthetic induction as reported by Butera et al. (1978). Mean duration of anaesthesia was 62.83 ± 5.62 minutes.

Quality of Anesthesia During Maintenance of Anesthesia

Quality of anaesthesia during maintenance was judged by muscle relaxation, intra arterial pressure and SpO_2. Excellent to good quality muscle relaxation was observed in all the horses maintained with triple drip.

Recovery in Animal After Anesthesia

Recovery period was divided into three stages as lateral recumbency with head up, sternal recumbency and standing time. After discontinuation of the anesthetic, mean time required for head up in lateral recumbency was 40.17 ± 2.90, for sternal recumbency 51.33 ± 5.162 and for standing time 63.833 ± 3.166. Thus, mean time required for complete recovery was 85.0± 4.38 with smooth and prolonged recovery.

Effect of Anaesthesia on Physiological and Clinical Parameters During Maintenance

The mean value of arterial blood pressure was recorded at different time interval was 114 ± 5.61 at 10 minutes after onset of anaesthesia (Table 6). There was a significant difference observed in the mean arterial pressure during anaesthesia ($P \leq 0.01$ and $P \leq 0.05$).

SPO_2 (%) was measured at different time interval, the mean value was 84.5 ± 2.56 %, 10 minutes after onset of anaesthesia. High significant differences were observed in the partial pressure of oxygen with Low partial pressure of oxygen. (Table 6).

No significant differences were observed in heart rate during maintenance of anaesthesia. Mean pulse rate before injection of pre anesthetic was 37.33 ± 1.22 with no significant variation in the pulse rate during study.

Clinical parameters recorded before induction of anaesthesia as well as at 15, 30, 45 and 60 minutes during anaesthesia and after complete recovery are presented in Table 7.

Effect Of Anesthesia On Hemato- Biochemical Parameters

Hemoglobin before, during and after surgery was 12.63± 0.62, 11.87 ± 0.45 and 12.97 ± 0.42 respectively. Non significant decrease in haemoglobin was observed during maintenance of anaesthesia which was returned to baseline after complete recovery. Non significant variation was reported in packed cell volume (PCV) and mean total erythrocyte count (TEC) during anaesthesia and following recovery in all the horses. Non significant increase in the neutrophil count and lymphocyte count was reported after complete recovery. Various haematological parameters recorded at various times interval are presented in Table 8.

Effect of Anesthesia on Biochemical Parameters

No significant variation was observed in the mean Serum Glutamic Pyruvate Transaminase (SGPT) and Serum Glutamate Oxaloacetate Transaminase (SGOT) in all the horses. Although significant decrease in the alkaline phosphatase enzyme was noted. Results showing enzyme profiling for liver function test and kidney function tests are presented in Table 9.

DISCUSSION

The results of the study showed usefulness of triple drip of Xylazine, Ketamine and Guaifenesin for maintenance of anesthesia in thoroughbred racing horses. After premedication with Xylazine hydrochloride horses showed signs of sedation like prolapse of penis, anal sphincter relaxation, shifting of weight, lowering of neck, drooling of lips and behavioural alteration which corroborate observations of Yamashita et. al. (2002), Thakur et al. (2011) and Nanda (2009). One horse was showed movement after sedation by Xylazine. This was because the noise created by the horse handlers and struggling of horses during injection of Xylazine. Similar finding were reported by Ratajczak et al. (1993), Kerr et al. (1972), Tripathi (2003), and Raut (2004).

With Xylazine, Ketamine and diazepam combination induction was smooth and similar findings were reported by Thakur et al. (2011) Chaturvedi (2005), Patil (2007) and Butera et al. (1978). Quality of induction was excellent in all the horses with presence of all characteristic signs of anaesthetic induction. More et al. (1993) and Pawade et al. (2000) reported smooth induction, excellent muscle relaxation and stable cardiopulmonary function in bovines when xylazine, ketamine and diazepam combination was used, same was observed in all the horses.

