Effect of isoflurane and sevoflurane anesthesia on coagulation parameters in dogs**

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ABSTRACT

The aim of this study was to investigate the effect of isoflurane (ISO) and sevoflurane (SEVO) anesthesia on coagulation parameters in dogs. A total of 12 dogs were used in the study in two groups as ISO (n=6) and SEVO (n=6), which were brought to the clinic for ovariohysterectomy. Premedication was performed by the intravenous administration of 0.3 mg/kg midazolam, followed by 5 mg/kg intravenous bolus propofol infusion. This was followed by 1.5% ISO administration in the ISO group and 2% sevoflurane administration in the SEVO group for anesthesia maintenance. Before anesthesia, prothrombin time (PT), active partial thromboplastin time (APTT), thrombin time (TT), and fibrinogen (FIB) level were measured at the 0th minute before anesthesia, at the 15th and 30th minutes during anesthesia, and at the 0th minute and the 1st hour after anesthesia. It was observed that the changes in TT, PT, APTT, and FIB level with time were not significant in the ISO and SEVO groups. It was determined that the changes in TT between the measurements in groups at the 30th minute during anesthesia and 0th minute after anesthesia were statistically significant (P<0.05).

Key words: Coagulation parameters, Dogs, Isoflurane, Sevoflurane.

INTRODUCTION

Inhalation anesthetics are widely used in clinical practice Steffey (1996). Inhalation anesthesia needs specific equipments and which may be possible under hospital conditions Saibaba et al (2016). These are considered to be unique because of the large number of anesthetic drugs discharged through the lungs. The desired depth of anesthesia develops rapidly. Special apparatuses are required for the use of anesthetics. Approximately 20 anesthetic agents are in use for more than 150 years. Fewer than 10 of these have found widespread use in clinical practice, of these, 5 in particular are clinically prescribed in North America. Isoflurane (ISO) and sevoflurane (SEVO) have been found to be widely used together Steffey (1996).

Inhalation anesthesia is an anesthetic method used to provide general anesthesia. It is easily used in all species, particularly in birds, reptiles, pets, and wild animals Steffey (1996), Skarda et al (1996) and Saritas (2014).

Evaluation of the thrombocyte counts and coagulation profile from citrate plasma samples at the laboratory level is recommended in diagnosing hemorrhagic diseases, in addition to the clinical determination of the duration of buccal mucosal bleeding. Determination of prothrombin time (PT), active partial thromboplastin time (APTT), and fibrinogen (FIB) and antithrombin III levels is required in the coagulation profile Kennerman and Kaya (2005). PT, is a test that commonly used to indicate of drugs for measuring the extrinsic blood coagulation system Gargy and Singla (2015). Determination of the duration of buccal mucosal bleeding, although applied at the clinical level, is not considered as an important indicator in diagnosing bleeding disorders. Pathological changes in one or more of a system composed of vascular wall, coagulation proteins, and thrombocytes are involved in the development of bleeding disorders. Thrombocyte count is accepted as an important diagnostic criterion that can be used at the clinical level for bleeding diseases Kennerman and Kaya (2005).

This study aimed to compare the effects of ISO and SEVO anesthesia on coagulation parameters in ovariohysterectomy (OHE) operation in dogs.

MATERIALS AND METHODS

Anesthetic interventions were carried out using an automatic anesthetic device operated by a closed system with automatic ventilation and digital control, double vaporizer, and sodalime SMS (SMS 2000 Vent-V Model). Coagulation parameters were measured using MT-TC TOKRA TURKEY device.

Animals: Twelve dogs, aged 1–4 years, which were brought to the Veterinary Health Practice and Research Center, Afyon Kocatepe University, Turkey, for OHE, were included in this study. The study started with the permission of the local ethics committee of the Experimental Animal Experiments and

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Application Center of Afyon Kocatepe University (dated 25.02.2016 and reference number AKÜ HADYEK-26-16).

The cases were divided into two groups: ISO (n = 6) and SEVO (n = 6). Midazolam (Dormicum, Roche, Switzerland) was administered intravenously at a dose of 0.3 mg/kg. Anesthesia induction was conducted by slowly injecting propofol intravenously at a dose of 6–7 mg/kg. Immediately, orotracheal intubation was performed using an appropriate endotracheal tube. For intubation, balloon-type disposable endotracheal tubes were used with an internal diameter of 7.0–9.0 mm according to the size of animal. The patient connector of the anesthesia device was attached to the endotracheal tube placed in the trachea of animal followed by mechanical ventilation. Spontaneous respiration was depressed with positive-pressure ventilation 14 times per minute, and ventilation was performed 14 times per minute with a tidal volume of 15 mL/kg. During the anesthesia, the heart rate and respiratory counts were monitored and recorded (Peta® KMA 800 Multichannel Monitor, Turkey).

