International Journal of Veterinary Sciences and Animal Husbandry 2024; 9(5): 358-362

ISSN: 2456-2912
VET 2024; 9(5): 358-362
© 2024 VET
www.veterinarypaper.com
Received: 09-06-2024
Accepted: 21-07-2024

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A clinical study on evaluation of anesthetic induction protocols for caesarean section in bitches

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Abstract
Two induction protocols *viz.* propofol and etomidate were used for performing caesarean section in bitches possessing viable foetuses. Animals of group I were premedicated with atropine sulphate @ 0.04 mg/Kg SC and butorphanol @ 0.2 mg/kg body weight, 10-15 minutes prior to induction; while animals of group II were given atropine sulphate only. General anaesthesia was induced by administering butorphanol @ 0.2 mg/Kg IV initially, followed by a mean total dose of 4.2 ± 1.10 mg/mL of propofol in group I and 1.58 ± 0.82 mg/mL of etomidate in group II. There is no significant difference between the two groups with respect to mean duration of anaesthesia, extubation time and response to pin prick. Significant difference was observed between the two protocols with respect to the onset of head righting reflex, sternal recumbency and standing position. The isoflurane sparing effect of etomidate is more significant when compared to that of propofol and this result has a direct bearing on the neonatal survival. High APGAR scores were observed in etomidate group when compared to the propofol group. Thus, although both induction agents are safe for both for the maternal and neonatal survival, relatively etomidate is considered as a better induction agent for caesarean section in bitches.

Keywords: Caesarean, bitches, propofol, etomidate, anesthesia

Introduction
During caesarean section in bitches, anaesthesia plays a crucial role in ensuring the safety and well-being of both the dam and the neonates, balancing the adequate analgesia and immobility in the dam while minimizing foetal exposure to anaesthetic agents. During pregnancy, a bitch undergoes a number of significant physiological and anatomical challenges (Pascoe and Moon, 2001 and Claude and Meyer, 2016) [25, 4] and further, any physiological deterioration in the bitch can lead to more pronounced effects in pups (Self, 2019) [33]. Hence, the drugs used for induction and maintenance of general anaesthesia for caesarean section in bitches which must be chosen cautiously. The anaesthetic goal for caesarean section in bitches is similar for all canine surgical patients, *viz.* delivery of the correct agents in a manner to ensure alleviation of pain and consciousness while affording minimal physiologic risk to the patient. Added factors for achieving the above task are the well-being of the foetuses, and a rapid, functional recovery of the dam to encourage appropriate mothering behaviour (Cain and Davidson, 2023) [1].
Induction with inhalant agents is the most commonly associated with struggling with excitement, with a significant risk of regurgitation. Both medetomidine and dexmedetomidine cause significantly decrease the cardiac output, while acepromazine should be avoided in dehydrated and compromised bitches (Moon *et al*., 1998) [19]. Most of the opioids cause respiratory and CNS depression in newly delivered neonates. Epidural anaesthesia/analgesia used alone for CS caesarean section has several disadvantages like hypotension (Kraus, 2016) [11]. Isoflurane or sevoflurane delivered in 100% oxygen reduce the likelihood of puppies spontaneously breathing on delivery (Moon-Massat and Erb, 2002) [20]. Poorly controlled pain in the dam can lead to reduced viability in puppies.
Butorphanol typically produces less sedation and respiratory depression than many of its group. Propofol followed by isoflurane has puppy survival rates equivalent to epidural anaesthesia and is associated with a positive effect on neonatal survival. Use of isoflurane for maintenance of general anaesthesia leads to more rapid recovery of the newly delivered

animals (Hall *et al.*, 2001) [10]. Etomidate has rapid onset, short duration of action, hemodynamic stability and preserves respiratory function and maintains higher levels of oxygenation (Chaudhary *et al.*, 2022) [3], thus, reducing the risk of neonatal depression.

Materials and Methods

A total of 12 full term pregnant bitches which were diagnosed to have with dystocia and referred from the Department of Veterinary Gynaecology and Obstetrics to the Department of Veterinary Surgery and Radiology for caesarean section were considered for the present study. Further, only those bitches with live foetuses were included in the present study, upon confirming viability through the foetal heart rate by transabdominal M-Mode ultrasonography. The bitches with foetal heart rate ranging between 170 and 230 were considered for the present study. The bitches possessing dead foetuses were excluded from the present study.

