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Peri-operative monitoring of general anaesthesia using xylazine+ butorphanol, ketamine + diazepam and isoflurane in ASA 2 equines

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ABSTRACT

The objective of the study was to evaluate the peri-operative monitoring of general anaesthesia using xylazine+butorphanol, ketamine+diazepam and Isoflurane in ASA 2 Equines. A total of 27 adult equines undergoing surgical treatment and for which general anaesthesia was necessary were included. The clinical observations included monitoring reflexes like palpebral and corneal, lacrimation, eyeball position, Pupil size, and physiological parameters such as heart rate and respiration rate, body condition score, weight, age, breed, gender, Intermittent positive pressure ventilation, oxygen saturation, end tidal carbon dioxide, Blood pressure, Isoflurane conc., and Oxygen flow rate. The overall sedation score was moderate in 59.26% (16/27), marked in 29.63% (8/27) and mild in 11.11% (n=3) equines. The recovery quality was mostly good but still 4 equines required xylazine @0.25mg/Kg, IV during recovery. One mare showed rough recovery. No mortality was recorded in any equine but morbidity (3.7%) in the form of rough recovery was recorded. The study concludes that systematic monitoring of general anaesthesia using physical parameters is required for all equines for a better outcome. Proper weighing of the equine is recommended for correct dose calculation and the conventional dose of xylazine + butorphanol and ketamine + diazepam used, may not be sufficient in ASA 2 equine of Marwari breed. One fourth dose of xylazine, intravenously may be recommended during the recovery period of ASA 2 equine, depending upon the pre-anaesthesia temperament to avoid rough recovery.

Keywords: Anaesthesia monitoring, Butorphanol, Diazepam, Equine, Recovery, Xylazine

Equine patients are highly sensitive and usually require general anaesthesia for most of the invasive procedures. Morbidity and mortality associated with general anaesthesia in equines is quite high in comparison to small animals like dogs and cats (Johnston *et al.* 2002). Morbidity and complications associated with general anaesthesia in equines includes; cardiac arrest, fractures, myopathy, myelopathy, non-specific internal damage, hypothermia, hypercarbia, hypoxaemia, hyperkalemic periodic paralysis, regurgitation and aspiration, cerebral necrosis, obstruction in airways, pulmonary oedema, post-anaesthetic colic and ileus, intravenous cannula problems, vaginal and uterine tears. Anaesthetic risk factors also affect the overall cost of surgery and it further increases if the equine is to be euthanized (Johnston *et al.* 2002). Due to the above explained morbidity and mortality reasons involved in the general anaesthesia of equines the peri-operative monitoring of general anaesthesia is mandatory in this species (Brodbelt *et al.* 2008). Proper peri-anaesthetic monitoring is also important to prevent possible injuries to anaesthetist, surgeon and other supporting members although it is very rare but cannot be neglected. In Indian context, the peri-operative monitoring of anaesthesia is not well developed in any animal species but is important so that timely intervention can be undertaken.

A single communication highlights the need of peri-operative monitoring of general anaesthesia in buffaloes suffering from diaphragmatic hernia (Singh *et al.* 2023). Therefore, the present study is planned to study the perioperative monitoring of general anaesthesia using xylazine+butorphanol, ketamine+diazepam and isoflurane in ASA 2 Equines.

MATERIALS AND METHODS

The present study was carried out on 61 equines, brought for surgical treatment to the Teaching Veterinary Hospital at Department of Veterinary Surgery and Radiology, College of Veterinary Science, GADVASU, Ludhiana from August 2022 to July 2023 and for which general anaesthesia was necessary. Due ethical permission was obtained from the Institutional animal ethics committee for a period of one year.

The equines were classified under various ASA groups (American Society for Anaesthesiologists) and anaesthetic protocols as per the case presentation. However, the ASA 2 equines were maximum presented (N=35) under a specific anaesthetic protocol (N=27) so, only 27 equines have been

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Fig. 1. Photograph showing procedure of taking (a) heart rate, (b) respiration rate from trachea, (c) mucous membrane and (d) capillary refill time from gum in equine during pre-anaesthetic period. HR: Heart rate (beats/min), RR: Respiration rate (breaths/min), MM: Mucous membrane, CRT: Capillary refill time

included in this communication for a conclusive study.

