CLINICAL, BIOCHEMICAL AND HAEMODYNAMIC EFFECTS OF THE INTRATHECAL KETAMINE FOR OVARIOHYSTERECTOMY IN BITCHES

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Abstract

The purpose of the study was to evaluate the effects of intrathecal (IT) ketamine HCl anesthesia on clinical values and some haemodynamic and biochemical parameters in bitches. An IT ketamine (10 mg/kg) was administered to 30 bitches with a spinal needle (18-22 G) in the lumbosacral space. The haemodynamic parameters were monitored and some biochemical values were assessed (blood gas, oxygen-haemoglobin, and electrolyte levels). The length and depth of anaesthesia was determined with a pinprick test, touching to the ligamenta lata uteri and incision. Anaesthesia took effect in less than 1 min in all dogs and has lasted an average of 95.9 min. In spite of the fact that the dogs recovered completely from the effects of dissociative anaesthesia, the anaesthesia in the some extremities was observed to be continued for an average of 17 min longer. The use of IT ketamine HCl raised blood pressure and did not have a depressive effect on respiratory and cardiac functions. It was concluded that ketamine HCl could be an appropriate alternative for ovariohysterectomy operations in bitches when the quality of the anaesthesia and the prevention of bradycardia and hypotension are considered.

Key words: bitches, anaesthesia, ketamine, ovariohysterectomy.

Intrathecal (IT) anaesthesia is a simple and more economic approach to anaesthesia that can be administered without the equipment and devices required for inhalation anaesthesia (16). Ketamine is a powerful analgesic that has become popular for short surgical procedures (2, 25). It results in dissociative anaesthesia characterised by deep analgesia and amnesia by revealing the connection between the thalamocortical center and the limbic system (8, 10, 12, 15, 22, 25). When it is administered intrathecally, it achieves a sensory and motor blockage (8, 23). Its mechanism of action is explained as antagonising the N methyl-D aspartate (NMDA) receptor in the dorsal horn of the spinal cord (18, 22, 23, 26) and reducing depolarisation by blocking sodium channels in a similar way to that of local anaesthetics (8, 13, 15, 17, 18, 23). Hypotension has been also reported to develop when it is administered as a local anaesthetic in the same way (8, 15, 23). In addition, hypotension appears to be beneficial to the respiratory system because of its bronchodilator effect (12, 15, 22). However, due to the fact that it induces local anaesthesia, it could be claimed that it is less desirable than local anaesthetics in terms of the length and quality of the anaesthetic effect (8, 13).

Intrathecal and epidural anesthesia are the techniques blocking the nerves in the subarachnoid space. The epidural dose is higher than that of IT ketamine HCl, because of systemic absorption in the epidural adipose tissue. Nerve blockage with the IT injection is much more rapid than an epidural injection. Therefore, it requires a smaller dose of anaesthetic administration because of its neurotoxicity and systemic effects (11).

Intrathecal administration of ketamine has been studied in both animals and humans (4, 8, 9). Studies on its neurotoxicity depending on preservative-free ketamine in rats, rabbits, and primates indicated the lack of neurotoxicity on the spinal cord (4, 9, 19). However, in spite of an available considerate clinical experience, there is still a controversy in both human and animal literature regarding the safety of ketamine for either IT or epidural administration (26).

Although the complications of spinal anaesthesia are generally a total blockage, bradycardia, and hypotension, the use of the agent in small amounts is one of the most important crucial advantages of this technique. Spinal or epidural anaesthesia is preferable to general anaesthesia in caesarean operation and ovariohysterectomy in terms of health of both mother and child (11).

The purpose of this study was to evaluate the effects of IT ketamine HCl anaesthesia on clinical values and some haemodynamic and biochemical parameters in bitches subjected to ovariohysterectomy.
**Material and Methods**

The study was conducted on 30 bitches, which were brought to the Department of Obstetrics and Gynecology for a routine ovariohysterectomy. The study was commenced after the permission, granted by the Kafkas University Local Animal Experimentation Board.

After atropinisation (Atrol-F®, Sanovel, 0.04 mg/kg), the bitches were sedated with xylazine HCl (2% Rompun®, Bayer, 0.5 mg/kg). The lumbosacral region was shaved and disinfected. At first local infiltration anaesthesia (Adokain®, Sanovel, 2 ml) was performed on the area from the skin to the spinal space. The spinal needle (18-22 G) was inserted in the lumbosacral space afterwards and a 10 mg/kg dose of ketamine HCl (10% Ketasol, Richter Pharma) was injected intrathecally as described by Torske and Dyson (28).

