

Case Report

Comparing the Clinical Efficacy of Mifepristone and Misoprostol Treatment Protocol for Induction of Parturition in Bitches

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ABSTRACT

Successful management of parturition induction is a challenging task in canine. This study made to assess the efficacy of antiprogesteragen mifepristone and prostaglandin misoprostol in induction of parturition in bitches. Total of 11 pregnant bitches with gestational age of more than 62 days confirmed by ultrasound scanning and not showing any sings of initiation of parturition were selected. Induction of parturition was initiated by mifepristone (3 mg/ kg b wt PO) twice a day or a combination of mifepristone (3 mg/ kg b wt PO) and misoprostol (200 µg for < 20 kg, 400 µg for > 20 kg b wt, i/vg) 12 h after second dose of mifepristone. The combination of both drugs mifepristone and misoprostol was more effective for parturition induction.

Keywords: Mifeioristone, Misoprostol, Pregnancy termination

It is frequently challenging to forecast the whelping date due to variations in ovulation timing, several breeding dates, and the prolonged survival of canine spermatozoa in the uterus. Due to numerous demands from worried dog owners, veterinarians are frequently under pressure to perform Caesarean sections, especially in valuable pregnancies (Reddy *et al.* 2014). Therefore, a key area of research in canine reproduction is the search for a safe and effective strategy for inducing whelping in bitches. For a pregnancy to persist, progesterone is essential. During pregnancy, the corpora lutea in dogs serve as the principal source of progesterone prior to the start of parturition, and plasma progesterone levels markedly decline as myometrial activity rises (Papa *et al.* 2020). Even though the causes of luteolysis are yet unknown, the abrupt drop in plasma

progesterone levels may be regarded as crucial for good whelping (Hoffmann, 1994). Aglepristone and mifepristone, progesterone receptor blockers, are competitive antagonists of the P4 receptor (Baan *et al.* 2005; Parmar *et al.* 2020). Misoprostol causes cervical ripening with softening and dilation of the cervix (Stephenson and Wing, 2015). Hence the objective of this study was to assess the efficacy of mifepristone single or in combination with misoprostol in induction of parturition in bitches.

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MATERIALS AND METHODS

Total 11 healthy full term pregnant bitches, with age ranging from 1.5 to 5 years and body weight ranging from 10.8 to 35.7 kg were used in this study at Sneh Vet lab and Clinic Bhadra, Bhiwani, Haryana, India. All bitches were examined for general status and history of mating. All bitches were subjected for X- ray examination to know the number of fetus and confirmation of pregnancy. The day of mating was considered to be day 0 of gestation. After the completion of the gestation period, bitches were also examined by ultrasonography for finding of live or dead fetuses. All the bitches were in normal pregnancy. In Group 1 (n=6) bitches were given Mifepristone 3 mg/kg body weight twice a day orally and misoprostol @ 200 µg for bitches with ≤ 20 kg body weight and 400 µg for bitches with > 20 kg body weight intra-vaginally 12 h after the second dose of mifepristone to induce the parturition. Animals of Group 2 (n=5) were given only the Mifepristone 3 mg/kg body weight twice a day till until the first pup was born. In some animals oxytocin was also used during whelping to enhance the process. Animals were monitored for the initiation and completion of whelping and complications, if any.

Blood samples were collected before treatment and 12 h after mifepristone treatment to assess serum progesterone profile by ELISA Technique. The data were expressed as mean ± SEs and were compared by student's 't' test.

RESULTS AND DISCUSSION

In the present study, after 2 to 3 days of treatment all the bitches whelped normally. Progesterone

concentration measured before treatment was on average 11.7 ± 0.89 ng/ml and 10.95 ± 0.50 ng/ml in group 1 and group 2, respectively, while 12 h after the treatment progesterone values were 4.27 ± 0.58 ng/ml and 4.69 ± 0.46 ng/ml in group 1 and group 2, respectively, which did not differ significantly between groups, though reduced highly significantly ($P < 0.01$) after treatment in both the groups (Table 1, 2). Mifepristone inhibits endogenous progesterone, sensitizing the uterus to prostaglandin contractile action (Sandhu, 2016), while Misoprostol is a synthetic prostaglandin E1 analog that selectively binds to EP2/EP3 receptors, it relaxes the cervix and stimulates uterine contractions (Weeks and Faundes, 2007). Expulsion of the first pup occurred between 21 and 40 h after the first treatment with mifepristone. Bitches in Group 1 (26.66 ± 2.30 h) had a significantly ($P < 0.05$) shorter average duration of onset of parturition than group 2 (33.2 ± 1.62 h). Thus, a combination of mifepristone and misoprostol was more effective than single mifepristone. These results agreed with Peetala *et al.* (2019). Furthermore, parturition happened within a rather shorter and predictable treatment period with mifepristone and misoprostol. Along with the treatment, oxytocin was used in some bitches to complete the parturition (Table 1, 2). In a study, mifepristone was given orally 57 days after mating until the first pup was born. Parturition occurred between 26 and 70 h following the initial therapy, with plasma progesterone levels ranging from 8.6 to 29.6 nmol/l (Van der Weyden *et al.*, 1989). The gestation length of the bitches with lower progesterone values was shorter than that of the bitches having higher progesterone values. Baan *et al.* (2005) also used oxytocin for expulsion of fetus

Table 1: Progesterone concentration and time of onset of parturition in bitches induced to parturite with mifepristone and misoprostol combination

Sl. No.	P4 before treatment (ng/ml)	P4 after 12 h of treatment (ng/ml)	Onset of parturition after treatment (h)	Oxytocin (IU) used during parturition
1	12.11	5.45	36	40
2	14.54	6.64	30	20
3	11.67	3.54	24	10
4	8.65	3.65	22	NA
5	9.78	2.99	21	NA
6	13.45	3.35	27	NA
Mean ± SE	11.7 ± 0.89	4.27 ± 0.58	26.66 ± 2.30	13.33

NA = Not used.



Table 2: Progesterone concentration and time of onset of parturition in bitches induced to parturite with mifepristone alone

Sl. No.	P4 before treatment (ng/ml)	P4 after 12 h of treatment (ng/ml)	Onset of parturition after treatment (h)	Oxytocin (IU) used during parturition
1	11.33	6.22	40	40
2	11.55	4.88	36	20
3	9.33	3.98	30	10
4	10.35	4.35	32	20
5	12.22	3.55	30	NA
Mean ± SE	10.95 ± 0.50	4.69 ± 0.46	33.2 ± 1.62	12.55

along with mifepristone. Parmar *et al.* (2020) also successfully used coprostenol and cabergolin in terminating mismated pregnancies in bitches.

In our study, the side effects from the mifepristone treatments were observed in three treated bitches as a slight depression and anorexia, which disappeared without any treatment. There were no complex side effects found in any of the bitches, which has previously been documented in dogs and cats (Galac, 2004). Very comparable results were also reported by Parmar *et al.* (2020) using coprostenol and cabergolin in terminating mismated pregnancies in bitches.

CONCLUSION

The progesterone-receptor blockers mifepristone and misoprostol were used to successfully induce parturition in 11 healthy bitches. Whelping started within a short and predictable time span. The combination of mifepristone and misoprostol was more effective for induction of canine parturition.

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