# CLINICO-PHYSIOLOGICAL AND HAEMODYNAMIC EVALUATION OF BUTORPHANOL -XYLAZINE/ DEXMEDETOMIDINE-KETAMINE ANAESTHESIA IN CANINE PYOMETRA PATIENTS

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Twelve female dogs subjected to ovariohysterectomy following pyometra to observe the effects of xylazine or dexmedetomidine along with buorphanol 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. $SpO_2$ 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.

**C**anine pyometra is a disease syndrom -e that affects intact bitches, causing a variety of clinical and pathological signs. In most cas -es of pyometra, the choice of treatment is ovario-hysterectomy (Pretzer, 2008). Alpha-2 agonists are commonly used sedatives in vete -rinary practice as they induce reliable and dose dependent sedation, analgesia and mus-cle relaxation. In dogs and cats, xylazine has been used alone or in combination with opioi -ds to provide sedation and analgesia for diag -nostic and minor surgical procedures. Combi -nations of butorphanol and alpha-2 adrenoce -ptor agonists provide reliable and uniform sedation in dogs and cats, although significant decreases in heart and respiratory rates are observed (Thurmon *et al*., 1996). Dexmedeto -midine reduces the dose requirement of opioi -ds and anaesthetic agents and attenuates the hemodynamic repsonses to tracheal intubatio-n, surgical stimuli along with cardiac and ren -al protective effects (Panzer *et al*., 2009). Ke -tamine has also been found to provide cardio -vascular stability when given along with opioids or alpha-2 agonists (White, 1983, Rafee *et al*., 2016). The present study was undertaken to compare the clinico-physiologi-cal 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. Atropi -ne was administered @ 0.04 mg/kg I/M follo -wed 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 µg/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 anaesthesia 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 ($SpO_2$) 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 dexmedetomidine 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 Rafee *et al*. (2015) also. Ketamine possesses excellent analgesic property and produces anaesthesia of shorter duration. Therefore, addition of alpha-2 agonist along with butorphanol produced analgesia and sedation of longer duration to perform the surgical intervention 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

**Table1: Mean ±S.E. values of heart rate (beats/min), respiratory rate (breaths/min), rectal temperature ($^0$C) and oxygen saturation ($SP0_2$%) at different time intervals in different groups**

| Parameter | Group | Time intervals (min) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | **0** | **10** | **15** | **30** | **45** | **60** | **75** | **90** |
| **HR** | A | 115.33± 2.67 | 124.67± 1.84** | 128.17± 3.74** | 133.50± 1.67** | 135.67± 2.40** | 136.83± 2.20** | 128.17± 2.82** | 121.33± 3.92 |
| | B | 120.67± 3.04 | 122.33± 2.74 | 128.50± 4.16 | 131.83± 2.71 | 133.17± 2.59** | 135.33± 2.53* | 125.83± 2.32 | 118.33± 4.55 |
| **RR** | A | 27.50± 2.33 | 22.67± 1.84* | 20.33± 1.99** | 19.67± 2.19** | 18.50± 1.26* | 18.17± 0.98* | 21.33± 1.05* | 25.33± 1.91 |
| | B | 28.33± 1.78 | 20.17± 1.64** | 19.33± 0.88** | 18.17± 1.01** | 17.50± 1.38** | 20.17± 1.74** | 21.17± 1.01* | 27.00± 1.69 |
| **RT** | A | 37.70± 0.49 | 37.13± 0.46* | 36.77± 0.44* | 37.00± 0.47* | 36.48± 0.44* | 36.72± 0.45* | 37.30± 0.38 | 37.08± 0.31 |
| | B | 37.23± 0.44 | 36.85± 0.42 | 36.28± 0.27* | 36.23± 0.37* | 36.05± 0.49* | 36.48± 0.20* | 37.02± 0.62 | 36.97± 0.39 |
| **$SPO_2$** | A | 89.50± 1.67 | 82.67± 1.65** | 81.17± 1.97* | 79.83± 0.70** | 79.17± 2.23** | 80.33± 2.29* | 84.50± 1.20* | 86.67± 1.50* |
| | B | 91.50± 1.06 | 84.83± 1.83** | 81.50± 1.54** | 80.17± 1.89** | 78.33± 1.45** | 80.67± 1.28** | 83.33± 2.30** | 84.67± 2.04** |

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 prioir 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 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 preanaesthetics as reported by Thurmon *et al.* (1996) also. Opioids produce dose dependent depression of ventilation primarily mediated by μ2 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 $SpO_2$ was recorded at most time intervals in both groups. Decrease in $SpO_2$ could possibly be due to certain degree of respiratory depression in both groups and this might also be responsible for reduced $SpO_2$ in the present study. Low $SpO_2$ is indicative of reduced arterial oxygenation and diminished tissue perfusion due to vasoconstriction as also recorded by Leppanen *et al*. (2006). Initial decrease in $SpO_2$ 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 $SpO_2$ 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**

Acharya, A. (2014). Comparative evaluation of xylazine and midazolam in combination with butorphanol/pentazocine as preanaesthetic to ketamine anaesthesia in canine patients. M.V.Sc. Thesis submitted to OUAT, Bhubaneswar, India.

