Evaluation of Bispectral Index (BIS) as an Indicator of Central Nervous System Depression in Horses Anesthetized with Propofol

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ABSTRACT. The bispectral index (BIS) was evaluated as an indicator of central nervous system (CNS) depression in horses anesthetized with propofol. Five non-premedicated horses were anesthetized with 7 mg/kg, IV propofol and the minimum infusion rate (MIR) of propofol required to maintain anesthesia was determined during intermittent positive pressure ventilation in each horse. The BIS was determined 20 min later and after stabilization at 2.0 MIR, 1.5 MIR, and 1.0 MIR. The BIS was also recorded after the cessation of propofol infusion when the horses regained spontaneous breathing and swallowing reflex. The MIR and plasma concentration (Cp) of propofol were 0.20 ± 0.03 mg/kg/min and 17.5 ± 4.0 µg/ml, respectively. The BIS value and Cp were 59 ± 13 and 26.7 ± 8.6 µg/ml at 2.0 MIR, 63 ± 9 and 22.9 ± 9.7 µg/ml at 1.5 MIR, 64 ± 13 and 20.1 ± 5.9 µg/ml at 1.0 MIR, 64 ± 24 and 13.0 ± 2.8 µg/ml at return of spontaneous breathing, and 91 ± 4 and 11.0 ± 3.4 µg/ml when the swallowing reflex returned, respectively. The BIS value was significantly less in anesthetized horses compared to horses once swallowing returned (p=0.025). The BIS value was significantly correlated with the propofol Cp (r=−0.625, p=0.001). There was not a significant difference in the BIS values during the MIR multiples of propofol. The BIS was a useful indicator of awakening but did not indicate the degree of CNS depression during propofol-anesthesia in horses.

KEY WORDS: bispectral index (BIS), equine, propofol.

Anesthesia can be subjectively evaluated on the basis of the degree of hypnosis, analgesia, and muscle relaxation. Arousal from anesthesia-induced hypnosis is a dynamic process that is dependent upon the degree of corticocerebral depression and nociceptive inhibition (analgesia) [14, 19, 38]. Inadequate analgesia in the presence of a sufficiently intense surgical stimulus may lead to activation of central nervous system (CNS) areas that mediate arousal [10]. A direct measure of cortical activity could provide a means of differentiating hypnosis from analgesia during anesthesia. The bispectral index (BIS) is an electroencephalographic (EEG)-based technology for measurement of the hypnotic effects of anesthetic agents in human patients [16]. The BIS number is inversely related to the depth of anesthesia and is currently used clinically as a measure of hypnosis and responsiveness in humans undergoing anesthetic procedures [17, 33, 35].

Propofol is a popular intravenous anesthetic in humans, dogs and cats. Although chemically unrelated to the ultrashort-acting hypnotic anesthetics thiopental, methohexitol, and etomidate, propofol acts by a similar mechanism of action, i.e., it potentiates γ-aminobutyric acid (GABA)-induced chloride current by binding with the β-subunit of GABA_A receptors at both spinal and supraspinal sites [18]. Propofol is unlikely to replace current induction techniques in horses such as α2-adrenoceptor agonist-ketamine, benzodiazepine-ketamine and guaifenesin-thiopental [22, 23, 31]. However, recovery from anesthesia is uneventful and generally typified by good skeletal muscle strength and minimum ataxia in horses anesthetized with propofol for prolonged periods [4–7, 11, 26–29, 36, 37]. Furthermore, cardiovascular function is maintained in horses anesthetized with propofol and supplemental sedatives and analgesics during controlled ventilation [4, 37].

The purpose of the study reported here was to determine whether BIS could be used to assess the hypnotic effect of propofol in horses. The authors hypothesized that BIS values would be inversely and linearly related to plasma concentrations of propofol.