The bitches of both the groups were premedicated with atropine sulphate @ 0.04 mg/Kg SC, 10-15 minutes prior to induction. General anaesthesia was induced in this group by administering butorphanol @ 0.2 mg/Kg IV initially. Propofol, loaded in another syringe by calculating @ 4 mg/kg was administered to the effect *i.e.* till when the relaxation of jaw muscles was achieved for satisfactory endotracheal intubation. Induction of general anaesthesia in group II was done by injecting etomidate. The syringe was loaded with etomidate after calculating at dose rate of 1 mg/Kg body weight and the drug was administered intravenously to the effect *i.e.* till when the relaxation of jaw muscles was achieved for satisfactory endotracheal intubation. The bitches induced and intubated on the preparation table were moved on to the surgery table. Preoxygenation of the dam was done for one minute prior to turning the isoflurane vaporizer on. General anaesthesia was maintained by connecting the endotracheal tube to the standard small animal anaesthetic machine with a precision vaporizer out of the circuit configuration, fitted with a rebreathing system. Surgical plane of anaesthesia was achieved by administration of isoflurane and oxygen mixture using appropriate machine settings. Upon connection, the oxygen flow rate into the circuit was set as per tidal volume of the animals. The inhalant agent vaporizer output was then set to an initial value of three to five percent for isoflurane. This output was maintained till when the animal reached surgical plane of anaesthesia.

Then, the vaporizer setting was maintained at 0.8 - five percent of isoflurane as per the requirement of the patient. Monitoring of general anaesthesia was done by as per standard norms. The anaesthetic protocols used in the present study have been summarized as following:

Results and Discussion

In the present study, the pregnant bitches were presented at a gestational age of 61 to 67 days and 6-13 hours after the beginning of the labour. The selected pregnant bitches were quickly screened and considered suitable for surgery. None of the bitches under study had a history of vomiting at the time of presentation or during the period of anaesthesia. However, Pascoe and Moon (2001) [25] and Thompson and Rioja (2016) [37] observed delayed gastric emptying, decreased lower oesophageal sphincter tone and regurgitation and aspiration pneumonia in periparturient bitches. The preoperative heart rates recorded an increase in the values when compared to their non-pregnant counterparts. Self (2019) [33] reported that, during pregnancy, the cardiovascular system of bitches exhibited increased preload, increased heart rate and reduced cardiovascular reserve due to the need to supply oxygen to the puppies and the physical exertion involved with parturition.

Fluids were administered @ surgical rate of fluid administration *i.e.* 10 ml/kg body weight as complications like cardiac diseases or hypoproteinaemia were not observed in any of the animals under study. Irrespective of the group, all the animals in the present study, were premedicated with atropine sulphate @ 0.04 mg/Kg SC, 10-15 minutes prior to induction. The heart rate was found increased progressively in both the groups. Salivation was not observed in any of the animals during the entire period of observation in the present study. Premedication with atropine sulphate was recommended for bitches undergoing caesarean section as it inhibited the action of acetylcholine on the muscarinic cholinergic receptors and corrected severe bradycardia secondary to increased vagal tone (Lemke, 2004) [16] and could prevent the development of heart blocks (Vesal *et al.*, 2011) [40]. Raffe (2015) [26] suggested to administer atropine sulphate to the dam if the objective was to increase fetal heart rate, long enough to allow delivery and proper resuscitation. Kantia *et al.* (2022) [14] used atropine sulphate at a dose rate of 0.02 mg/Kg body weight IM in dogs and observed a significant reduction in the induction doses and recovery times.

General anaesthesia was induced by administering butorphanol @ 0.2 mg/Kg IV initially, followed by propofol @ 4 mg/kg in group I; and etomidate at dose rate of 1 mg/Kg body weight in group II, administered to the effect *i.e.* till when the relaxation of jaw muscles was achieved for satisfactory endotracheal intubation. The quality of induction observed in both the groups was assessed objectively through the following parameters. The mean total doses of propofol in group I and etomidate in group II used in the present study were 4.2 ± 1.10 mg/kg of and 1.58 ± 0.82 mg/kg respectively.

Table 2: Drugs and doses employed and the time taken for induction in groups I and II (n=6 in each group)

Groups	Induction agents used	Doses employed (mg/kg)	Time taken for induction (in seconds)	Time taken for intubation (in seconds)
Group I	Propofol	4.2 ± 1.10	73^{a} ± 4.91	118^{a} ± 2.31
Group II	Etomidate	1.58 ± 0.82	65^{b} ± 2.91	102^{b} ± 2.59

In contrast to the findings of the present study, comparatively higher induction doses of propofol *i.e.* 5-8 mg/kg in unpremedicated dogs were used by Glowaski and Wetmore (1999) [9] and 3.32-6.92 mg/kg body weight; while a lesser dose of 2.2 mg/kg body weight was used by Ko *et al.* (2001) [15] Ferreira *et al.* (2015) [7] and Dar *et al.* (2019) [5] in dogs. Saini (2017) [30] and Dar *et al.* (2019) [5] also used etomidate at a rate similar to the present study; while Pablo and Bailey (1999) [24] and Sams *et al.* (2008) [31] used a little higher dose of 2.8 mg/kg in premedicated dogs. The variations in the dose rates can be attributed to the type of preanesthetic used and the physiological status of the animals.