Excellent to good quality muscle relaxation was observed in all the horses maintained with triple drip as reported by Thakur et al. (2011). The muscle relaxation is largely attributed to guaifenesin which acts centrally by depressing or blocking nerve impulse transmission at subcortical areas of brain, brainstem, and spinal cord (Cullen, 1996). However,

Table 6: Effect of infusion of Xylazine, Ketamine and Guaifenesine on clinical parameters

	Time (minutes) after initiation of anaesthesia					
Variable	10	20	30	40	50	60
Mean blood pressure (mm of Hg)	104± 4.32	94.67 ± 4.78	75.83 ± 4.36	78.33 ± 5.31	82.5 ± 4.66	90.33 ± 6.33
Saturated Partial Pressure of Oxgen (SpO_2) (%)	98.5± 0.35	99.00±00.00	98.83 ± 0.17	98.83 ± 0.17	98.83 ± 0.17	98.83 ± 0.17

Table 7: Effect of infusion of Xylazine, Ketamine and Guaifenesine on clinical parameters

		Time (minutes) after initiation of anaesthesia				
Variable	**Before induction of Pre anaesthetic**	**15**	**30**	**45**	**60**	**After complete recovery**
Heart rate (beats/minute)	37.0± 1.53	35.5± 1.72	36.5 ± 2.07	37.33 ± 0.96	36.67 ± 2.06	34.67 ± 0.89
Pulse rate (beats/minute)	37.0± 1.53	35.5± 1.72	36.5 ± 2.07	37.33 ± 0.96	37.33 ± 1.92	34.0 ± 0.89
Respiration rate (breats/minute)	15.83 ±0.55	4.5 ± 0.95	6.0	6.0	2.83 ± 0.40	14.83± 0.40
Rectal Temperature (°F),	100.27 ± 0.28	100.0 ± 0.22	99.6 ± 0.20	99.47 ± 0.13	99.28 ± 11	99.95 ± 0.22

Table 8: Effect of infusion of Xylazine, Ketamine and Guaifenesine on hematological parameters

	Time of infusion of anaesthesia		
Variable	**Before anaesthesia**	**during anaesthesia**	**After anaesthesia**
Haemoglobin (gm/dl)	12.63± 0.62	11.87 ± 0.45	12.97 ± 0.42
Packed cell Volume (%)	37.85 ± 2.67	38.80 ± 1.98	39.85 ± 2.74
Total Erythrocyte Count (10^6/cumm)	7.75 ±0.37	7.52 ± 015	7.83 ±0.37
otal Leukocyte Count (10^3/µl)	7.22± 0.58	8.25 ± 1.23	11.88± 1.64
Neutrophils (%)	45.67± 0.92	46.17± 0.91	64.67± 2.94
Lymphocyte (%)	48.16± 0.70	48.50± 1.38	30.83 ± 3.00
Monocyte (%)	2.17± 0.47	2.17± 0.55	2.5 ±0.68
Eosinophil (%)	4.0 ± 0.36	3.17±0.65	2.0 ± 0.36
Platelet count (10^5/µL)	7.50 ± 0.23	7.39 ± 0.23	7.47 ± 0.29

Table 9: Effect of infusion of Xylazine, Ketamine and Guaifenesine on biochemical parameters

	Time of infusion of anaesthesia		
Variable	**Before anaesthesia**	**during anaesthesia**	**After anaesthesia**
SGPT (IU/L)	12.34± 1.03	12.97± 1.41	26.47±6.70
SGOT(IU/L)	386.7± 44.99	388.67±35.59	372.78±43.19
Alkaline Phosphatase(IU/L)	137.08±23.63	133.55±35.05	151.32±28.45
BUN (mg%)	11.38 ± 1.65	14.5 ± 2.80	13.11± 2.19
Serum creatinine(mg%)	1.75 ± 0.12	1.86 ± 0.11	1.97 ± 0.17

Lin et al. (1993), Baetge et al. (2007) and Matthews et al. (1991) observed merely excellent quality muscle relaxation in horses and similar findings were reported by More et al. (1991) and Pawade et al. (2000) in bovines. Thurmon*et al.* (1997) recorded good quality muscle relaxation in ponies maintained with triple drip of Detomidine-Ketamine-Xylazine.