MATERIALS AND METHODS

Experimental animals: Five thoroughbred horses (4 mares and 1 gelding) aged 2 to 16 years (12.4 ± 5.9 years, mean ± SD) and weighing from 480 to 578 kg (531 ± 49 kg) were the subjects of this study. All horses had their right carotid arteries surgically repositioned to a subcutaneous location at least 1 month before beginning this study. The horses were judged to be in good to excellent health based upon the results of a physical examination, complete blood cell count and serum biochemical analysis. Food, but not water, was withheld from the horses for 12 hr before experiment. The horses were owned by the university and cared for according to the principles of the “Guide for the Care
and Use of Laboratory Animals” prepared by Rakuno Gakuen University. The Animal Care and Use Committee of Rakuno Gakuen University approved the study.

Experimental protocol: Each horse was anesthetized with propofol alone to determine the individual minimum infusion rate (MIR) in response to electrical stimulation as described below. Subsequently, each horse was sequentially infused with propofol for 20 min at 2.0, 1.5 and 1.0 times each animal’s predetermined propofol MIR. The BIS and other physiologic parameters were recorded after 20 min of equilibration at each propofol MIR multiple. Arterial blood samples were obtained at the end of each MIR multiple of propofol and after stopping the propofol infusion when the horse regained spontaneous breathing, a swallowing reflex and a standing position. Plasma concentrations of propofol in arterial blood samples were analyzed by high performance liquid chromatography (HPLC). The target plasma concentration required to prevent a positive response to surgical stimulation in 50% of the patients (Cp50) for propofol was determined from the plasma propofol concentration in arterial blood samples obtained when the MIR was identified.

Anesthesia: All horses were restrained by a swinging-door for induction to anesthesia, following the placement of a 14-gauge, 13.3-cm catheter (Angiocath, Becton Dickinson Japan, Inc., Tokyo, Japan) into the right jugular vein. The horses were anesthetized by administering 7 mg/kg IV of 1% propofol (Frezofol, Sawai Pharmaceutical Co., Osaka, Japan) at a constant rate of 2 mg/kg/min through the 14-gauge catheter. The swing-door was opened after the horse collapsed and the horse was rolled to lateral recumbency. The horses were orotracheally intubated, hoisted and repositioned in left lateral recumbency on a 20-cm thick foam pad. Additional padding was used to support the horses’ upper rear legs in a natural position. Anesthesia was maintained by infusing (Subrateck-3030, JMS Co., Hiroshima, Japan) propofol through the 14-gauge catheter. Propofol was infused at 0.2 mg/kg/min for 40 min before determination of the MIR. The endotracheal tube was connected to a large animal circle system that incorporated a ventilator (Mallard Aspect Medical Systems, Natick, MA, U.S.A.) and was placed and zeroed at the level of the mid-sternum.

Heart rate (beats/min), a base-apex electrocardiogram and arterial blood pressure were recorded by a multiparameter anesthetic monitoring system (DS-5300, Fukuda Denshi Co., Tokyo, Japan). Arterial blood samples were anaerobically collected from the 18-gauge catheter into heparin rinsed syringes. The partial pressure of arterial O2 (PaO2) and PaCO2 were determined by a blood gas analyzer (Rapidlab 348, Bayer Medical Co. Tokyo, Japan).