Twelve cases brought to the clinic for OHE were included in the study. All of these cases were found to have good overall health status. After general anesthesia, routine OHE was performed with median laparotomy under aseptic conditions. Operative procedures for all cases were performed by the same investigator who was an expert in the field. All of the operations were completed within approximately 25–30 min. Desketooprofen tromamol (Arveles 25 mg / ml amp.) was applied at a dose of 1 mg / kg i.v when needed as a postoperative analgesic. All of these cases were found to have physiological limits.

Measurement of coagulation parameters: Venous blood samples were taken from the citrated tubes at the 0th minute (Z₀) before anesthesia, 15th (Z₁) and 30th (Z₂) minutes during general anesthesia, and 0th (Z₀) and 60th (Z₄) minute after anesthesia. TT, PT, APTT, and FIB level were measured using a coagulometer (MT-TC Coagulometer, Tokra, Turkey).

Statistical analysis: Repeated-measures analysis of variance was used to determine the differences in clotting factors over time within the group. The independent-samples t test was used to determine the differences between the groups. Data were shown as mean value ±standard deviation. The significance level of P<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The changes in TT, PT, APTT, and FIB level with time were not found to be significant in the ISO and SEVO groups. The difference between the Z₀ and Z₄ measurements of TT was statistically significant (P<0.05); however, TT levels in both groups were within the physiological limits (Table 1).

During anesthesia, heart and respiratory rates of all animals in the ISO and SEVO groups remained within normal physiological limits.

When TT values are found to be high, hereditary causes such as afibrinogenemia, hypofibrinogenemia, and dysfibrinogenemia, as well as acquired conditions such as heparin therapy or contamination and disseminated intravascular coagulation should be investigated Seligsohn and Coller (2001). It is equivalent to APTT but less reliable. It measures the conversion of fibrinogen into fibrin Aktas et al (2005). Van Lue et al. (2007) reported that the TT level in venous blood samples was 11.34 ± 1.49 g/L.

In this study, the decreases in TT values in Z₂ and Z₃ in the ISO group were found to be statistically significant compared with the TT values in Z₀ in the ISO and SEVO groups (P<0.05).

Regarding the TT values in both groups, the differences between intraoperative and postoperative values were statistically significant. However, these changes were within the reference values, supporting the findings of Van Lue et al. (2007).

Munro et al. (1997) conducted a study on humans and reported that the thrombocyte counts were less than 1.1%, PT increased 0.4%–4.8% and APTT increased 0%–15.6% in preoperative tests conducted on asymptomatic individuals.

<table>
<thead>
<tr>
<th>Time</th>
<th>Group</th>
<th>TT (s)</th>
<th>PT (s)</th>
<th>APTT (s)</th>
<th>Fibrinogen (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z₀</td>
<td>ISO</td>
<td>9.36± 2.4</td>
<td>12.13± 2.5</td>
<td>14.25± 4.4</td>
<td>532.9± 194.3</td>
</tr>
<tr>
<td></td>
<td>SEVO</td>
<td>11.2± 1.7</td>
<td>12.1± 5.1</td>
<td>13.3± 5.1</td>
<td>439.6± 145.3</td>
</tr>
<tr>
<td>Z₁</td>
<td>ISO</td>
<td>7.20± 1.5</td>
<td>12.33± 3.2</td>
<td>15.55± 3.4</td>
<td>361.3± 185.3</td>
</tr>
<tr>
<td></td>
<td>SEVO</td>
<td>8.5± 3.5</td>
<td>12.01± 5</td>
<td>14.6± 6.1</td>
<td>333± 141.7</td>
</tr>
<tr>
<td>Z₂</td>
<td>ISO</td>
<td>8.20±1.9</td>
<td>12.23± 1.9</td>
<td>13.21± 1.3</td>
<td>407± 216.2</td>
</tr>
<tr>
<td></td>
<td>SEVO</td>
<td>10.9± 1.2</td>
<td>9.5± 4.2</td>
<td>13.7± 5.1</td>
<td>359.7± 151.9</td>
</tr>
<tr>
<td>Z₃</td>
<td>ISO</td>
<td>6.53±1.5*</td>
<td>13.08± 4.6</td>
<td>13.36± 4.7</td>
<td>479.7± 124.7</td>
</tr>
<tr>
<td></td>
<td>SEVO</td>
<td>9.4± 1.5</td>
<td>10.9± 2.2</td>
<td>8.4± 6.7</td>
<td>396± 123.5</td>
</tr>
<tr>
<td>Z₄</td>
<td>ISO</td>
<td>7.6± 1.3</td>
<td>12.38± 2.2</td>
<td>11.16± 3.6</td>
<td>401.6± 55.3</td>
</tr>
<tr>
<td></td>
<td>SEVO</td>
<td>7.2± 2.4</td>
<td>11.3± 1.8</td>
<td>11.5± 5.9</td>
<td>324.8± 104.5</td>
</tr>
</tbody>
</table>

