Propofol and ketamine with isoflurane in dexmedetomidine and butorphanol premedicated dogs for ovariohysterectomy

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Abstract
The study was conducted to evaluate propofol and ketamine with isoflurane in dexmedetomidine and butorphanol premedicated twelve numbers of female dogs undergoing elective ovariohysterectomy. Animals were randomly divided into Group A and B comprising of six animals in each group. The animals in both the groups were administered glycopyrrolate @ 0.01 mg/kg IM. Fifteen minutes later, the animals were administered dexmedetomidine @5µg/kg IV and Butorphanol @ 0.1mg/kg IV. Two minutes later, induction of anaesthesia was done with propofol IV till effect in Group A and with ketamine IV till effect in Group B. The anaesthesia was maintained with isoflurane in both the groups. The mean induction times (Sec) in Group A were recorded as 34.83 ± 2.44 and in Group 36.17 ± 1.87 respectively. The induction doses of propofol (Group A) and ketamine (Group B) were 0.67±0.07 and 2.55± 0.24 respectively. The recovery time (min) was recorded as 6.17±0.59 and 6.68±0.54 in Group A and B respectively. The mean values of vaporizer settings (%) for isoflurane were recorded as 1.34±0.06 and 1.28±0.07 respectively in Group A and B. Quality of anaesthesia was excellent in both the group and the clinical parameters remained with the physiological limit.

Keywords: Propofol ketamine isoflurane dog

Introduction
It is well known that almost all anaesthetic agent exhibit evidence of some deleterious effects on the body which may be of short or long duration and no such agent has been found so far which is totally free from one or more unwanted effect. Anaesthetic protocols involving single agent have largely been abandoned in favour of protocols that incorporate multiple agents from different classes to achieve sedation, analgesia and muscle relaxation together, which is also known as balanced anaesthesia. In balanced anaesthesia, two or more drugs or techniques are combined to achieve all the components of anaesthesia and at the same time the side effects of an individual agent is mitigated by the others. For this purpose, different classes of pre-anaesthetic agents are used along with induction or maintenance agents to achieve cardiovascular and respiratory stability, reduction of secretions together with ideal components of anaesthesia. In order to optimize the advantages afforded by premedication, it is important to select premedicants, induction and maintenance agents based on the need of the individual patient. The present study has been undertaken to compare propofol and ketamine with isoflurane in butorphanol and dexmedetomidine premedicated dogs.

Materials and Methods
The clinical study was carried out on twelve numbers of female dogs with mean body weight of 15.48 ± 1.22 kg and a mean age of 2.75±0.38 years presented for elective ovariohysterectomy. Animals were randomly divided into two groups (Group A and B) comprising of six animals in each group. The animals in both the groups were administered with glycopyrrolate @ 0.01 mg/kg IM. Fifteen minutes after administration of glycopyrrolate, the animals were administered dexmedetomidine @5µg/kg IV and Butorphanol @ 0.1mg/kg IV. Two minutes after administration of dexmedetomidine and butorphanol, induction of anaesthesia was done with propofol IV till effect in Group A and with ketamine IV till effect in Group B. The anaesthesia was maintained with isoflurane in both the groups. The heart rate, respiratory rate and rectal temperature were recorded at 0 minute (before premedication) and 20 minutes, 40 minutes and 60 minutes (during maintenance).
Induction Time was recorded (in seconds) from administration of the induction agent till the animal is anaesthetized. The mean dose (mg/Kg) required for induction of anaesthesia were recorded in both the groups. The overall quality of induction was scored as per the method described by Amengu et al. (2013) [2] and scores were given as 0- Calm transition, no paddling, 1- Occasional, slow paddling movements, 2- Moderate, sustained paddling movements and 3- Marked paddling, struggling or vocalisation. Intubation quality was assessed as per the method described by Amengu et al. (2013) [2] and scores were given as 0- Easy intubation, 1- Mild coughing, 2- Pronounced coughing and 3- Swallowing, coughing and gagging. The quality of analgesia was assessed as per the method described by Sabbe et al. (1994) [23] and scores were given as 0- Normal pedal reflex, 1- Immediate withdrawal, 2- Slow reflex, 3- Withdrawal of foot only after pinching with increased intensity for 3 seconds and 4- No response. The muscle relaxation was judged as per the method described by Ahmad et al. (2013) [1] and scores were given as 0- Not allowing opening of the jaws, 1- Resistant to opening of the jaws and closed quickly, 2- Less resistance to opening of the jaws and closed slowly and 3- No resistance and jaws remain open. The anaesthetic depth was assessed as per the method described by Ahmad et al. (2013) [1] and scores were given as 0- Intact and strong (quick blink), 1- Intact but weak (slow response), 2- Very weak (very slow and occasional response) and 3- Abolished (no response). Recovery time (minutes) was recorded as time from discontinuation Vaporizer setting till return of swallowing reflex and removal of endotracheal tube. Quality of recovery: Quality of recovery was assessed as per the method described by Jimenez et al. (2012) [12] and scores were given from 1 to 6. The vaporizer settings were decreased or increased to maintain the surgical plane of anaesthesia as required by the animals with a fresh gas flow (FGF) of 10 ml/kg/minute and the percentage of vaporizer settings were recorded at regular time intervals. The data obtained were analyzed using statistical package SPSS version 16. One way ANOVA based on Fisher’s Least Significant Difference method was used to determine the significant difference among the different treatments and time intervals. The significant values in the ANOVA were further tested through Duncan multiple range test considered significant when P<0.05.

