Twelve female dogs subjected to ovariohysterectomy following pyometra to observe the effects of xylazine or dexmedetomidine along with butorphanol to ketamine anaesthesia on clinico-physiological and hemodynamic parameters. Atropine (0.04 mg/kg) followed 5 min later by butorphanol (0.2mg/kg) were administered I/M to each animal in both groups. The animals were randomly distributed into groups A and B having 06 animals in each group. In group A, xylazine (0.5 mg/kg I/M) and in group B dexmedetomidine (10 μg/kg I/M) was administered at 5 minutes interval along with butorphanol. After 10 minutes, anaesthesia was induced with ketamine as single bolus in both groups followed by maintenance with ketamine I/V as and when needed. Adequate muscle relaxation, sedation and analgesia necessary for surgical intervention followed by smooth and uneventful recovery was achieved in both groups. An early weak time and down time was recorded in the animals of group B. However, the animals of group B regained recovery and attained sternal and standing position after a longer duration as compared to group A. The dose sparing effect on ketamine was significantly higher in group B as compared to group A. Heart rate showed significant increase (P<0.001) after premedication followed by further increase during post-induction period in both groups. Respiration rate and rectal temperature remained decreased in both groups. SpO₂ revealed significant decrease after premedication and during post-induction period in both groups. It was concluded that xylazine/dexmedetomidine-butorphanol combination produced a comparable degree of clinico-physiological and haemodynamic stability during ketamine anaesthesia in dogs undergoing ovariohysterectomy following pyometra.

Keywords: Butorphanol, Dexmedetomidine, Ketamine, Ovariohysterectomy, Xylazine.

Canine pyometra is a disease syndrome that affects intact bitches, causing a variety of clinical and pathological signs. In most cases of pyometra, the choice of treatment is ovario-hysterectomy (Pretzer, 2008). Alpha-2 agonists are commonly used sedatives in veterinary practice as they induce reliable and dose dependent sedation, analgesia and muscle relaxation. In dogs and cats, xylazine has been used alone or in combination with opioids or alpha-2 agonists (White, 1983, Rafee et al., 2016). The present study was undertaken to compare the clinico-physiological and haemodynamic effects of ketamine anaesthesia in canine pyometra patients premedicated with butorphanol-xylazine/dexmedetomidine combination.

Materials and Methods
The study was conducted on 12 adult female dogs subjected to ovariohysterectomy for surgical management of pyometra. Atropine was administered @ 0.04 mg/kg I/M followed after 5 minutes with butorphanol @0.2 mg/ kg in both groups. However, in group A, xylazine @ 0.5 mg/kg body weight I/M while dexmedetomidine @ 10 g/kg body weight I/M was administered in group B in separate syringe along with butorphanol. Ten minutes after premedication, anaesthesia was induced with ketamine administered I/V in both group -s. Maintenance of surgical anaesthesia was
made by incremental doses of ketamine I/V as and when needed during surgery.

Weak time and down time were recorded as the time elapsed from the time of injection of drugs to the time of onset on incoordination/ataxia or drowsiness, and till the animal attained sternal recumbency, respectively. Recovery time was recorded as time elapsed from completion of surgery till reappearance of pedal reflex. Sternal recumbency time and complete recovery time were recorded as the time elapsed after completion of surgical procedure until the animals attained sternal recumbency for recovery, and stood and walked unassisted, respectively.

Palpebral reflex as a measure of depth of sedation and jaw relaxation as a measure of muscle relaxation were used to monitor the depth of anesthesia at 0, 10, 15, 30, 45, 60, 75 and 90 min.

Jaw relaxation, palpebral reflex and pedal reflex were scored as: 0. Animal not allowing to open the jaw, intact and strong reflex (strong withdrawal) as, 1. Animal resists opening of jaws and closes quickly, intact but weak blink (slow response), intact but weak pedal reflex (animal responding slowly) as, 2. Less resistance to opening the jaws and closed slowly, very weak (very slow and occasional response) as, 3. No resistance and jaws remain open, abolished blink reflex and pedal reflex, respectively.

Heart rate (HR-beats/min) was monitored with non-invasive blood pressure monitor from ulnar artery and respiratory rate (RR-breaths/min) was measured by counting the excursion of thoracoabdomen at 0, 10, 15, 30, 45, 60, 75 and 90 min intervals. Rectal temperature (RT) was recorded with the help of a digital thermometer. Oxygen saturation of hemoglobin (SpO₂) was measured with pulse oxymeter. The sensor was applied on the pinna or tip of the animal ear after clipping hair at the site and cleaned with 70% alcohol or tip.

Analysis of variance (ANOVA) and Duncan’s multiple range tests (DMRT) were used to compare the means at different intervals among different groups. Paired “t” test was used to compare the mean values at different levels with their respective base value in each group. For non-parametric observations Kruskal-Wallis one-way test was used to compare the mean between the groups at corresponding intervals. Statistical significance was assessed at P<0.05.

