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RESEARCH ARTICLE

Determination of Propofol and Isoflurane Anesthesia Depth with Bispectral Index Monitorization in Dogs Undergoing Ovariohysterectomy Procedure

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Summary

In this study, 12 bitches were used to compare anesthetic depth by bispectral index (BIS) monitoring and vital parameters under propofol and isoflurane anesthesia. The animals were randomly divided into two groups (n=6) for ovariohysterectomy. All animals were premedicated with atropine sulphate (0.04 mg/kg, sc) and midazolam (0.3 mg/kg, iv). The induction of anesthesia was achieved by propofol (5 mg/kg, iv) in groups. General anesthesia was maintained with propofol (0.4 mg/kg/min.) in first group (PRO group) and 2% isoflurane in second group (ISO group). Non-invasive systolic (SAP), diastolic (DAP), mean arterial blood pressure (MAP), heart rate (HR), respiratory rate (RR), haemoglobin oxygen saturation (SpO_2) and BIS were measured before anesthesia (0 min, T0), maintenance of anesthesia (T5, T10, T15), end of anesthesia (T30) and additionally BIS also measured at 5 min after the terminating of anesthesia (T35). HR, RR, SAP and DAP did not significantly differ between groups. The MAP value did not show any significant difference within both groups. However, the MAP value detected on T5, T10, T15 and T30 was higher in PRO group than those detected in ISO group ($P<0.05$). The BIS values detected at all measured times in PRO and ISO groups were lower than those detected before anesthesia. The BIS value detected on T5 and T10 was higher in ISO group, whereas the value determined at T15 was higher in PRO group ($P<0.05$). In conclusion, it is suggested that bispectral index is a useful tool for monitoring depth of anesthesia in veterinary practice and total intravenous anesthesia with propofol may be used as an alternative to isoflurane anesthesia.

Keywords: *Bispectral Index, Dog, Isoflurane, Propofol*

Ovariohisterektomi Yapılan Köpeklerde Propofol ve İzofloran Anestezisinin Derinliğinin Bispektral İndeks Monitörizasyonu ile Belirlenmesi

Özet

Bu çalışmada, propofol ve izofluran anestezisinde anestezi derinliğinin bispektral indeks (BIS) ve vital parametrelerin izlenmesi ile karşılaştırılması için 12 adet dişi köpek kullanıldı. Hayvanlar ovariohisterektomi operasyonu için rastgele iki gruba bölündü (n=6 her grupta). Hayvanlar atropin sülfat (0.04 mg/kg, sc) ve midazolam (0.3 mg/kg, iv) ile premedike edildi. Anestezi indüksiyonu gruplarda propofol (5 mg/kg, iv) ile sağlandı. Genel anestezi ilk grupta propofol (PRO grubu) ile ikinci grupta %2 izofluran (ISO grubu) ile devam ettirildi. Non-invaziv sistolik (SAP), diastolik (DAP), ortalama arteriyel kan basıncı (MAP), nabız sayısı (HR), solunum sayısı (RR), hemoglobin oksijen saturasyonu (SpO_2) ve BIS anestezi öncesi (0. dakika, T0), anestezi boyunca (T5, T10, T15) ve anestezi sonunda (T30) ölçülürken BIS ölçümü anestezi sonlandırıldıktan 5 dakika sonra (T35) da ölçüldü. HR, RR, SAP ve DAP değerleri gruplar arasında farklılık göstermedi. MAP değeri her iki grup içinde istatiktiksel olarak farklılık oluşturmadı. Bununla birlikte, T5, T10, T15 ve T30 ölçüm zamanlarında PRO grubundaki MAP değerinin ISO grubuna göre yüksek olduğu belirlendi ($P<0.05$). PRO ve ISO gruplarında tüm ölçüm zamanlarındaki BIS değerlerinin anestezi öncesi değere göre daha düşük olduğu izlendi. BIS değerinin ISO grubunda T5 veT10 zamanında, PRO grubunda ise T15 zamanında yüksek olduğu gözlendi ($P<0.05$). Sonuç olarak, bispektral indeksin veteriner pratikte anestezi derinliğinin ölçümünde faydalı olduğu ve propofol ile yürütülen total intravenöz anestezinin izofluran anestezisine alternatif olarak kullanılabileceği ileri sürülmektedir.