The mean induction times in group I and II were 73 ± 4.91 and 65 ± 2.91 seconds respectively. The mean intubation times in group I and II were 118 ± 2.31 and 102 ± 2.59 seconds respectively. Although both agents used in the present study are good for induction, relatively rapid induction and quick intubation were observed in etomidate group in the present study. Further, etomidate group had a greater number of superior induction scores in the present study.

Table 3: Scores for quality of induction (n=6 in each group)

Score	Quality of induction	Group I		Group II	
		No. of animals	%	Number of animals	%
0	Unacceptable	0	0	0	0
1	Poor	0	0	0	0
2	Fair	0	0	0	0
3	Good	4	66.67	2	33.33
4	Excellent	2	33.33	4	66.67

Hall *et al.* (2001) [10] reported that timely endotracheal intubation after induction with propofol, was challenging in dogs, which could be due to its rapid clearance as explained by Weaver and Raptopoulos (1990) [42]. A smooth induction with propofol with a relatively higher induction time. Contradictory to the findings of the present study, Sams *et al.* (2008) [31] and Dar *et al.* (2019) [5] reported smooth and rapid induction with propofol when compared to that of etomidate. The difficulty experienced at the time of endotracheal tube intubation due to preservation of the laryngeal reflex (Saini, 2017, Liu *et al*., 2018 and Dar *et al.*, 2019) [30, 18, 5] myoclonus and vomiting (Sams *et al.*, 2008) [31] during etomidate induction were not observed in the present study.

The mechanisms of jaw muscle relaxation are different with respect to propofol and etomidate, where in, the former acts at peripheral or central level and could affect any part of the motor pathway, from cortical motor neurons to muscle cells (Ummenhofer *et al*., 1998) [39] while the latter produces hypnosis, amnesia, and inhibition of nociceptive responses through its actions at one class of neuronal ion channels, GABA A receptors (Forman 2011) [8]. In the present study, etomidate group had a greater number of superior scores for the quality of transfer in the present study. This period corresponds to the transit between endotracheal tube intubation and switching of the isoflurane after preoxygenation. During this period, the bitches remained anaesthetized with or without palpebral reflex. Evaluation of general anaesthesia was done by the assessment of the following parameters.

Table 4: Scores for grading the variables of quality of transfer (n=6 in each group)

Score	Quality of transfer	Group I		Group II	
		Number of animals	%	Number of animals	%
0	Unacceptable	0	0	0	0
1	Poor	0	0	0	0
2	Fair	0	0	0	0
3	Good	3	50	1	16.67
4	Excellent	3	50	5	83.33

In the present study, among physiological parameters, the temperature first decreased and then increased non-significantly in both the groups. These findings are in tune with those recorded by Jadon *et al.* (2008) [12] and Cecen *et al.* (2009) [2]. The decreased body temperature could be due to the decrease in the skeletal muscle tone, shivering threshold, vasodilation and impairment of thermoregulatory control as explained by Muir and Gadawski (1998) [22]. Epstein *et al.* (2013) [6] attributed the hypothermia during isoflurane anaesthesia to induction of peripheral vasodilatation and muscle relaxation. In the present study, among haematological parameters, non-significant changes were observed in TEC, Hb, PCV and TLC in both the groups. Among various biochemical parameters estimated in the present study, serum creatinine, blood urea nitrogen and serum albumin showed non-significant variations in both the groups.

In the present study, the volume of isoflurane liquid used was arrived as 19.22 ± 0.39 ml/animal/hour in group I and 15.99 ± 0.29 ml/animal/hour in group II. The difference in the consumption of isoflurane liquid between groups was statistically significant (P<0.05). Hence, isoflurane consumption was observed at a lower level in etomidate group when compared to propofol group. This feature is desirable during anaesthesia in any protocol as all volatile anaesthetic agents cause a dose-related respiratory depression in dogs (Mutoh *et al.*, 1997) [23]. Further, isoflurane is a profound respiratory depressant (Ramankutty, 2008) [27] and it reduces the blood pressure due to decreased peripheral circulatory resistance (Steffey and Howland, 1977) [35].