**Results and Discussion**

A non-significantly (P>0.05) lower weak time (2.93±0.17 v/s 3.38±0.22 min) and down time (4.37±0.28 v/s 4.08±0.19 min) was recorded in the animals of group B which could be attributed to earlier onset of action of dexmedetomididine due to its lipophilic property as also reported by Amarpal et al. (1996) and Rafee et al. (2016). Reduction in weak time following administration of dexmedetomidine along with butorphanol has also been reported in dogs by Ahmad (2010) and Rafee et al. (2015).

The animals of group A had significantly (P<0.05) shorter recovery time (16.33±1.98 v/s 22.67±1.73 min) after completion of surgical procedure. However, there was no significant (P>0.05) difference in sternal recumbency time (23.17±2.14 v/s 28.00±2.28 min) and complete recovery time (37.50±2.00 v/s 39.83±2.07) between two groups. The prolonged recovery time recorded in group B may be due to the synergistic actions of dexmedetomidine and butorphanol which might have enhanced the effects of ketamine as also reported earlier in dogs by Acharya (2014) and Rafee et al. (2016). A non-significantly (P>0.05) increased sternal recumbency time and standing recovery time in group B probably resulted from the synergistic action of various drugs resulting in deeper sedation and reduced metabolic activity to delay redistribution and metabolism of the drugs.

Excellent muscle relaxation was recorded from 15 min onwards up to 45 min interval and thereafter, muscle tone regained gradual strength in both groups. Resistance to opening the mouth is fully lost in moderate anaesthesia as also recorded by Tranquilli et al. (2007). In the present study, mild relaxation was recorded in both groups after premedication at 10 min and after recovery period. Comparison between groups revealed that the jaw relaxation values were significantly (P<0.05) higher at 60 and 75 min interval in group B. The findings of the present study conformed
to the observations of earlier researchers viz. Selmi et al. (2003), who reported greater muscle relaxation when dexmedetomidine or medetomidine was combined with opioids and/or ketamine in small animals.

During ketamine anaesthesia, the palpebral reflex remained moderately depressed but not completely abolished till 45 min interval. Thereafter, mild palpebral reflex was recorded at most of the time intervals till completion of the observation period. Similar observations were reported by Rafee et al. (2015) during dexmedetomidine-butorphanol premedication prior to ketamine anaesthesia where mild to moderate palpebral reflex was recorded in dogs undergoing ovariohysterectomy. Pedal reflex was completely abolished from 10 min onwards till 60 min interval. Thereafter, pedal reflex was very slow at 75 min interval in group B. Alpha-2 agonists produce analgesia by stimulating α-2 receptors at various sites in the pain pathway within the brain and spinal cord. Butorphanol is a central-acting analgesic which ameliorates the signs of superficial and visceral pain when administered I/V but is effective for only 30 to 90 minutes. Therefore, in the present study butorphanol and alpha-2 agonist combination might have produced better analgesia by a similar synergistic mechanism as reported earlier in dogs by Acharya (2014) also.

Comparison between groups revealed a significantly (P<0.05) lower induction dose of ketamine in group B as compared to group A (4.29±0.31 and 5.96±0.37 mg/kg) which might be due to synergistic interaction between dexmedetomidine and butorphanol. The reduction in induction dose of ketamine following administration of dexmedetomidine along with opioids has also been reported in dogs by Ahmad (2010). However, there was no significant (P>0.05) difference between maintenance dose of ketamine in both groups (2.29±0.16 and 2.04±0.17 mg/kg). Reduced ketamine dose for maintenance (2-3mg/kg) has also been reported with dexmedetomidine-butorphanol premedication in canine patients as also mentioned by Acharya (2014).

In both groups, HR increased after administration of preanaesthetic administration (Table- 1). Heart rate increased significantly (p<0.01) high following preanaesthetic administration in