Anahtar sözcükler: *Bispektral İndeks, Köpek, izofloran, Propofol*

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INTRODUCTION

Inhalation anesthetics are widely used in veterinary medicine and the basic advantage of these anesthetics is their independent hepatic and renal system elimination. Therefore, the biotransformation of inhalant anesthetics and morbidity and mortality is very low, as compared to other anesthetics [1,2].

The application of total intravenous anesthesia (TIVA), an alternative to inhalant anesthetics, has an increasing popularity with the advent of the infusion pump technology to induce anesthesia in small animal practice [3]. TIVA is a general anesthesia technique which is used to induction of anesthesia by intravenously given drugs and maintains the anesthesia [4]. Propofol (2,6-diisopropylphenol) is an intravenously using anesthetic agent in alkyl phenol family [4,5].

Recently, bispectral index (BIS) monitoring has been developed to utilize the depth of anesthesia by estimating electroencephalogram (EEG) signals [1,6,7]. BIS, numerical value of EEG derivative is used for evaluation of depression of central nervous system (CNS) in human medicine. The depressive effect of sedative and anesthetic agents on CNS in human is correlated to BIS [8]. It has been reported that BIS is used for the evaluation of CNS depression in dogs anesthetized with isoflurane, sevoflurane or propofol [6,9,10], however there are limited reports in veterinary medicine. It has been indicated that the frequency of nociceptive stimuli and the sensitivity of anesthetics affects the BIS value [11]. Therefore, this study was designed to compare anesthetic depth by BIS monitoring and vital parameters in ovariohysterectomized dogs anesthetized by propofol and isoflurane.

MATERIAL and METHODS

All procedures were approved by local ethical committee of Experimental Animal Research Center, Afyon Kocatepe University (Reference No: 65-11, Date: 03.10.2011) and the approval of the owners were also received.

Animals

In this study, 12 bitches which referred to animal hospital for elective ovariohysterectomy, in different breeds, aged between 1 and 6, weighing at 22±4 kg were used. Clinical aspect, hematologic and biochemical parameters of the animals were examined. Dogs having abnormal hematologic and biochemical parameters were excluded from the study. The animals were not allowed to eat 12 hours before the surgery, however water intake was allowed until four hours prior to ovariohysterectomy.

Anesthesia

The dogs were randomly divided into two groups (n=6). The left *v. cephalica accessoria* were catheterized in all dogs using a 20 gauge catheter for administration of intravenously given fluids in both groups. An additional 20 gauge catheter was placed in the right *v. cephalica accessoria* for infusion of anesthetics.

Atropine sulphate (Atropin 2%, Vetaş, Turkey) at 0.04 mg/kg was administered subcutaneously (sc) approximately 45 min before general anesthesia. The dogs were premedicated with midazolam (Dormicum, Roche, Turkey) at a dose of 0.3 mg/kg intravenously. When the sedation was achieved, the induction of anesthesia in both groups was performed with propofol (Propofol 1%, Fresenius Kabi, Germany) which was slowly administered at a dose of 5 mg/kg intravenously by manual injection over a period of about 60 sec to effect. General anesthesia was induced with the infusion pump (Medifusion DI-2000, Korea) of propofol at a dose of 0.4 mg/kg/min in the first group (PRO group). Immediately after tracheal intubation, the dogs in second group (ISO group) were connected to anesthesia machine (SMS 2000 Classic Anesthesia System with Vent-V Automatic Ventilator. SMS, Turkey). General anesthesia was maintained with 2% isoflurane (Forane Liquid, Abbott Company USA). All general anesthesia procedure was ended after 30 min in both groups. The dogs in group ISO was extubated at the end of the anesthesia. During general anesthesia, lactated ringers solution was infused at a dose of 10 ml/kg per hour in both groups. Moreover, $PaCO_2$ and pH values were stabilized between 35-45 mmHg and 7.35-7.45, respectively in groups (Gastat Mini, Japan).

Surgery

Ovariohysterectomy was performed by a median line laparatomy and ended in 30 min in both groups. The induction of anesthesia in groups was terminated after the measurement of last data at the end of the surgery. However, the study was ended after the measurement of BIS that was performed 5 min after ending of infusion in group PRO, and 5 min after terminating of induction of anesthesia in group ISO.

Skin incision was performed in 5 min after the induction of general anesthesia. Ovaries and uterine body were removed in a routine manner. The closure of incision line was achieved in approximately 25 min after the skin incision and the anesthesia was terminated. Dexketoprofen Trometamol (Arveles, UFSA, Turkey) at a dose of 1 mg/kg was administered intravenously to control prophylactic postoperative pain in both groups.