The ASA 2 equines are those suffering from mild systemic disease such as febrile, laryngeal dysfunction, mild impaction, pregnancy or laminitis. In the present report, 27 equines were classified under ASA 2 and were suffering from recto-vaginal injuries (n=16), fractures (n=2), eye affections (n=4) and miscellaneous other conditions like umbilical hernia, abscesses, contracture (n=5). All the equines were more than 4 months of age.

Pre-anaesthetic assessment of equines undergoing general anaesthesia

Signalment: Documentation of the equine's weight, age, breed, gender and surgical treatment was recorded.

Physiological observations

Heart rate (beats/min) (HR): The heart rate was taken from over the chest at 3-4th ICS with a stethoscope and was counted for a minute (Fig. 1a). During anesthesia, the Heart rate was recorded every 5 min form the Multipara Monitor. The Pulse rate, if required was taken from the facial artery.

Respiration rate (breaths/min) (RR): The respiration rate was counted by placing the stethoscope on the trachea in the neck region (Fig. 1b) in the pre-anesthetic period. and during anaesthesia from the rebreathing bag every 5 min.

Mucous membrane (*MM*) color: MM color was recorded by reverting the MM of the eye as pale, pink, congested (Fig. 1c).

Capillary refill time (CRT): CRT was recorded by pressing the thumb on the gums and recording the refill time in sec as 1 sec, >1 sec, <2 sec, 2 sec, <3 sec, 3 sec, >3 sec and so on (Fig. 1d). These classifications were given numerical numbers for statistical analysis as mentioned in results.

BCS score: The body condition score (BCS) of all the equines was recorded as per Henneke *et al.* 1983. (Poor: 1, Very thin: 2, Thin: 3, Moderately thin: 4, Moderate: 5, Moderately fat: 6, Fleshy: 7, Fat: 8 and Extremely Fat: 9)

Body weight (b.wt): All the equines were weighed before dose calculations unless in emergency cases.

All the equines were administered tetanus toxoid prior to surgery. The equines were brought to the anaesthesia room and were allowed to stand close to a wall. The equines were pre-anaesthetized using a combination of xylazine (1.1 mg/kg body weight) and butorphanol (0.02 mg/kg), intravenously in a standing position. Once the sedation mark was achieved, the anaesthesia was induced with a combination of ketamine (2.2 mg/kg) and diazepam (0.02 mg/kg), intravenously in standing position only. When the equine lied on the ground, a mouth gag was applied and endotracheal tube of suitable diameter was placed (Fig. 2a). The quality of sedation was evaluated using a simple descriptive scale as described by Nannarone *et al.* 2021 (Table 1).

Once tracheal intubation was done, the equine was transported to the operation table through a ceiling mounted motorized hoist (Fig. 2b). The endotracheal tube was attached to the anaesthesia machine for oxygen delivery and inhalant anaesthesia of Isoflurane was used for maintenance mixed in 100% oxygen (Fig. 2c).

Peri-anaesthetic monitoring of parameters in equine: Apart from the HR, RR, CRT and the MM mentioned above the other parameters recorded were as follows:

Oxygen hemoglobin saturation in blood (%): Oxygen hemoglobin saturation in blood (SpO_2) was measured by the pulse oximeter of multi-para monitor (Fig. 3a) placed on the tongue, nostrils or lip commissure of the equine during anaesthesia (Fig. 3b).