Results and Discussion
The heart rate at different time intervals decreased non-significantly in Group A with highest fall at 20 min (103.50±5.42). In Group B, the heart rate increased initially at 20 min (127.83±4.61) and thereafter decreased gradually. Similar findings were also reported by Chen et al. (2012) with isoflurane anaesthesia premedicated with dexmedetomidine, Ahmad et al. (2013) [1] with dexmedetomidine, midazolam, fentanyl and ketamine combinations in dog and (Kurdi et al., 2014) with ketamine. The initial non-significant decrease in heart rate observed in Group A might be due to the effect of butorphanol and dexmedetomidine as both the drugs caused decrease heart rate in animals as mentioned by Greene et al. (1990) [8] and Pypendop and Verstegen (1998). The dexmedetomidine causes a vasoconstriction in both the pulmonary and systemic circulations initially and then elicits a decrease in heart rate and cardiac output with a slight depressive effect on ventilation (Pascoe, 2015) [22]. In Group B, the rise in heart rate might be due to cardiac stimulatory effects of ketamine Kumar et al. (2014) [14]. Ketamine stimulates the cardiovascular system resulting in increased heart rate principally through the sympathetic nervous system (Kolawole, 2001) [13]. Ketamine has an antagonistic interaction with mono-amnergic, muscarinic and nicotinic receptors and produces anticholinergic symptoms (Pai and Heining, 2007) [21]. The respiratory rate did not show any significant variation between the groups at different time intervals. A decreasing trend in respiratory rate from pre-induction values was observed in both the groups till the end of the observation period. The changes were found to be significant in Group A (P<0.05) and Group B (P<0.01). The decreased respiratory rate observed might be due to depression of respiratory centre caused by isoflurane (Galloway et al. 2004), ketamine (Narayanam et al. 2011) [19] and propofol (Suarez et al., 2012). The respiratory depression with ketamine anaesthesia might also be due to airway relaxation by acting on various receptors, inflammatory cascades and bronchial smooth muscles as reported by Goel and Agrawal (2013) [7]. The rectal temperature between the groups did not show any significant difference at different observation periods where as the rectal temperature decreased at different time intervals in both the groups after administration of anaesthesia till the end of the observation period with non significant variations. The decreased rectal temperature recorded in the present study might be due depression of the thermoregulatory centre or depression of the basal metabolic rate or reduction in peripheral circulation or due to muscle relaxation (Ahmad et al., 2013) [1]. The mean induction times (Sec) in Group A were recorded as 34.83 ± 2.44 and in Group 36.17 ± 1.87, respectively. The shorter induction times observed in the present study might be due to the synergistic effect of dexmedetomidine and butorphanol which caused sufficient degree of sedation prior to induction. Dexmedetomidine has rapid onset of action owing to its lipophilic properties (Arunkumar et al., 2017b) [3]. Congdon et al. (2011) [5] also observed potent sedation enabling minor clinical procedures in dogs with intramuscular administration of dexmedetomidine @10 mcg/kg. Similarly, Trimble et al. (2018) [30] also reported high sedation with butorphanol and dexmedetomidine in dog. The induction doses (mg/kg) of propofol in Group A was 0.67±0.07 and ketamine in Group B was 2.55±0.24. The induction doses of propofol and ketamine recorded in the present study were lower than their general recommended doses with and without premedication in dog. The induction in the total dose of induction agent in the present study might be due to the synergistic action of dexmedetomidine and butorphanol (Jena et al. 2014) [11] with the induction agents. The premedication with alpha2adrenoceptor and opioid might have reduced the induction dose of propofol and ketamine. A reduction in the induction dose of propofol by 20 to 80% when administered in combination with sedative or analgesic agents was reported by Short and Bufalari (1999) [25]. Sharma et al. (2014) also observed similar reduction in dose of ketamine with butorphanol and dexmedetomidine premedication in dogs and opined that dexmedetomidine along with butorphanol reduced the induction dose rate of ketamine up to 61%. All the groups were recorded with induction score of zero. During the anaesthetic induction the animals in all the groups were recorded with calm transition, without paddling movement, salivation, nausea and vomition. An excellent jaw relaxation was observed in animals of both the groups and all the animals were recorded with easy intubation. The analgesic score were recorded as 4 in both the groups. The animals showed excellent analgesia sufficient for performing surgical operation showing no response to noxious stimuli and