Measuring of Vital Parameters

Before premedication (0 min, T0) and every 5 min during anesthesia (T5, T10, T15) and end of anesthesia (T30), non-invasive systolic (SAP), diastolic (DAP), mean arterial blood pressure (MAP), heart rate (HR), respiratory rate (RR), haemoglobin oxygen saturation (SpO_2) were recorded in both groups using a multi-channel monitor

(KMA PETAS 800 multi-channel monitor, PETAS, Turkey). However, the RR in ISO group was 14 per minute due to mechanic ventilation. In PRO group, ovariohysterectomy was performed under spontaneous ventilation; thereby RR per minute was recorded. During SpO_2 measurement, SpO_2 probe was placed to the tongue of dogs and the probe was connected to the monitor for recording the data.

For ECG monitoring, ECG electrodes were attached to all four extremities of dogs and, ECG tracings from lead II were monitored and recorded on the multi-channel monitor.

Measurement of BIS

Before general anesthesia, frontal-temporal part of cranium was shaved and the skin was defatted by ether. BIS electrodes using in human medicine were adapted to the dogs. The sensors for assessing the BIS (Quatro, Aspect Medical Systems International B.V., Netherlands) were attached by 5 electrodes in a frontal-temporal configuration. Three electrodes were connected to frontal area, whereas electrode 4 and 5 was placed into temporal area in front of left and right ear, respectively. Before premedication (0 min, T0), every 5 min during anesthesia (T5, T10, T15) and end of anesthesia (T30) and 5 min after the terminating of anesthesia (T35), BIS activity was continuously recorded by the BIS monitor (Bispectral Index Monitor, A-2000 PIN: 185-0070, BIS XP Platform Aspect Medical Systems Inc., USA) following the monitor-sensor connection.

Statistical analysis

Data were analyzed with the SPSS 16.0 (SPSS Inc, for Windows) software package. A one-way ANOVA test was used to compare the groups. Test significance levels within and between groups were checked using Duncan's test. Descriptive results are expressed as means ± standard deviation. For all comparative tests, a value of $P<0.05$ was considered significant.

RESULTS

The values of HR, RR, SAP, DAP, MAP, SpO_2 and BIS in group PRO and ISO are given in *Table 1*.

The RR did not differ significantly at measured times in both groups. The RR rate was stable in ISO group due to mechanic ventilation, whereas it did not show any significant difference at measured times in PRO group.

The SAP and DAP in group PRO and ISO showed no significant changes at measured times.

The MAP in group ISO decreased (P<0.05) at T5, T10, T15 and T30, as compared to T0 (P<0.05) *(Table 1, Fig. 1)*. However, no decrement was observed in PRO group.

Oxygen saturation exhibited normal values in both PRO and ISO groups.

The BIS values detected at all measured times in PRO and ISO groups were lower than those detected before anesthesia. When the BIS values were compared between groups, it was observed that the value detected on T5 was higher in ISO group, whereas the value determined at T15 was higher in PRO group (P<0.05) *(Table 1, Fig. 2)*.

DISCUSSION

The present study clearly demonstrated the application of BIS monitoring in ovariohysterectomized dogs

Table1. *Heart rate, respiratory rate, systolic, diastolic and mean arterial blood pressures, SpO_2 and BIS values in propofol and isoflurane groups. (Mean ± SD) (n=6)*

Tablo 1. *Propofol ve izofluran gruplarında kalp frekansı, solunum sayısı, sistolik, diastolik ve ortalama arteriyal kan basınc ile SpO_2 ve BİS değerleri. (Ort ± SD) (n=6)*