Blood pressure (mm Hg): The suitable size (4 inch) pressure sensor cuff was placed on the base of the tail to record blood pressure in the multipara monitor (Fig. 3c). If the surgery was in the perineal region, it was difficult

Table 1. Table showing the sedation quality scoring system by Nannarone *et al.* 2021

Score	Sedation quality
No sedation (0)	Animal alert, no ataxia (equine required more sedation)
Mild sedation (1)	Slightly lowered head (up to shoulder), some response to intervention, mild ataxia.
Moderate sedation (2)	Lowered head (up to elbow), slight response to intervention, moderate ataxia.
Marked sedation (3)	Lowered head (up to knee), animal attempt to or become recumbent, no response to intervention, marked ataxia.

Fig. 2. Photograph showing (a) the procedure of endotracheal intubation in equine, (b) transfer of equine on ceiling mounted hoist, and (c) equine connected to inhalant anaesthesia machine.

to place the cuff and take readings. The systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) were recorded every 5 min, wherever possible.

Capnography (*ETCO$_2$*): The ETCO$_2$ (End tidal carbon dioxide) levels were recorded using a capnograph placed on the side port of the 'Y' piece of corrugated inhalation and exhalation pipes (Fig. 3b). The readings were recorded from the Multipara monitor every 5 minutes.

Palpebral reflex: The palpebral reflex was given numerical value as per the presentation. If no reflex=0, lateral palpebral reflex present=1, medial and lateral palpebral present=2. The palpebral reflex was recorded by lightly touching the lateral palpabra and if present also checking the medial one.

Lacrimation: Lacrimation was recorded as present or absent as 1 or 0, respectively (Fig. 3d).

Corneal reflex: Corneal reflex was recorded no reflex '0', mild '1' and moderate '2' by touching the cornea.

Position of eyeball: Position was eyeball was classified as ventromedial (Fig. 3e) or central (Fig. 3f). Central was given numerical value '0' if present in light plane, ventromedial as '1' and central in deep plane as '2'.

Size of pupil: The size of pupil was recorded as constricted as '0' (Fig. 3g) and dilated as '1' (Fig. 3h).

Nystagmus: Nystagmus was recorded as present or absent as '1' or '0'.

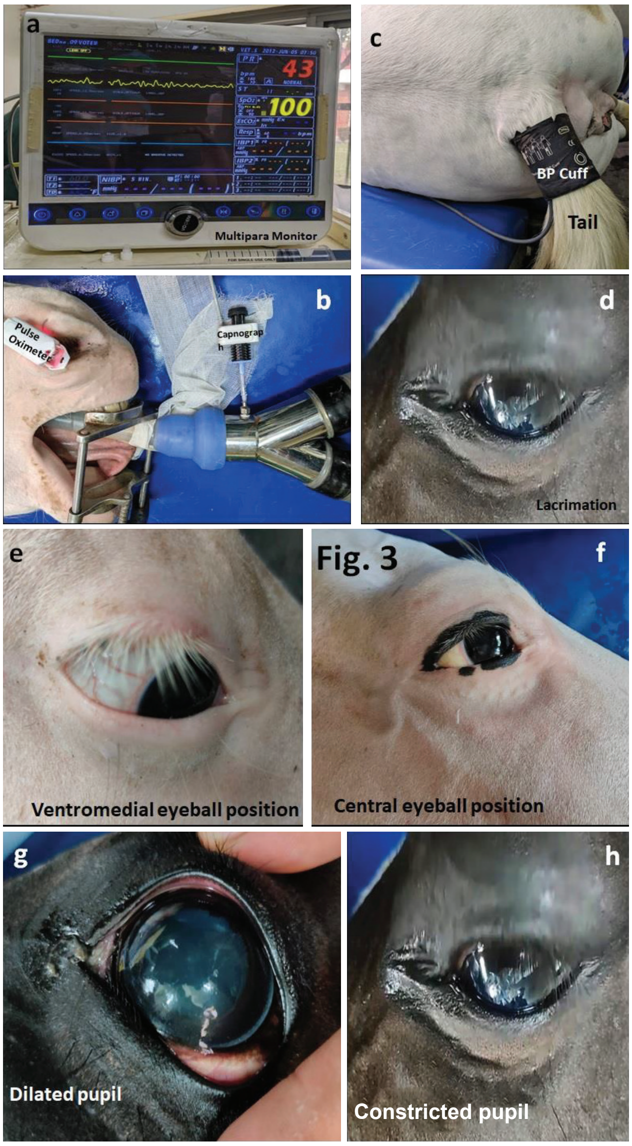

Fig. 3. Photograph showing (a) multipara monitor, (b) placement of pulse oximeter and capnograph, (c) blood pressure cuff on tail, (d) lacrimation, (e) ventromedial eyeball position, (f) central eyeball, (g) dilated pupil, and (h) normal/ constricted pupil.