After the injection of the anaesthetic agent, the onset and end of anaesthesia were evaluated with deep pinpricks performed every 5 min on the thorax, inguinal region, rear extremities, perineum, and tail. As soon as the dogs were laid in the supine position on the operating table, a ovariohysterectomy was performed with a routine operating technique by entering the laparatomy incision, which began approximately 1 cm caudal to the belly button and extended for 5 cm to the posterior along the center line. During the ovariohysterectomy, regular checks were performed to determine whether or not the ovaries, uterus, and ligamenta lata uteri were sensitive to touch or dissection.

The animals were monitored (Veteriner Monitör® MMED6000DP S6-V) and initial values for arterial blood pressure, electrocardiography, (EKG) pulse rate, respiration, and body temperature were recorded, as well as measurements at the 5th, 15th, 30th, 60th, 90th, and 120th min of anaesthesia. During these procedures, three measurements were taken for each dog and the averages, were calculated. Furthermore, venous blood was used to determine blood gases, oxygen-haemoglobin levels, and the amounts of some electrolytes (IDEXX VetStat® Electrolyte and Blood Gas Analyzer) using venous blood from the beginning, and at the 30th and 60th min. With regard to biochemical measurements, venous blood was also taken prior to the procedure at the 5th, 15th, 60th, and 120th min after the IT injection and serum glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and creatinine levels were determined colorimetrically.

Extremity derivations were used in the EKG evaluation. QT values were corrected according to the heart rate and the adjusted QT (QTc) values, were calculated. The formula, developed by Fridericia (7) (QTcF = QT/(RR)1/3) was used for this purpose as appropriate.

The time taken to recover from dissociative anaesthesia, as well as the analgesic difference between the rear extremities and front extremities at the end of this period and the how long this lasted, were determined.

As concerns the postoperative care, suitable antibiotics and analgesic agent were applied and daily nursing procedure was also performed.

The statistical evaluation of the parametric samples was performed by one-way ANOVA method using the Minitab 12 programme. The non-parametric data was statistically analysed by Kruskal-Wallis test.

**Results**

The data was evaluated in terms of clinical, haemodynamic, and biochemical values. Clinically, dissociative anaesthesia was achieved in all bitches in less than 1 min. Anaesthesia lasted from maximum of 150 min to minimum of 55 min, averaging 95.9 min. After they emerged from dissociative anaesthesia, anaesthesia has continued in the rear extremities. The difference varied between 7 and 35 min. The average delay in the rear extremities was 17.45 min.

During the ovariohysterectomy, no response from the animals to touching the ovary or to pulling the ligamenta lata uteri was observed.

There was a statistically significant difference in the pulse rate (P<0.05) between the values at beginning of sedation and at the 5th, 15th, 30th, and 60th min of anaesthesia, but the mentioned difference disappeared at the 60th and 120th min. A statistically significant difference (P<0.05) was also observed in the respiration values at the beginning, sedation, and the 5th and 15th min of anaesthesia, but this difference was not significant as it concerns the other time intervals.

The systolic and diastolic values were a parallel with each other. Significant difference was found at the beginning, sedation, and the first 5 min of anaesthesia (P<0.05). Neither statistically significant difference was found during the evaluation of EKG data, nor in the body temperature.

There was a statistically significant difference in glucose levels concerning the beginning, and the 60th and 120th min in BUN levels between the beginning, and the 60th and 120th min, in AST activity between the beginning, and the 15th, 60th, and 120th min, and for glucose between the beginning and 60th and 120th min (P<0.05). No statistically significant difference was found in blood gases, oxygen-haemoglobin, and electrolyte levels between the initial values and the 30th and 60th min of anaesthesia.