Determination of MIR and Cp50 of propofol: The MIR and Cp50 for propofol were determined as previously reported [30]. The MIR was determined by judging the horses response (gross purposeful movement) to an electrical stimulus applied to the upper oral mucosa after infusing propofol for 20 min while increasing or decreasing the infusion rate in 0.02 mg/kg/min steps from 0.2 mg/kg/min. The electrical stimulus (50 V, 5 Hz, 10 msec) was applied for 60 sec using an electrical stimulator (SEN3301, Nihon Kohden Co., Tokyo, Japan). Gross purposeful movement was defined as substantial movement of the head or extremities and did not include chewing, swallowing, or increases in respiratory rate or effort. Spontaneous movement before applying the stimulus was judged as a “positive” response. The absence of gross purposeful movement to electrical stimulation was judged as a “negative” response. The infusion rate of propofol was increased when the horse demonstrated a “positive” response to the stimulation, and the infusion rate was decreased when the horse demonstrated a “negative” response. Then, the horse was retested for the appropriate response after a 20 min of re-equilibration period. Testing continued until the infusion rate at which the horse demonstrated the change in response to the stimulation from “negative” to “positive” or from “positive” to “negative” in triplicate. Mean values were calculated between the infusion rate at which the horse demonstrated a “negative” response and the next lower infusion rate at which the horse demonstrated a “positive” response, or between the infusion rate at which the horse demonstrated a “positive” response and the next higher infusion rate at which the horse demonstrated a “negative” response. The MIR was considered to be the average of these three mean values.

The plasma concentration of propofol determined from arterial blood samples obtained just before the stimulation to determine MIR. The mean plasma propofol concentration (Cp50) was calculated between two samples obtained when the horse demonstrated a “negative” response and the next “positive” response or when the horse demonstrated a “positive” response and the next “negative” response. The Cp50 for each horse was determined as the average of these three mean values.

Measurement of BIS: The BIS value was measured every 5 sec for the last 5 min of each 20 min infusion period, and the average BIS value determined for the recording period at each propofol MIR multiple. The BIS value was determined using a BIS monitor with version 3,21 software (A-2000, Aspect Medical Systems, Natick, MA, U.S.A.) and was reported as a unitless whole numbers ranging from 0 and
100. Filters for elimination of electrical noise were set at 2 Hz of the low-frequency cutoff, at 50 Hz of the 50/60 Hz filter, and at 70 Hz of the high-frequency cutoff. The monitor required an initial skin electrode impedance < 7.5 kΩ and thereafter provided for continuous impedance checking with impedance < 2 kΩ at 16 Hz. High-frequency activity (70 to 110 Hz) was identified as electromyographic (EMG) activity measured in dB and was graphed in real time with the BIS. The monitor had automatic artifact detection and displayed a signal quality index (SQI) as a function of good epochs and suppressed epochs over the previous 120 epochs (61.5 sec) used for BIS calculation. The percentage of epochs in the past 63 sec in which the EEG signal was suppressed was expressed as the suppression ratio (SR). Burst suppression was identified as an isoelectric EEG for at least 1 sec and was indicated as an increased SR (i.e., SR > 1).

**Placement of electrodes for BIS measurement:** The use of needle electrodes as a feasible alternative to proprietary adhesive one-piece patch electrodes recommended by the BIS manufacturer has been validated in animals [18]. Subdermal spiral needle electrodes (TN204–035, Unique Medical Co., Tokyo, Japan) were used in the present study to avoid potential lead failure associated with poor skin contact and to allow each of three leads to be placed individually. A modified patient interface cable was connected to the BIS cable distal to the analog-to digital converter, and three spiral needle electrodes were attached to this cable. The three spiral needle electrodes were screwed into the subdermal space through skin at the following locations: the primary lead was placed on the midline of the frontal bone 2 cm caudal to the lateral canthus of the eyes; the secondary lead (ground) was placed 1 cm medial to the dorsal edge of the right orbital opening over the frontal bone; and the third lead was placed 5 cm caudal to the lateral canthus on the right zygomatic process of the temporal bone.

**Measurement of plasma propofol concentration:** Arterial blood samples (8 ml) collected from the 18-gauge catheter placed into the raised right carotid artery were mixed with heparin sodium (10 unit per 1 ml of blood). The blood samples were immediately centrifuged (1,580 × g for 15 min) to separate plasma. The plasma samples were stored at −80°C until HPLC analysis. Each plasma sample (200 µl) was mixed with 100% methanol (400 µl) and the top clear layer (300 µl) was obtained by centrifugation (1,580 × g for 15 min). Another 100% methanol (400 µl) was mixed with the precipitate and the top clear layer (300 µl) was also obtained by centrifugation. These 2 layers were combined in a tube as an extract. The extract (200 µl) was mixed with purified water (600 µl) and stored at −80°C until HPLC analysis.