Isoflurane concentration in %: Isoflurane concentration was recorded every five minutes in numerical value 1 to 5.

Oxygen flow rate mL/Kg/min: The oxygen flow rate was recorded in numerical value as per the body weight as 6-12 l/min/kg.

Muscle movement: Muscle movement during surgery was given numerical value '0' if not present and '1' if mild limb movement was present.

Intermittent positive pressure ventilation (IPPV): IPPV was administered to the equines wherever required.

Recovery quality: The recovery was recorded as the time of sitting of the equine after switching off the Isoflurane concentration, the time of standing, and number of attempts the equine made for standing. The recovery was score 1-5

Table 2. Recovery scoring system as described by Young and Taylor 1993

Scoring	Recovery quality
1 (excellent)	Excellent, perfect, no ataxia, stand at 1st attempt as if rising from rest.
2 (good)	Stand after 1st or 2nd attempt, some weakness, ataxia, and may knuckle slightly after standing.
3 (fair)	Stands after several attempts, moderate weakness/ataxia, may knuckle on fetlocks after standing.
4 (marginal)	Multiple attempts to stand, very ataxic when finally standing and commonly falls down again, sustains injury.
5 (poor)	Multiple attempts to stand, could make many desperate attempts to stand in between exhausted episodes, fail to stand because of PAM or neuropathy.

Note: The data was statistically analysed using excel Microsoft 2010.

as per the scoring system described by Young and Taylor 1993 (Table 2).

RESULTS AND DISCUSSION

An anaesthesia record sheet was standardized for recording of all the parameters at suitable intervals from the pre-anaesthetic to recovery period for equine (Supplementary Table 1) for single side of a paper. The perioperative monitoring of the anaesthesia was done based on the record sheet developed.

The average body weight of the equines was 320.11±69.74 kgs. All the equines were of Marwari breed and had an average age of 60.07 ± 35.62 months. The average BCS of the equines was 4.85 ± 0.99. The duration of anaesthesia was 96.96 ± 33.20 min. On an average, the equines showed the head down upto knee in 2.72 ± 0.68 min and lying down in 2.74 min. Topping of anaesthesia with a combination of xylazine and ketamine in equal quantity was required in 51.8% equines (14/27) for endotracheal intubation and shifting to the operation table for attachment to isoflurane anaesthesia. The size of endotracheal tube ranged from 16-22mm (internal diameter). Out of 27 equine, 18 (66.67%) were placed in dorsal recumbency while 9 were in lateral as per the need of the surgery. The overall sedation score was moderate in 59.26% (16/27), marked in 29.63% (8/27) and mild in 11.11% (n=3) equines.

Butorphanol @0.02mg/kg has clear sedative effect when combined with xylazine and no ataxia is recorded, however, at a higher dose ataxia is common (Taylor *et al.* 2016, De Grauw and Loon 2020). Butorphanol is reported to be the best opioid which produces good sedation with no response to external stimuli and no excitatory effects (Clarke and Paton 1988). Even, in standing sedation, if mixed with butorphanol, the dose of xylazine is reduced (Ringer *et al.* 2012) or in TIVA (total intravenous anaesthesia) it decreases the top ups (Straticò *et al.* 2021). Sufficient sedation is recommended to when the head of the equine is lowered up to its knee level or nearly 50% to its initial standing position (Ringer *et al.* 2012) due to significant muscle relaxation provided by xylazine (Hubbell *et al.* 1999). A higher dose of Ketamine (5 mg/kg) is recommended to provide faster induction and better surgical condition under field anaesthesia (Harðardóttir *et al.* 2019) as compared to the recommended dose of 2.2 mg/kg.