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 o deemed University, IVRI, Izatnagar, India.

Amarpal, Pawde, A.M., Singh, G.R., Pratap, K. and Kumar, N. (1996). Clinical evaluation of medetomidine with or without pentazocine in atropinized dogs. *Indian J. Anim. Sci.*, **66**: 219-222.

Gutstein, H.B. and Akil, H. (2001). Opioid analgesics. In: Goodman and Gilman's The pharmacological basis of therapeutic -s, Harman, J.G., Limbird, L.E. and Goodman L.S. and Gilman, A. (Eds.). 10th edn., Mcgraw Hill, New York, U.S.A. Pp. 569-619.

Innes, I.R. and Nickerson, M. (1975). Atropine, scopolamine and related antimuscarinic drugs. In: Pharmacolog-ical basis of therapeutics, Goodman, L.S. and Gilman, A. (Eds.). 5th edn., Macmillan Publishing Co. Inc., New York, U.S.A. Pp. 514-532.

Leppanen, M.K., McKusick, B.C., Granholm, M.M., Westerholm, F.C., Tulama, R. and Short, C.E. (2006). Clinical efficacy and safety of dexmedetomidine and buprenorphine, butorphanol or diazepam for canine hip radiography. *J. Small Anim. Pract.*, **47**: 663-669.

Muir, W.W., Ford, J.L., Karpa, G.E., Harriso-n and Gadawski, J.E. (1999). Effects of intramuscular administration of low doses of medetomidine and medetomidine-butorphanol in middle-aged and old dogs. *J. Am. Vet. Med. Assoc.*, **215**: 1116-1120.

Panzer, O., Moitra, V. and Sladen, R.N. (2009). Pharmacology of sedative-analgesic agents dexmedetomidine, rimefentanil, ketamine, volatile anesthetics, and the role of peripheral mu antagonists. *Crit. Care Clin.*, **25**: 451-469.

Pretzer, S.D. (2008). Clinical presentation of canine pyometra & mucometra: A review. *Theriogenology*, **70**: 359-363.

Rafee, M.A., Kinjavdekar, P., Amarpal and Aithal, H.P. (2015). Effect of dexmedetomidine with or without butorphanol on the clinico-physiological and haemodynamic stability in dogs undergoing ovariohysterectomy in midazolam and ketamine anaesthesia. *Int. J. Sci. Res. Pub.*, **5**: 1-7.

Rafee, M.A., Kinjavdekar, P., Amarpal and Aithal, H.P. (2016). Clinico-physiological and haemodynamic changes during midazolam-ketamine anaesthesia in dogs premedicated with dexmedetomidine with or without pentazocine. *Indian J. Vet. Surg.*, **37**(2): 82-87.

Selmi, A.L., Mendes, G.M., Lins, B., Figueiredo, J.P. and Baebudo-Selmi, G.R. (2003). Evaluation of the sedative and cardiorespiratory effects of dexmedetomidine, dexmedetomidine-butorphanol and dexmedetomidine-ketamine in cats. *J. Am. Vet. Med. Assoc.*, **222**: 37-41.

Sinclair, M.D. (2003). A review of the physiological effects of alpha-2 agonists related to the clinical use of medetomidine in small animal practice. *Can. Vet. J.*, **44**: 885-897.

Thurmon, J.C., Tranquilli, W.J. and Benson, G.J. (1996). Preanaesthetics and anesthetic adjuncts. In: Veterinary Anaesthesia. Lumb, W.V. and Jones, E.W. (Eds.). 3rd edn., Williams and Wilkins, Philadelphia, U.S.A. Pp. 731-746.

Tranquilli, W.J., Thurmon, J.C. and Grimm, K.A. (2007). Lumb & Jones' Veterinary Anesthesia and Analgesia. 4th edn., Blackwell Publishing Ltd, Oxford, U.K. Pp. 16

Virtanen, R. (1989). Pharmacological profiles of medetomidine and its antagonist, atipamezole. *Acta Vet. Scand.*, **85**: 29-37.

White, P.H. (1983). Use of continuous infusion versus intermittent bolus administration of fentanyl or ketamine during outpatient anaesthesia, *Anaesthesiology*, **59**: 294-300.