The plasma concentration of propofol was determined by HPLC consisting of dual pump (DP-8020, Tosy, Tokyo, Japan), auto-sampler (AS-8020, Tosy), reversed-phase column (TSK-GEL ODS-80TS, Tosy), integration software (LC8020, Tosy), degasser (GASTORR 702, Eyela Co., Tokyo, Japan), and intelligent fluorescence detector (FP-2020 plus, JASCO Co., Tokyo, Japan). Propofol within each extract sample was separated with the reversed-phase column using a linear gradient mobile phase from methanol-water-ammonium acetate (24:75:94:0.06) to 100% methanol delivered at 1 ml/min and detected by the fluorescence detector set at 276 nm (excitation) and 310 nm (emission). The limit of detection for propofol was 0.05 µg/ml.

**Statistical analysis:** Data are reported as mean ± standard deviation (SD). Data from each MIR multiple were compared using one-way factorial ANOVA and Fisher’s PLSD test. The relationship between BIS values and the propofol plasma concentration from the MIR multiples and during recovery were analyzed using Pearson’s correlation coefficient (r). The level of significance was set at p<0.05.

**RESULTS**

**Induction and maintenance of anesthesia and recovery:** Rising of the head and transient stiffening of the neck muscles was observed in all horses during induction to anesthesia. Transition to lateral recumbency occurred at a propofol dose of 4.1 ± 0.3 mg/kg (3.7 to 4.3 mg/kg). Strong paddling lasting about one min was a common feature early after recumbency. All horses became quiet once the 7 mg/kg dose of propofol was completed. The horses were easily intubated, breathed spontaneously and maintained a brisk palpebral response. The horses developed tachycardia and hypertension during propofol infusion, and oxygenation and ventilation maintained by IPPV (Table 1). The time required to determine the MIR and BIS values was 200 ± 15 min.

Recovery from anesthesia was uneventful in all horses. The horses regained spontaneous breathing at 16 ± 6 min and swallowing reflex at 26 ± 9 min after the cessation of propofol infusion. The horses stood with support using head and tail ropes at 124 ± 44 min after the cessation of propofol infusion. One horse (16 years old, mare) showed mild ataxia after standing and the other four horses stood without ataxia.

**MIR and Cp50 of propofol:** The propofol was infused at a rate of 0.24 mg/kg/min in a younger gelding (2 years old) after the first 40 min period following induction to anesthesia because of a light anesthetic plane. The first MIR was determined at 77 ± 12 min after induction to anesthesia. The second and third MIR determinations were obtained at 100 ± 92 and 121 ± 18 min after induction to anesthesia. The average MIR and Cp50 were 0.21 ± 0.03 mg/kg/min and 17.5 ± 4.0 mg/ml (Fig. 1).

**Changes in the plasma concentration of propofol and BIS value:** Propofol infusion at rates of 2.0 MIR and 1.5 MIR produced stable anesthesia in all horses. The horses showed a light plane of anesthesia at 1.0 MIR. The plasma propofol concentrations were 26.7 ± 8.6 µg/ml at the end of the 20 min infusion of 2.0 MIR propofol, 22.9 ± 9.7 µg/ml at 1.5 MIR, 20.1 ± 5.9 µg/ml at 1.0 MIR, 13.0 ± 2.8 µg/ml when the horses began to breath spontaneously and 11.0 ± 2.9 µg/ml when the horses regained the swallowing reflex (plots in Fig. 2). The mean plasma propofol concentration was lower when the propofol infusion rate was decreased, but there
was no significant difference between the 2.0 MIR vs 1.5 MIR (p=0.118). The plasma propofol concentration significantly decreased after the cessation of propofol infusion (p=0.001) and it was significantly lower than 2.0 MIR and 1.5 MIR (p=0.003 and p=0.025, respectively) when horses regained spontaneous breathing. The propofol plasma concentration was significantly lower than 2.0 MIR, 1.5 MIR and 1.0 MIR when horses regained the swallowing reflex (p=0.002, p=0.012 and p=0.047, respectively). The propofol plasma concentration was 7.7 ± 4.4 µg/ml when the horses stood up. The apparent elimination half-life (t1/2) was estimated to be 63.0 ± 30.8 min from the terminal log-linear portion of the post-infusion decay of the propofol plasma concentration versus time (Fig. 3).