Monitoring of anaesthesia during maintenance: The initial isoflurane concentration was high, and remained at 2.0 or 2.5, which was higher than the MAC value mentioned in literature (Steffey *et al.* 1977). Butorphanol is supposed to reduce the MAC of inhalant anaesthesia (Matthews and Lindsay 1990, Doherty *et al.* 1997), but was not seen in the present protocol.

The oxygen flow rate was initially kept higher and was almost 20 mL/kg body weight in a partial rebreathing circuit which was slowly increased to 33 and 25 mL/kg near to the end of surgery. The eyeball was mostly in central position of deep plane of anaesthesia. Butorphanol can deepen the plane of anaesthesia and obtund surgical stimulation (Hofmeister *et al.* 2008). Most of the equines had both lateral and medial palpebral reflex present at the start of surgery which later converted to only lateral reflex. Ketamine keeps the spontaneous palpebral reflex active and makes it unrelated to the actual depth of anaesthesia (Stefanik *et al.* 2021). The initial palpebral reflex could be due to short half-life of 10–15 min of ketamine (Lin *et al.* 2015), after which the isoflurane masks ketamine effect. The pupil got dilated in between the surgery. Opioids are also reported to cause lightening of anaesthetic plane in isoflurane anesthetized horses in certain circumstances (Steffey *et al.* 2003). The corneal reflex was mostly present, and was either strong or in between mild and strong. In rare cases it occasionally comes to 'no' reflex. The anaesthesia protocol of xylazine-butorphanol-guaifenesin-ketamine is supposed to reduce the lacrimation, palpebral and corneal reflexes (Thakur *et al.* 2011). Lacrimation was mostly present at the start of anaesthesia which gradually reduced or stopped. The α -2 agonist in combination with butorphanol decrease tear production in equines (Muir 2009, Bianchi *et al.* 2015).

Nystagmus was absent in all equines indicating sufficient anaesthetic plane (Taylor and Clarke 2006). Mild muscle movement was present in between in one or two equines in between the surgery. The CRT was almost constant throughout the surgery. Overall low heart rate was recorded. Butorphanol is supposed to affect the heart rate in equines (Robertson *et al.* 1981, Knych *et al.* 2013) however; few reports also indicate no change in heart rate or no decrease below baseline (Matthews and Lindsay 1990). The colour of MM remained constant throughout the anaesthesia. The MAP is recommended to be maintained at 70 mmHg or higher to provide adequate muscle perfusion (Richey *et al.* 1990), which was almost seen in all the equines, although

Table 3. Table showing the monitoring of various parameters at different time intervals

Parameter	0 min	10 min	20 min	30 min	40 min	50 min	60 min	70 min	80 min	90 min	100 min	110 min
Isoflurane conc. in %	4.05	3.26	2.9	2.7	2.6	2.4	2.2	2.0	2.3	2.5	2.0	2.0
O2 flow rate mL/Kg/min	8.6	8.3	8.4	8.5	8.6	8.9	9.0	8.7	8.0	8.0	8.0	8.0
Eyeball position	1.2	1.4	1.5	1.6	1.7	1.6	1.8	1.7	1.5	1.0	1.0	1.0
Palpabral reflex	1.8	0.7	0.4	0.3	0.2	0	0	0	0	0	0	0
Pupil size	0.09	0.05	0.15	0.21	0.27	0.2	0.4	0	0	0	0	0
Corneal reflex	2	2	1.8	1.7	1.6	1.5	1.2	1	1	2	2	2
Lacrimation	0.6	0.6	0.4	0.2	0.2	0.1	0	0	0	0	0	0
Nystagmus	0	0	0	0	0	0	0	0	0	0	0	0
Muscle movement	0.1	0.08	0	0.04	0	0	0	0	0	0	0	0
CRT	1.3	1.3	1.3	1.3	1.3	1.4	0.8	1	1.5	3	3	3
Pulse rate	37.3	37.5	39.2	38.8	38.3	38.2	38	37.3	36	32	32	32
Mucous membrane	2	2	2	2	1.9	1.9	1.8	1.7	1.5	1	1	1
Systolic BP	102.0	94.1	88.1	93.0	93.6	89.0	116.5	85.0	130.0	99.0		
Diastolic BP	74.3	70.0	58.0	64.1	69.0	63.5	89.5	56.5				
MAP	83.2	77.6	66.7	73.3	77.0	71.7	98.0	65.0	72.0			
RR	7.2	6.7	6.9	7.7	7.2	5.9	5.2	6.7	5.5	7	8	8
SPO2	97.2	97.8	97.3	97.3	96.9	95.5	98	98	94	96	100	99
$ETCO_2$	47	47.5	45.5	43.1	46.3	47.5	44.5	50.5	51	38	33	33