Z₀, 0th minute before anesthesia; Z₁, 15th minute under anesthesia; Z₂, 30th minute under anesthesia; Z₃, 0th minute after anesthesia; Z₄, 60th minute after anesthesia. The differences between groups are statistically significant (P<0.05).
PT is used for a mix of initial tissue factors and phospholipids. It is measured as a parameter to evaluate the extrinsic coagulation pathways Brainard (2015). In this test, the time from the extrinsic pathway to fibrin clot formation is measured by adding plasma calcium and prothromboplastin (tissue factor). If the levels of factor VII found in the extrinsic pathway, factors X and V found in the common pathway, prothrombin, and fibrinogen are normal, PT is found to be normal. PT elongation is not observed until the aforementioned values drop below 10% of the normal. PT elongation is seen only in inherited factor VII deficiency. It is also seen in liver diseases, vitamin K deficiency, and the use of inhibitors against factor VII Roger and Bithell (1999). Chohan et al. (2011) reported that the initial value of PT was 7.8 ± 0.8 (6.7–9.1) s. Van Lue et al. (2007) applied general anesthesia using ISO following a minor surgery and propofol induction on dogs and determined the PT values of blood samples as 7.23 ± 0.70 s.

The PT values in the ISO and SEVO groups were compared in this study, and no statistically significant differences were found ($P > 0.05$).

In the present study, it was found that the initial PT values did not significantly change compared with the intraoperative and postoperative values, in line with the literature.

APTT is used to measure intrinsic factors (factors XII, XI, IX, and VIII) and the common coagulation pathway Chohan et al. (2011). During APTT measurement, the time from the intrinsic pathway to the fibrin clot formation is measured by adding an activator such as phospholipids, calcium, and ellagic acid or kaolin to the plasma. APTT elongation is not seen until the level of clotting factors drops as low as 15%–30% below normal. APTT prolongation is seen in the absence of inherited factors VIII, IX, XI, or XII. APTT is prolonged in the presence of specific or nonspecific inhibitors against the aforementioned factors, following heparin therapy, and in the presence of antiphospholipid antibodies. Rare hereditary causes such as the deficiency of factor XII, prekallikrein, and HMWK should be considered in patients with a history of prolonged APTT without bleeding. The prolonged TT in patients with high APTT values supports the presence of heparin. Factor XIII may be lacking in patients with normal PT and APTT values and a history of serious bleeding Turgut et al. (2000) Sencan (2004). Chohan et al. (2011) found the APTT level in healthy dogs to be 11.2 ± 0.6 s. Van Lue et al. (2007) reported the APTT level as 13.85 ± 5.12 s.

The differences between the APTT values in the ISO and SEVO groups were not statistically significant ($P > 0.05$).

Fibrinogen forms in the parenchyma cells of the liver. It is a soluble plasma protein. It is transformed into a nonsoluble fibrin. It is not found in the serum. Its molecular
weight is 380,000 D Yilmaz, (2000). TT depends on the level of blood fibrinogen and is determined by measuring fibrin formation in the common pathway Brainard (2015). Van Lue et al. (2007) found the fibrinogen levels in venous blood samples as 2.23 ± 0.94 g/L. They also reported decreased arterial fibrinogen levels and prolonged TT.

In this study, no statistical differences were found between the fibrinogen values in the ISO and SEVO groups (P > 0.05).

The results in both groups were within normal limits in the present study. The combination of two anesthetics did not have an adverse effect on the plasminogen level, and these data were in parallel with the literature. The TT values were also within normal limits. In this respect, it differs from the mentioned report. This suggests that the use of acepromazine had an effect in premedication in the study.

Amarpal et al. (1999) demonstrated that ketamine given epidurally to dogs before fracture repair decreased post-operative pain for up to 15 days as compared to dogs receiving saline. Epidurally administered opioids have been shown to provide analgesia for both visceral and somatic pain that can persist in the dog for 10-24 hours Ram et al (2014). In this study, no statistically significant differences were found between the two groups. However, the preoperative, intraoperative, and postoperative findings of this study were found to be higher compared with the aforementioned two studies. The data suggested that the midazolam–propofol–ISO and midazolam–propofol–SEVO anesthesia had no negative effects on the coagulation parameters.

Therefore, it was concluded that ISO and SEVO anesthesia applied during OHE in this study had no adverse effect on the coagulation parameters and hence they could be used safely in patients with coagulation disorders in clinical practice. Studies with more detailed parameters should be conducted to validate the findings of this study.

REFERENCES