The BIS values were 59 ± 13 at 2.0 MIR, 63 ± 9 at 1.5 MIR, 64 ± 13 at 1.0 MIR, 64 ± 24 when horses regained spontaneous breathing and 91 ± 4 when horses regained swallowing reflex (columns in Fig. 2). The BIS values remained at approximately 60 to 70 during propofol infusion and increased when horses regained SPB, and SWR (p=0.025). The BIS recorded when horses regained SWR was significantly higher than those recorded at 2.0 MIR, 1.5 MIR, 1.0 MIR and SPB (p=0.005, p=0.011, p=0.012 and 0.010, respectively).

Fig. 1. Minimum infusion rate (MIR) of propofol and its corresponding plasma concentration (Cp50) in horses. Plots and error bars represent mean values and standard deviations (SD) for 5 horses. Vertical error bars represent SD of MIR (●) and Cp50 (●). Horizontal error bars represent SD of the times when horses demonstrated a change in response to the electrical stimulation (i.e. time of MIR determination).

Fig. 2. Bispectral index (BIS) values and plasma propofol concentrations at multiple MIR and when horses regained spontaneous breathing (SPB) and a swallowing reflex (SWR). Columns and error bars represent mean values and standard deviations (SD) of BIS values for 5 horses. Plots and error bars represent mean values and SD of plasma concentration of propofol. The BIS values remained at approximately 60 to 70 during propofol infusion and increased when horses regained SPB, and SWR (p=0.025). The BIS recorded when horses regained SWR was significantly higher than those recorded at 2.0 MIR, 1.5 MIR, 1.0 MIR and SPB (p=0.005, p=0.011, p=0.012 and 0.010, respectively).

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Table 1. Heart rate (HR), mean arterial blood pressure (MABP), respiratory rate (RR), and arterial partial pressure of oxygen (PaO2) and carbon dioxide (PaCO2) during the determination of minimum infusion rate (MIR) of propofol and during the infusion of propofol MIR multiple in horses

<table>
<thead>
<tr>
<th></th>
<th>40 min after induction</th>
<th>Determination of MIR</th>
<th>2.0MIR</th>
<th>1.5MIR</th>
<th>1.0MIR</th>
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</thead>
<tbody>
<tr>
<td>Number of data</td>
<td>5</td>
<td>15*</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>69 ± 27</td>
<td>74 ± 17</td>
<td>58 ± 14</td>
<td>55 ± 11</td>
<td>56 ± 13</td>
</tr>
<tr>
<td>MABP (mmHg)</td>
<td>153 ± 19</td>
<td>163 ± 17</td>
<td>153 ± 23</td>
<td>154 ± 26</td>
<td>153 ± 23</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>6</td>
<td>7.0 ± 1.6</td>
<td>6</td>
<td>6</td>
<td>6.6 ± 0.9</td>
</tr>
<tr>
<td>PaO2 (mmHg)</td>
<td>444 ± 91</td>
<td>493 ± 56</td>
<td>508 ± 19</td>
<td>502 ± 29</td>
<td>511 ± 23</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>47 ± 4</td>
<td>46 ± 5</td>
<td>45 ± 6</td>
<td>44 ± 7</td>
<td>46 ± 5</td>
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</table>

Data are expressed as mean ± standard deviation for 5 horses. * Three data recorded just before electrical stimulation that produced changes in response to the stimulation were obtained from each horse.