tolerated the surgery well. The analgesia observed in the present study might be due to the synergistic effect of butorphanol and dexmedetomidine (Kuusela et al., 2000) [15] as propofol and isoflurane provides minimal analgesia (Branson, 2007; Neto et al., 2007) [20] although ketamine provides profound analgesia (Hall et al. 2014) [8]. Butorphanol has strong agonist activity at the kappa and sigma receptors. It exerts its effect by inhibiting the transmission of nociceptive stimulation in the dorsal horn of the spinal cord, activating descending inhibitory pathways, inhibiting supra spinal afferent pathways and causing a decrease in the release of neurotransmitters in the spinal cord (Schnellbacher, 2010) [24]. The analgesic effect by dexmedetomidine is mediated at spinal level and by interruption of nociceptive pathways to the ventral root of the dorsal horn which reduce spinal reflexes (Talukder and Hikasa 2009) [28]. Dexmedetomidine activates α2-adrenergic receptors reducing the transmission of nociceptive signals like substance P (Bekker and Sturaitis, 2005) [4]. Ketamine inhibits ion-channels at the membrane levels and acts on the opioid receptors to exhibit antinociceptive effects (Sleigh et al., 2014; Demirkiran et al., 2002) [26, 6]. The muscle relaxation score were recorded as three in both the groups. All the animals showed excellent muscle relaxation enabling intubation and the surgical procedure. The excellent muscle relaxation observed in all the groups might be due to dexmedetomidine, as all alpha-2 adrenoceptor agonists including dexmedetomidine are known to produce good muscle relaxation (Lemke, 2007) [16] which is attributed to inhibition of intraneuronal transmission of impulses by alpha-2 agonists at the level of central nervous system (Marjorie 2001) [17]. The muscle relaxation might also be enhanced due to butorphanol, propofol and isoflurane as co-administration of anaesthetics, sedatives, hypnotics or opioids with dexmedetomidine is likely to lead to an enhancement of their effects (Naaz and Ozair, 2014) [18]. The animals in both the groups had an abolised palpebral reflex during the procedure and scored as 3. The depth of anaesthesia observed in the present study might be attributed to the synergistic effects of dexmedetomidine and butorphanol with the induction and maintenance agents (Naaz and Ozair, 2014) [18] and it might also be attributed to the action of propofol, isoflurane (Arunkumar et al., 2017b) [3] and ketamine (Hazra et al. 2008). The recovery time (min) were recorded as 6.17±0.59 and 6.68±0.54 in Group A and B, respectively. The shorter recovery time recorded might be due to the shorter duration of sedative action of dexmedetomidine due rapid biotransformation with elimination half life of 47 min (Kuusela et al., 2000) [15]. It might be attributed to rapid redistribution from the brain to other tissues, quick biodegradation of the agents by the hepatic enzyme systems and efficient elimination from plasma by metabolism as described by Watkins et al. (1987) [31] and Zoran et al. (1993) [32]. The shorter recovery with isoflurane might also be due to the reduced percent of isoflurane requirement to maintain adequate plane of anaesthesia which might have caused quick recovery. In both the groups 33.33% animals were recorded with score 3 and 66.66% were recorded with score 4. The smooth recovery observed in the present study might be due to the combined effects of pre-anesthetic and anesthetic agents. The mean values of vaporizer settings (%) for isoflurane were recorded as 1.34±0.06 and 1.28±0.07, respectively in Group A and B. The reduction in the maintenance dose in the present study might be due to the use of dexmedetomidine and butorphanol as pre-anesthetic agents. Reduction in maintenance dose of anaesthetic agent due to use of sedatives and opioids were also reported by various workers. Intravenous injection of butorphanol at dose rate of 0.1 and 0.3 mg/kg reduced the anaesthetic requirement by 11% and 16%, respectively (Trim, 1983) [29]. Similar findings of decreased maintenance dose were also reported by Khan et al. (1999) with dexmedetomidine on isoflurane. Administration of butorphanol alone significantly reduces the MAC of isoflurane in dogs (Ko et al., 2000).

**Conclusion**

Dexmedetomidine and butorphanol premedication significantly reduced the doses of induction and maintenance agents and provides excellent quality anaesthesia for performing major abdominal operation in dogs at the same time keeping the vital parameters within the physiological limit.

**References**


12. Jimenez CP, Mathis A, Mora SS, Brodbelt D, Aibihai H. Evaluation of the quality of the recovery after administration of propofol or alfaxalone for induction of

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