Time (min)	Group	HR Pulse/min	RR	SAP (mmHg)	DAP (mmHg)	MAP (mmHg)	SpO_2 %	BIS
T0	PRO ISO	120.3±15.0 115.6±14.3	24.8±2.2 26±4.0	162.5±14.4 153.1±20.6	92.1±17.6 85.1±20.4	130.8±11.8^{a} 110.1±23.0	98.1±0.7 98.1±0.7	100±0.0^{a} 100±0.0^{a}
T5	PRO ISO	133±1.6 125±7.6	21.1±3.8 14±0.0	160.6±7.8 139.3±15.1	86.6±14.5 71.1±15.8	123.5±7.4^{ab*} 94.8±9.7	97.8±0.9 98.1±0.4	59.3±14.9^{cd*} 70±13.2^{bc}
T10	PRO ISO	129.5±7.6 124.6±18.3	21.1±3.6 14±0.0	159.8±10.5 135.3±18.8	86.6±20.7 72.6±21.3	123.8±11.4^{ab*} 97.5±15.1	97.3±0.8 97.1±0.7	56.3±3.6^{d} 59.5±13.7^{cd}
T15	PRO ISO	131.3±8.7 121.8±12.2	19.3±2.4 14±0.0	163.8±14.6 139.1±25.1	88.5±19.6 74.6±15.6	121.5±10.5^{abc*} 102.5±23.8	98±0.8 98±0.8	56.1±7.5^{d*} 47.5±10.6^{de}
T30	PRO ISO	130.5±15.8 119.3±13.9	21.5±3.8 14±0.0	148.1±26.6 139.6±21.8	91.3±19.1 80.1±20.2	117.3±16.7^{abcd*} 104.3±15.6	97.6±0.8 97.5±0.5	51.3±10.1^{de} 42.5±9.2^{e}
T35	PRO ISO							75.0±3.7^{b} 77.6±8.2^{b}

** There is significant difference between groups (P<0.05). The values with different letters in the same column have significant difference (P<0.05)*
HR: *heart rate,* ***RR:*** *respiratory rate,* ***SAP:*** *systolic arterial blood pressure,* ***DAP:*** *diastolic arterial blood pressure,* ***MAP:*** *mean arterial blood pressure,* ***SpO_2:*** *haemoglobin oxygen saturation,* ***BIS:*** *bispecteral index*

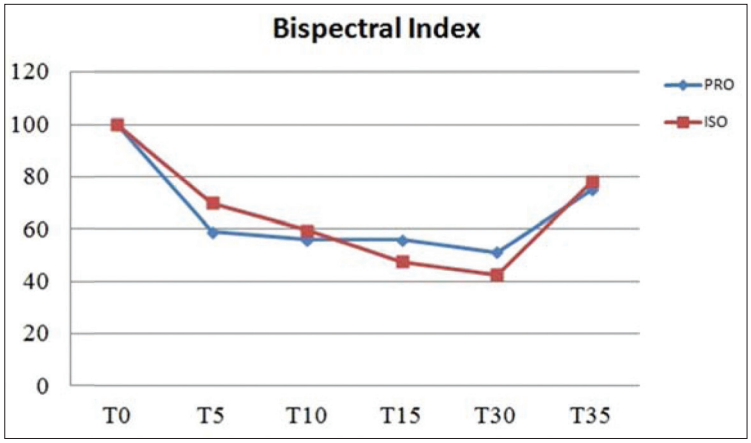
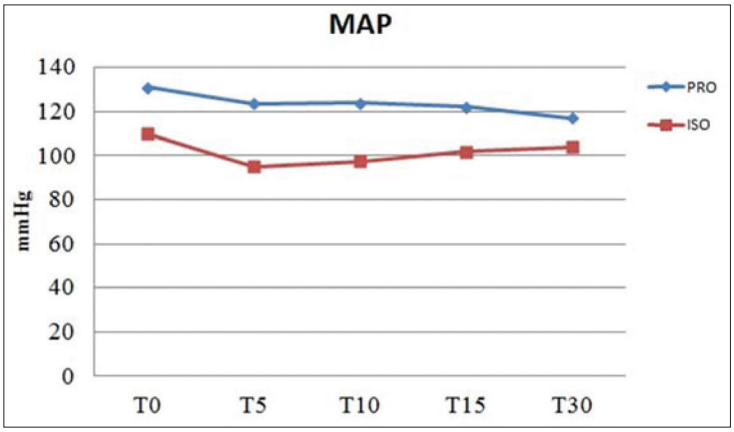