DISCUSSION

This is the first study to report the MIR of propofol in non-premedicated horses. The MIR and calculated Cp50 for propofol were 0.21 ± 0.03 mg/kg/min and 17.5 ± 4.0 mg/ml,
respectively. These values are greater than for those reported for horses administered xylazine [30]. As suspected, the BIS values correlated with the plasma propofol concentrations, however, there was not any significant difference in the BIS values during the maintenance phase of general anesthesia. The BIS values increased immediately as the horse regained a swallowing reflex.

The evaluation of BIS as an objective measure of hypnosis and hypnotic titration ideally requires comparison to a gold standard. Unfortunately, no such standard exists and it is well recognized that traditional end points for describing the stages and planes of anesthesia based on physical signs (Guedel signs: palpebral reflexes, eyeball position, and corneal reflexes, muscle tone) often fail to discriminate between degrees of hypnosis. Lack of movement in response to a noxious stimulus is used to define anesthetic potency for inhalant anesthetics and is also thought to predict the level of unconsciousness produced by these drugs [34]. Multiples of minimum alveolar concentration (MAC) for inhalation anesthetics is considered the most appropriate independent variable for objective BIS assessment in dogs and cats [12, 20–22]. Thus, we chose to evaluate multiples of the MIR for propofol in horses. It has been reported that the plasma propofol concentration reached almost stable at 15 to 20 min following changing infusion rate of propofol in horses [30]. The MIR concept, however, is not considered as useful as MAC because the pharmacokinetics of intravenous anesthetics can vary considerably among horses and the MIR is considered to be a time-dependent (context sensitive) variable [15]. Therefore, MIR values were initially determined for each individual horse and subsequent BIS measurements made during titration of propofol to an infusion rate expressed as a multiple of each horse’s MIR. Furthermore, we measured propofol plasma concentrations simultaneous with BIS recordings. This additional experimental step helped to minimize individual variability as a source of error and to establish the relationship between BIS and propofol MIR multiples in our horses.

The administration of propofol (4 mg/kg IV) to non-premedicated horses produces short-term anesthesia and rapid and smooth recovery, however, leg paddling and tachycardia (60 to 80 beats/min) during induction to anesthesia and lateral recumbency is common [22]. Transition to lateral recumbency was achieved at the propofol dose of 4.1 ± 0.3 mg/kg and strong paddling was a common feature early in the recumbent phase in the present study. Increased arterial blood pressure was also observed when the horses were tachycardic. Recovery from anesthesia was uneventful and similar to previous reports [4–7, 11, 26–29, 36, 37]. The plasma concentration of propofol declined rapidly after the cessation of propofol infusion and the estimated t1/2 of propofol in the present study (63.0 ± 30.8 min) was similar to that reported in a previous study in ponies (69.0 ± 8.0 min) [28]. The horses required 124 ± 44 min to stand after 200 ± 15 min infusion of propofol. The longer recovery time was likely due to the accumulation of propofol in peripheral tissues thereby influencing the rate of drug elimination and recovery.

The BIS is considered a good indicator of CNS depression in humans and cumulative deep hypnotic time (BIS < 45) has been shown to be an independent predictor of mor-

Table 2. Signal quality index (SQI), electromyografic (EMG) activity, and suppression ratio (SR) recorded at multiple minimum infusion rate (MIR) and when horses regained spontaneous breathing or the swallowing reflex