The mean arterial blood pressure was decreased after induction in comparison to initial pressure, which was subsequently increased after 40 minutes. Similar trend observed by Green et al. (1986) in horses and Taylor et al. (2008) in donkeys. However, Batram et al. (1991) reported increase in MAP, 30 minute after induction of anaesthesia in horses.

Wagner et al. (2008) and Steffy et al. (1987) reported that unlike other species, less variation in the heart rate during anaesthesia in the horses makes it an unreliable indicator for the depth of anaesthesia. Taylor et al. (2008) reported same observation with Triple drip of Detomidine- Ketamine - Guaifenesin in pregnant ponies during laparot-

omy and in donkeys. But Green et al. (1986) and Lin et al. (1983) reported significant decrease in the heart rate in horses maintained with Xylazine-Ketamine - Guaifenesin triple drip. Mama et al. (2005) found that presence of reflex activity at a surgical plane of anesthesia can also confound evaluation of anesthetic depth and may lead to inappropriate drug dosing.

Non Significant decrease in rectal temperature was observed in all horses during maintenance of anaesthesia. Taylor et al. (2008) reported decrease in the temperature during maintenance of anaesthesia in the donkeys with Triple Drip of Xylazine-Ketamine-Guaifenesin.Nonsignificant decreases in heart rate and respiration rate were observed after induction and during anaesthesia (Table 7). However, the changes recorded were within normal range in all the horses. A similar trend was observed following continuous intravenous triple drip of Xylazine-ketamine-guaifenesin.

During maintenance of anaesthesia non significant decrease in haemoglobin which was returned to baseline after complete recovery were also reported by Nanda (2009), Thakur et al. (2011), Jackson and Lundavell (1970) and Young et al. (1993) after using triple drip in equines. Decrease in haemoglobin might be due to splanchnic pooling of erythrocyte. No change in TEC could be due to assignment of diagnostic and surgical procedures where minimal vasculature and less loss of blood occurred. Non significant increase in total leukocyte count (TLC) was noted after complete recovery which may be due to excitement, pain or fear in the horses leading to redistribution and flushing effect (Benjamin, 1998). Non significant increase in the neutrophil count and lymphocyte count was reported after complete recovery which could be due to normal inflammatory response following surgical procedures. However no statistical significance was noted for monocyte, eosinophil and platelet count during anaesthesia and could be attributed to maintenance of normal homeostasis by triple drip of Xylazine, ketamine and Guaifenesin.

Significant decrease in the alkaline phosphatase enzyme was noted but it has no clinical relevance because of wide range of alkaline phosphatase in horses. The minimal changes in the hepatic enzyme profile in horses maintained with triple drip of Xylazine-Ketamine- Guaifenesin indicates less hepatic damage. Non significant increase in the blood urea nitrogen and non significant increase in the serum creatinine was reported which might be due to decrease renal blood flow and consequent decrease glomerular filtration rate.

CONCLUSION

It was concluded that Xylazine, Ketamine and Guaifenesine combination can safely be used for total intravenous anaesthesia for short-term procedures in equines under field conditions where the monitoring facilities are meager. The combination produces minimal side effects without any hepatic or renal toxicity but needs further intensive study.

This combination can be used safely for maintenance of anesthesia during orthopedic surgery where recovery is smooth expected.

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CONFLICT OF INTEREST

The authors declare they have no conflicts of interest with regard to the work presented in this report.

AUTHORS CONTRIBUTION

Satyawan M.Agivale did research work as study protocol and prepared the manuscript for submission, G.S.Khandekar guided for planning of work, S.D.Tripathi member of research committee and helped in editing the manuscript and P. Sawandkar helped in execution of research methodology.

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