a few times it, went below 70 mmHg, as hypotension is routinely noticed in inhalant anaesthesia (Wilson *et al.* 2003) leading to decreased cardiac output upto 50% from awake horses (Mizuno *et al.* 1994). No medication was given during surgery for occasional lower heart rate. The respiration at 10 minutes was quite low. Butorphanol is supposed to increase the respiratory depression (Clarke *et al.* 1991) but not to the extent of serious effect (Robertson *et al.* 1981). Xylaine and ketamibe combination is supposed to cause a significant depression in respiratory rate (Rings and Muir 1982, Cuvelliez *et al.* 1995). Even isoflurane lead to significant respiratory depression as also observed in this study in comparison to pre-anaesthesia RR (Serteyn *et al.* 1988). IPPV (Intermittent positive pressure ventilation) was given in 3 equines due to very less or no respiration during the procedure. However, it is recommended to start IPPV immediately after induction for a better gas exchange in equines (Wolff and Moens 2010) to prevent alveolar collapse (Day *et al.* 1995). The SPO_2 of dropped to 94 in few equines but that could be because the probe was not staying properly on tongue, lip or nostrils and hence may have given wrong reading. A less reliability on the pulse oximeters has been recommended by anaesthesiologists for equine as they tend to show lesser values (Whitehair *et al.* 1990). The $ETCO_2$ was almost within the normal range.

Recovery Quality: The average sitting time of the equines was 8.85 minutes and the average standing time was 36.19 min. The equine on an average made 2.65 attempts to stand. On score basis, 88.88% (n=24) had recovered ‘good’ with a score of ‘2’, while 7.47% (n=2) had fair recovery (Score 3) and one equine had marginal recovery (Score 4). Out of 27 equine, 4 (14.81%) required 0.25 mg/kg, IV dose of xylazine during recovery which increased the recovery time but made it smoother (Taylor and Clarke 1999, Santos *et al.* 2003, Loomes and Louro 2022), while one was administered dobutamine during recovery, due to hypotension. A 0.25 mg/Kg IV dose of xylazine is recommended during recovery to increase its quality (Lda *et al.* 2013). It is also reported that the recovery quality is negatively related to the duration of anaesthesia (Young and Taylor 1993). There was a lot of difference in sitting and standing time in the equine, as Isoflurane tend to increase this time interval (Matthews *et al.* 1992, Whitehair *et al.* 1993, Grosenbaugh and Muir 1998). One mare showed rough recovery with falling multiple times before standing (3.7%).

The study concludes that systematic monitoring of general anaesthesia using physical parameters is required for all equines for a better outcome. Proper weighing of the equine is recommended for correct dose calculation and the conventional dose of xylazine + butorphanol and ketamine + diazepam used, may not be sufficient in ASA 2 equine of Marwari breed. One fourth dose of xylazine, intravenously may be recommended during the recovery period of ASA 2 equine, depending upon the pre-anaesthesia temperament to avoid rough recovery.

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