**Discussion**

In addition to the existing positive effects of local anaesthetics commonly used for IT anaesthesia on the quality and length of anaesthesia, there are reports indicating a depressive effect of IT anaesthesia on the circulatory and respiratory systems (8, 11, 16, 21, 27). The purpose of this study was to eliminate the negative effects by using ketamine with the same technique.
It is said that ketamine HCl administered intrathecally not only antagonises the NMDA receptors, but it also creates a sensory and motor blockage by blocking the calcium channels (2, 8, 10, 16, 17). Some researchers (6, 20) have also noted that the effect of ketamine could be used for postoperative analgesia. Though local anaesthesia is achieved by use of ketamine intrathecally, it is claimed that neurotoxicity and vasotoxicity can develop (18, 26). Another study (23) has reported the development of spinal myelopathy depending on the dose, but there was no evidence that intrathecal ketamine caused a nerve damage. On the other side, the results of studies conducted on rats, rabbits, and primates with ketamine (0.3-0.6 mg/kg/IT) have proved that neurotoxicity must be taken seriously (9, 22). In our study, none of the bitches exhibited any direct clinical symptoms or changes in behaviour referring to spinal anaesthesia complications. In addition, there were no abnormal findings in bitches’ general condition such as whimpering, loss of appetite, and lethargy after emerging from anaesthesia or in the postoperative period.

During anaesthesia, when ketamine was administrated epidurally, no significant changes in the pulse rate and arterial blood pressure were observed (12, 16). In addition, when ketamine was administrated intrathecally, also no changes in arterial blood pressure between initial and during anaesthesia values, and pulse and respiration rates were found (10). On the contrary, in this study, some statistically significant differences (Table 1) in pulse rate and arterial blood pressure (1 min) and that even though the dissociative anaesthesia ended 95 min later, the anaesthesia has continued in the back legs and inguinal region (for other 17 min) as shown by clinical observation and pinprick tests.

Though local anaesthesia is achieved by use of ketamine intrathecally, it is claimed that neurotoxicity and vasotoxicity can develop (18, 26). Another study (23) has reported the development of spinal myelopathy depending on the dose, but there was no evidence that

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### Table 1

Haemodynamic parameters and evaluation periods

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>0 min</th>
<th>5th min</th>
<th>15th min</th>
<th>30th min</th>
<th>60th min</th>
<th>120th min</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>89.8±10.44&lt;sup&gt;a&lt;/sup&gt;</td>
<td>48.3±5.44&lt;sup&gt;a&lt;/sup&gt;</td>
<td>56.5±7.13&lt;sup&gt;a&lt;/sup&gt;</td>
<td>65.5±8.14&lt;sup&gt;a&lt;/sup&gt;</td>
<td>74.2±9.45&lt;sup&gt;a&lt;/sup&gt;</td>
<td>82.4±8.56&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>R</td>
<td>24.2±5.17&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16.1±3.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>18.5±4.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19.8±4.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21.8±3.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>23.5±4.45&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>S</td>
<td>148.1±23.86&lt;sup&gt;a&lt;/sup&gt;</td>
<td>107.95±18.57&lt;sup&gt;a&lt;/sup&gt;</td>
<td>124.6±19.38&lt;sup&gt;a&lt;/sup&gt;</td>
<td>132.4±18.98&lt;sup&gt;a&lt;/sup&gt;</td>
<td>139.5±21.29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>147.7±23.01&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>D</td>
<td>99.75±5.83&lt;sup&gt;a&lt;/sup&gt;</td>
<td>88.25±6.29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>91.9±6.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>94.55±5.52&lt;sup&gt;a&lt;/sup&gt;</td>
<td>96.4±6.21&lt;sup&gt;a&lt;/sup&gt;</td>
<td>98.15±5.94&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>T</td>
<td>38.6±0.56&lt;sup&gt;a&lt;/sup&gt;</td>
<td>38.74±0.37&lt;sup&gt;a&lt;/sup&gt;</td>
<td>38.84±0.71&lt;sup&gt;a&lt;/sup&gt;</td>
<td>38.64±0.58&lt;sup&gt;a&lt;/sup&gt;</td>
<td>38.5±0.49&lt;sup&gt;a&lt;/sup&gt;</td>
<td>38.5±0.53&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

P - pulse, R – respiration, S - systolic value, D - diastolic value, T – temperature; Differences between average values are shown by different letters (a-d) on the same line (P<0.05).