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>0</th>
<th>10</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>75</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>115.33±2.67</td>
<td>124.67±1.84**</td>
<td>128.17±3.74**</td>
<td>133.50±1.67**</td>
<td>135.67±2.40**</td>
<td>136.83±2.20**</td>
<td>128.17±2.82**</td>
<td>121.33±3.92</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>120.67±3.04</td>
<td>122.33±2.74</td>
<td>128.50±4.16</td>
<td>131.83±2.71</td>
<td>133.17±2.59**</td>
<td>135.33±2.53*</td>
<td>128.17±2.82**</td>
<td>118.33±4.55</td>
<td></td>
</tr>
<tr>
<td><strong>RR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>27.50±2.33</td>
<td>22.67±1.84*</td>
<td>20.33±1.99**</td>
<td>19.67±2.19**</td>
<td>18.50±1.26*</td>
<td>18.17±0.98*</td>
<td>21.33±1.05*</td>
<td>25.33±1.91</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>28.33±1.78</td>
<td>20.17±1.64**</td>
<td>19.33±0.88**</td>
<td>18.17±1.01**</td>
<td>17.50±1.38**</td>
<td>20.17±1.74**</td>
<td>21.17±1.01**</td>
<td>27.00±1.69</td>
<td></td>
</tr>
<tr>
<td><strong>RT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>37.70±0.49</td>
<td>37.13±0.46*</td>
<td>36.77±0.44*</td>
<td>37.00±0.47*</td>
<td>36.48±0.44*</td>
<td>36.72±0.45*</td>
<td>37.30±0.38</td>
<td>37.08±0.31</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>37.23±0.44</td>
<td>36.85±0.42</td>
<td>36.28±0.27*</td>
<td>36.23±0.37*</td>
<td>36.05±0.49*</td>
<td>36.48±0.20*</td>
<td>37.02±0.62</td>
<td>36.97±0.39</td>
<td></td>
</tr>
<tr>
<td><strong>SPO2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>89.50±1.67</td>
<td>82.67±1.65**</td>
<td>81.17±1.97*</td>
<td>79.83±0.70**</td>
<td>79.17±2.23**</td>
<td>80.33±2.29*</td>
<td>84.50±1.20*</td>
<td>86.67±1.50**</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>91.50±1.06</td>
<td>84.83±1.83**</td>
<td>81.50±1.54**</td>
<td>80.17±1.89**</td>
<td>78.33±1.45**</td>
<td>80.67±1.28**</td>
<td>83.33±2.30**</td>
<td>84.67±2.04**</td>
<td></td>
</tr>
</tbody>
</table>
group A. However, HR started decreasing gradually at 75 and 90 minutes interval but still the values were significantly (p<0.01) higher as compared to baseline. Heart rate in group B revealed a non-significant increase (p>0.05) after preanesthetic administration till 30 minutes interval. A significant (p<0.05) increase in HR was recorded at 45 and 60 minute interval followed by gradual decrease but the values were non-significantly (p>0.05) increased as compared to baseline. Comparison between groups revealed no significant (p>0.05) difference in HR at different time intervals. Initial increase in HR even after the administration of alpha-2 agonists with opioids might be attributed to the effect of atropine. The increase in heart rate by atropine is due to the antagonistic activity of atropine with acetylcholine at postganglionic effector sites as also reported by Innes and Nickerson (1975). The findings of increased HR following administration of dexmedetomidine along with opioids prior to ketamine anaesthesia in dogs has also been reported by Rafee et al. (2016).

A significant (p<0.05) decrease in respiratory rate was recorded in both groups as compared to the baseline values at most of the time intervals during the observation period and comparison between groups revealed no significant (p>0.05) differences at any time interval. Respiratory depression associated with alpha-2 agonists might be secondary to the CNS depression produced by alpha-2 adrenoceptors stimulation as also mentioned by Sinclair (2003) or due to direct depression of the respiratory centers by preanesthetics as reported by Thurmon et al. (1996) also. Opioids produce dose dependent depression of ventilation primarily mediated by 2 receptors, leading to a direct depressant effect on brain-stem respiratory centre as also reported by Gutstein and Akil (2001). Decreased RR values following administration of alpha-2 agonists along with butorphanol and ketamine anaesthesia in dogs have also been reported by Rafee et al. (2016).

Rectal temperature decreased significantly (p<0.05) below the baseline in both groups till 45 min interval followed by non-significantly (p>0.05) decreased RT till the end of observation period. This might be attributed to a decrease in the skeletal muscle tone, reduced metabolic rate, muscle relaxation, depression of thermoregulatory center and peripheral vasodilation as also reported by Virtanen et al. (1989). Reduced RT values following administration of opioids along with alpha-2 agonist and ketamine anaesthesia has also been reported in dogs by Acharya (2014) and Rafee et al. (2015).

A highly significant (P<0.01) decrease in SpO2 was recorded at most time intervals in both groups. Decrease in SpO2 could possibly be due to certain degree of respiratory depression in both groups and this might also be responsible for reduced SpO2 in the present study. Low SpO2 is indicative of reduced arterial oxygenation and diminished tissue perfusion due to vasoconstriction as also recorded by Leppanen et al. (2006). Initial decrease in SpO2 in both groups may be attributable to vasoconstriction caused by alpha-2 agonists as also mentioned by Thurmon et al. (1996). The findings of decreased SpO2 values due to depression of respiration caused by butorphanol along with alpha-2 agonists and ketamine anaesthesia has also been reported in dogs by Muir et al. (1999).

The results suggest that butorphanol along with xylazine/dexmedetomidine produced comparable degree of clinicophysiological and hemodynamic effects during ketamine anaesthesia in pyometra affected dogs undergoing ovariohysterectomy and may be recommended for balanced anaesthesia in critically ill canine patients.

References


Ahmad, R.A. (2010). Studies on sedative, analgesic and anaesthetic effects of...
dexmedetomidine and its combination with midazolam, fentanyl and ketamine in dogs. M.V.Sc. thesis submitted to deemed University, IVRI, Izatnagar, India.