<table>
<thead>
<tr>
<th>MIR</th>
<th>SQI (%)</th>
<th>EMG (dB)</th>
<th>SR (%)</th>
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<tbody>
<tr>
<td>2.0 MIR</td>
<td>99.2 ± 9.8</td>
<td>44.6 ± 6.7</td>
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</tr>
<tr>
<td>1.5 MIR</td>
<td>84.5 ± 11.7</td>
<td>42.8 ± 7.3</td>
<td>0</td>
</tr>
<tr>
<td>1.0 MIR</td>
<td>84.6 ± 12.7</td>
<td>43.4 ± 6.9</td>
<td>0</td>
</tr>
<tr>
<td>Spontaneous breathing</td>
<td>81.4 ± 10.3</td>
<td>45.6 ± 5.7</td>
<td>0</td>
</tr>
<tr>
<td>Swallow reflex</td>
<td>53.8 ± 17.6*</td>
<td>63.6 ± 23.1</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard deviation for 5 horses. *Significantly different from 2.0 MIR, 1.5 MIR, 1.0 MIR and spontaneous breathing (p<0.001, p=0.001, p=0.001 and 0.002, respectively).

Fig. 3. Semilogarithmic plots of propofol plasma concentration versus time after the cessation of propofol infusion in 5 horses.

Fig. 4. Relationship between bispectral index (BIS) value and propofol plasma concentration in horses (n=25, r=-0.625, p=0.001).
tality [3, 17, 33]. The BIS values are greater than 90 in unmedicated awake humans while values smaller than 60 are a strong indication of unconsciousness and greater than 60 are suggestive of returning consciousness [16, 33]. The BIS value is also useful for predicting changes in the anesthetic depth of sevoflurane and isoflurane anesthesia in pigs, goats, dogs and cats and has been shown to be inversely and linearly correlated to the end tidal isoflurane and sevoflurane concentrations [2, 12, 20, 21, 24, 25]. Studies in detomidine (10 μg/kg IV) and butorphanol (10 μg/kg IV) premedicated horses followed by induction with ketamine (2.5 μg/kg IV) and diazepam (40 μg /kg IV) did not show a downward trend in the BIS during isoflurane anesthesia, although the BIS increased during recovery from anesthesia prior to movement [13]. These authors concluded that BIS was not a good indicator of the depth of anesthesia [13]. Similar observations have been made in human pediatric populations [32, 35]. We were unable to find significant difference in BIS values during propofol infusion between 2.0 and 1.0 MIR consistent with these earlier studies in horses and humans. On the other hand, the BIS values were significantly correlated with the plasma propofol concentration and significantly increased immediately when the horse regaining a swallowing reflex. It is thought that he BIS is a useful indicator of awakening but not a precise indicator of the degree of CNS depression in propofol-anesthetized horses.

The BIS values in our horses were somewhat higher and remained around 60 although all horses remained unconscious during propofol infusion. Exogenous catecholamine administration, EMG activity and burst suppression are known to increase BIS values in humans and may have contributed to our higher BIS values [1,8,9]. In addition burst suppression of the EEG has been reported at deep planes of anesthesia for most anesthetic agents and causes a paradoxical increase in the BIS value related to the monitor’s interpretation of preburst EEG patterns as high-frequency activity [9]. We did not observe burst suppression in our horses. On the other hand, tachycardia and hypertension did occur during anesthesia in our horses, suggesting that plasma levels of endogenous catecholamine or lighter planes of anesthesia may have occurred. Epinephrine (15 μg /kg IV) has been reported to increase heart rate (from 68 to 96 beats/min), arterial blood pressure (from 107/60 to 140/70 mmHg), and BIS values (from 63 to 76) in human patients during propofol infusion [1]. EMG activities in our horses were not substantial but somewhat higher than those recorded in horses anesthetized with isoflurane at an end-tidal concentration of 1.4% and 1.9% [13]. The contribution of endogenous catecholamine and EMG activity could have affected the BIS value in our horses and requires further investigation.

We conclude that BIS is a useful indicator of awakening but not a precise indicator of the degree of CNS depression in propofol-anesthetized horses. BIS values were significantly correlated with the propofol plasma concentrations in horses recovering from anesthesia, however, there was no relationship between BIS values and propofol plasma concentrations during the maintenance phase of anesthesia.

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