### Table 2

Distribution of biochemical parameters according to anaesthesia intervals

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>0 min</th>
<th>5th min</th>
<th>15th min</th>
<th>30th min</th>
<th>60th min</th>
<th>120th min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>65.97±7.43&lt;sup&gt;a&lt;/sup&gt;</td>
<td>68.35±7.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>70.75±9.81&lt;sup&gt;a&lt;/sup&gt;</td>
<td>76.65±10.05&lt;sup&gt;a&lt;/sup&gt;</td>
<td>84.39±13.39&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>40.05±10.27&lt;sup&gt;a&lt;/sup&gt;</td>
<td>37.04±10.54&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34.43±9.81&lt;sup&gt;a&lt;/sup&gt;</td>
<td>36.36±4.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>33.04±9.44&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>53.13±11.66&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47.58±10.96&lt;sup&gt;a&lt;/sup&gt;</td>
<td>44.08±10.68&lt;sup&gt;a&lt;/sup&gt;</td>
<td>39.5±10.23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>41.69±10.54&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>BUN</td>
<td>7.08±1.97&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9.27±2.72&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.64±3.12&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16.4±4.02&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19.28±3.75&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Creatine</td>
<td>0.66±0.12&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.71±0.12&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.79±0.11&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.88±0.15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.95±0.16&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

Differences between average values are shown by different letters (a-b) on the same line (p<0.05).

### Table 3

Blood gases, oxygen-haemoglobin, and electrolyte values according to anaesthesia intervals

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>pH</th>
<th>pCO&lt;sub&gt;2&lt;/sub&gt; (mmHg)</th>
<th>HCO&lt;sub&gt;3&lt;/sub&gt; (mmol/L)</th>
<th>BE (mmol/L)</th>
<th>AnGap (mmol/L)</th>
<th>PO&lt;sub&gt;2&lt;/sub&gt; (mmHg)</th>
<th>tHb (g/dL)</th>
<th>SO&lt;sub&gt;2&lt;/sub&gt; (%)</th>
<th>Na (mmol/L)</th>
<th>K (mmol/L)</th>
<th>Cl (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning</td>
<td>7.43</td>
<td>33.7</td>
<td>20.62</td>
<td>1.88</td>
<td>22.88</td>
<td>40.9</td>
<td>15.32</td>
<td>72.50</td>
<td>155.2</td>
<td>4.66</td>
<td>116.1</td>
</tr>
<tr>
<td>30th min</td>
<td>7.35</td>
<td>41.33</td>
<td>21.47</td>
<td>3.23</td>
<td>26.1</td>
<td>35.66</td>
<td>17.03</td>
<td>65.66</td>
<td>155.67</td>
<td>4.54</td>
<td>115.0</td>
</tr>
<tr>
<td>60th min</td>
<td>7.36</td>
<td>41.30</td>
<td>21.73</td>
<td>2.67</td>
<td>22.78</td>
<td>38.5</td>
<td>16.33</td>
<td>67.8</td>
<td>155.0</td>
<td>4.6</td>
<td>112.67</td>
</tr>
</tbody>
</table>

P - pulse, R – respiration, S - systolic value, D - diastolic value, T – temperature; Differences between average values are shown by different letters (a-b) on the same line (P<0.05).
the clinical point of view because they could be attributed to sedation rather than to the effect of intrathecal ketamine HCl. Additionally, some differences were also noticed in respiratory values (Table 1), but there was no a depressive effect in a clinical sense when respiration quality was taken into consideration. There was no statistically significant difference between the initial values and those at subsequent intervals in terms of the body temperature.

Some of the studies conducted on dogs (3, 14) have reported that no statistically significant difference was found as regards the initial values and those under anaesthesia for blood gases and electrolyte balance when a combination of xylazine and ketamine was administered intravenously (1). In this study, it was confirmed that intrathecal administration of ketamine did not affect these values and the same results can be found in the literature (3, 14).

Some authors indicated that an increase in pulse rate, respiration, and systolic blood pressure values to 20% or more during the operation, are considered to be an indication of intraoperative pain (1, 24). In our study, pulse and respiration rates and systolic values were almost the same as the initial values. Consequently, there was no evidence of intraoperative pain in this sense or any other indication during the operation. Even though there was a statistically significant difference (P<0.05) between the initial values and the values observed during anaesthesia in biochemical parameters. However, the obtained values were in the range with the reference values (5).

In conclusion, when the effects on clinical and some haemodynamic and biochemical values are taken into consideration, the anaesthesia achieved in dogs using IT ketamine HCl creates a possibility of recommending it as a possible alternative anaesthesia suitable for ovariohysterectomy (as the anaesthesia is dissociative and spinal anaesthesia continues even after the dissociative effect subsides). Based on all mentioned characteristics of IT ketamine HCl, we consider it as a possible alternative anaesthesia appropriate for the operating procedures in which spinal anaesthesia can be used, including orthopedic procedures.

**References**