Table 5: Mean vaporizer setting and total quantity of isoflurane liquid consumed per animal in groups I and II (n=6 each)

	Mean fresh gas flow (mL)	Mean vaporizer* setting (%)	Mean duration of anaesthesia* (minutes)	Saturated gas volume (vol %) For isoflurane	Isoflurane liquid used* (ml/animal/hour)
Group –I	2,535 ± 30.26	3.28 ± 0.57	45.0 ± 0.58	194.7	19.22* ± 0.39
Group –II	2,260 ± 28.35	2.87 ± 0.32	48.0 ± 0.57	194.7	15.99** ± 0.29

During a caesarean section in bitches, the use of isoflurane may expose the foetus to elevated levels of volatile agents, which can impact the central nervous system and in turn, affect neonatal vitality and the overall outcome of the procedure (Wang *et al.*, 2009) [41]. The minimum alveolar concentration of inhalant anaesthetics decreases up to 40% in parturients. Inhalant-sparing techniques such as incision blocks, epidural and parenteral analgesia will help avoid high inhalant concentration and reduce foetal cardiopulmonary and CNS depression Ames (2015) and Raffe (2015) [26].

Significant difference was observed between the two protocols with respect to the onset of head righting reflex, sternal recumbency and standing position. In group I, out of six animals, one animal (16.67) had a score of 2- Fair, four (66.67%) had score of "3-Good" and one (16.66%) had a score of "4-Excellent". In group II, out of six animals, two (33.33%) had a score of "3-Good" and four (66.67%) had a score of "4-Excellent". Objective assessment of recovery also graded etomidate as superior to propofol.

Table 6: Traits of recovery in terms of time lines in groups I and II (n=6 each)

	Duration of anaesthesia (min)	Extubation time (min)	Response to pin prick (min)	Onset of head righting reflex (min)	Sternal recumbency (min)	Standing position (min)
Group I	45 ± 0.58	9.83 ± 0.54	14.83 ± 0.16	23.00^{1} ± 0.58	49.67^{1} ± 0.42	102.16^{1} ± 0.83
Group II	48 ± 0.57	7.50 ± 0.34	11.33 ± 0.21	16.5^{2} ± 0.50	30.17^{2} ± 0.31	86.66^{2} ± 0.84

In the present study, no significant adverse effects were observed in both the groups. However, the bitches in group I, induced with butorphanol and propofol showed transient changes like apnoea, occasional and transient tachycardia and

decreased diastolic pressure that became normal within one minute were observed. Similar to the findings of the present study in group I, apnoea was also observed by Lerche *et al.* (2000) [17], Stegmann and Bester (2001) [36], Dar *et al.* (2019) [5] and Jones *et al.* (2021) [13]; while Sano *et al.* (2003) [32] documented apnoea and tachycardia in dogs, when propofol was used for induction. The side effects of etomidate induction like excitement, myoclonus, pain on injection, vomiting, and apnoea during induction (Muir and Mason, 1989, Sams *et al.*, 2008, Rodriguez *et al.*, 2012) [21, 31, 29] superficial thrombophlebitis (Reves, 2005) [28], difficulty at the time of endotracheal tube intubation due to preservation of laryngeal reflex regurgitation and hypersalivation (Dar *et al.*, 2019) [5] and gagging (Jones *et al.*, 2021) [13] were not observed in the present study. The side effects of individual drugs could be mitigated in the present study due to use of the induction agents at lower doses and their dose sparing effect on isoflurane.

Conclusion

1. When caesarean section in bitches is opted, the selection of the induction agents must be based on the M-mode ultrasonographic screening of the foetal heart rate and those with 170-230 must be given either butorphanol-propofol or etomidate.
2. The pre-surgical preparations should be finished before inducing the anaesthesia.
3. There is no significant difference between the two groups with respect to mean duration of anaesthesia, extubation time and response to pin prick. Significant difference was observed between the two protocols with respect to the onset of head righting reflex, sternal recumbency and standing position.
4. The isoflurane sparing effect of etomidate is more significant when compared to that of propofol and this result has a direct bearing on the neonatal survival.
5. Thus, although both induction agents are safe for both for the maternal and neonatal survival, relatively etomidate is considered as a better induction agent for caesarean section in bitches.

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How to Cite This Article
Sreedhar N, Prasad VD, Sreenu M, Srinivas M, Ravindra DS. A clinical study on evaluation of anesthetic induction protocols for caesarean section in bitches. International Journal of Veterinary Sciences and Animal Husbandry. 2024;9(5):358-362.

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