Fig 1. BIS value of dogs in PRO and ISO groups

Şekil 1. PRO ve ISO grubu köpeklerde BİS değerleri

Fig 2. Mean arterial pressure (MAP) of dogs in PRO and ISO groups

Şekil 2. PRO ve ISO grubu köpeklerde ortalama arteriyel kan basıncı



anesthetized with propofol and isoflurane anesthesia. In human medicine, bispectral monitoring has been used to quantify the degree of hypnosis as a result of amount of used anesthetic [1,12] and is also described in dogs and other species [1,8,13-15]. In the human, a BIS value of 90 or higher indicates wakefulness, while a score under 50 is ideal for surgical procedures [16]. Compagnol et al.[17] reported that BIS value was 66, 63, and 47 under 1.5%, 2.3% and 3% isoflurane anesthesia, respectively and a weak correlation was evident between BIS value and the concentration of anesthetic drug. Moreover, Mattos-Junior et al.[1] studied BIS values during ovariohysterectomy operation under halothane, isoflurane and sevoflurane anesthesia in dogs premedicated with acepromazine or acepromazine + meperidine. In their study, BIS values were measured 15 min after premedication, 10 min after general anesthesia, during ligation of pedicle of right ovary, closure of muscles, closure of skin and 10 min after termination of general anesthesia. They also reported that total anesthesia was maintained longer than 60 min and BIS value in halothane group was lower than those in isoflurane group and higher than those in sevoflurane group. In this study, it was found that MAP and BIS values detected at except T5 in ISO group was lower than those in PRO group.

Ibrahim et al.[12] indicated that the measurement of BIS was more effective to detect the level of hypnosis in patients sedated with propofol as compared to isoflurane. Hatshbach et al.[18] compared the BIS value in ovariohysterectomized dogs under propofol anesthesia or propofol anesthesia combined with remifentanyl and the BIS value was found between 73 and 79. In the present study, BIS value throughout the general anesthesia in PRO group was measured between 51 and 59. In PRO and ISO groups, premedication was performed by midazolam and induction was conducted by propofol, however TIVA was maintained by propofol at a dose of 0.4 mg/kg per min in PRO group.

Propofol which is characterized by tranquilising and fast anesthesia induction has been reported to have short duration of recovery when it is used as constant rate infusion (CRI) for maintenance of anesthesia and decreases HR and MAP under therapeutic dose range [4]. In current study, SAP and DAP values in PRO and ISO groups were compared, no significant difference was observed. However, it was determined that MAP value detected during premedication in PRO group was higher than those detected during other measured times but MAP value decreased all measured times in ISO group. Unlike Suarez et al.[4] reported a decrement in HR, it was observed that HR value did not show any significant difference between groups. The researchers also indicated that the infusion of propofol and alphaxolane had adequate anesthesia for ovariohysterectomy in dogs premedicated with acepromazine and morphine however, ventilatory support

was needed due to long-term hypoventilation caused by using of these anesthetic agents [4]. In the present study, all ovariohysterectomie procedure was ended in 30 min and SpO_2 value in PRO group which TIVA was used, was in normal range throughout the surgery. Therefore, ventilatory support was not needed in this study.

Mattos-Junior et al.[1] stated that a change in anesthetic depth was based on ocular movements and the presence or absence of palpebral reflexes and slow intravenous infusion of Fentanyl bolus was administered, when HR and MAP value increased at 20%. In this study, reflex was disappeared after the induction of anesthesia and no narcotic agent was used. Moreover, the depth of surgical anesthesia was clearly achieved in both groups, since the BIS values confirmed this observation. Furthermore, increasing salivation, vomiting and excitation findings were in agreement with Matos-Junior et al.[1].

BIS is a quantitative method to detect the depressive effect of anesthetics such as sevoflurane, isoflurane or propofol on central nervous system (CNS) in dog [6,9,10,19]. However, BIS may not reflect changes in depth of anesthesia in dogs anesthetized with isoflurane in the absence of noxious stimulation [6,17]. In current study, the depth of anesthesia changed parallel to BIS and MAP values during surgery.

Yamashita et al.[20] reported that BIS monitoring was an indicator to detect intraoperative awareness but did not show the degree of CNS depression. In this study, BIS value decreased parallel to depth of anesthesia and no reflex response was present related to anesthesia either in dogs of ISO group or PRO group during surgical procedure.

In a study which was compared the propofol and isoflurane anesthesia without any surgical approach in rabbits premedicated with dexmedetomidin by Saritas et al.[21], BIS value was found to parallel to MAP and HR values but depth of anesthesia was higher in propofol group. Moreover, it was emphasized that general anesthesia in isoflurane group induced by glove-mask method altered the depth of anesthesia.

It was concluded that BIS monitorization should be taken into consideration together with vital parameters, especially MAP for monitoring of anesthetic depth. Moreover, it is suggested that total intravenous anesthesia with propofol may be used as an alternative to isoflurane anesthesia.

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