# EVALUATION OF THERAPEUTIC PROTOCOLS FOR INDUCTION OF WHELPING IN BITCHES

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## ABSTRACT

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A total of 29 full term pregnant bitches not showing signs of whelping were utilized for induction. The mean duration of time interval from starting of treatment to beginning of whelping, duration of whelping and inter pup intervals (in hours) were 34.46 ± 4.70, 8.17 ± 1.52 and 3.20 ± 1.04 respectively in cloprostenol group, 40.48 ± 6.47, 4.22 ± 0.80 and 1.13 ± 0.18 respectively in dinoprostone plus cloprostenol group and 26.98 ± 4.51, 5.9 ± 1.43 and 1.02 ± 0.16 in mifepristone plus cloprostenol group. Duration of whelping was 8.34 ± 0.40 and inter pup interval was 1.31 ± 0.13 hrs in the control group. Whelping was induced successfully in three treatment groups, but dinoprostone plus cloprostenol was a better protocol because it required less obstetrical assistance, shorter duration of whelping. Followed by mifepristone plus cloprostenol group and cloprostenol group.

Keywords: Whelping; Cloprostenol; Dinoprostone; Mifepristone; Induction.

Progesterone is necessary for maintaining pregnancy in mammals (Heap et al., 1997). In dogs, Progesterone is secreted only from the corpus luteum (Tsutsui et al., 1989). In bitches whelping takes place with an average gestation length of 61.4 days, when bitch are mated once on the guidance of the preovulatory increase of the plasma progesterone concentration (Okkens et al., 2001). One to two days prior to whelping, plasma progesterone concentration decreases rapidly (Vander Weyden et al 1989). As a result of deceases in progesterone and rise in $PGF_{2\alpha}$ concentration, myometrial activity gradually increases, which leads to onset of whelping. It remains unclear which signal(s) trigger(s) these hormonal changes associated with whelping in bitches. In bitches whelping dates are difficult to predict due to lot of variation in ovulation time. Prolonged gestation in single or two pup pregnancy leads to foetal over size resulting in dystocia. Once dystocia ensues, medical treatment and obstetrical assistance may not suffice necessitating caesarean section. Caesarean section invariably involves anaesthetic surgical risk, expensive and leads to unsatisfactory pup survival rate, often due to use of improper anaesthetic protocols. These complications can be avoided by medical induction of whelping. The literature is scanty on this aspect. Therefore, the efficacy of different protocols for induction of whelping in full term bitches in ensuing safe delivery of pups was also assessed as part of the present study.

Clinical cases of 29 bitches of different breeds and age groups presented to the Teaching Veterinary Hospitals of College of Veterinary Science, Rajendrannagar, Hyderabad (AP) with history of more than 60 days from last mating, but not showing any signs of whelping were utilized for medical induction of parturition. This study was carried out from October

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2007 to May 2009. Pregnancy in these bitches was confirmed by ultrasonography using a B- mode ultrasound scanner ( Esaote piemedical Benelux B.V., P.O.Box 1132,6201 BC, Maastricht) with a 5 MHz linear transabdominal transducer. Gestational age was estimated by correlating the crown rump length and cardiac diameter with the standard graph recommended by Khan (2004). A standard lateral abdominal radiograph was obtained not only to confirm pregnancy, but also to count the number of fetuses and to assess approximate fetal age by looking at their teeth and other bones growth.

The bitches were randomly distributed into four groups: Group1 (n =6) bitches were treated with cloprostenol 2.5ug/kg b wt, sc (Vetmate 2 ml vial each ml contains 250ug cloprostenol, Vetcare, Bangalore, 560 106, India), Atropine Sulphate 0.04 mg/kg b wt, sc (Tropine 1ml ampoule contains 0.6mg Atropine sulphate) 10- 15 minutes prior to cloprostenol administration. Bitches in Group 2 (n= 10) were administered dinoprostone gel 0.5mg (Cerviprime gel contains 0.5mg of dinoprostone in 3gm base, its supplied in a syringe with detachable plastic nozzle, Astrazeneca Pharma India Limited, 12th Mile, Bellary Road, Banalore, India) intra cervical and anterior portion of vagina by using the syringe and the plastic nozzle supplied with the packing. Following this cloprostenol and atropine sulphate was administered in the same manner as in the Group1. Group 3 (n=7) bitches were treated with mifepristone 10mg /kg b wt po ( MT Pill , each tablet contains 200 mg mifepristone, Cipla Ltd., Kumrek, Rangpo Sikkim – 737132, India.) as a single dose. If the bitch did not whelp within 24 hours, cloprostenol and atropine sulphate was administered in the same manner as in the Group 1. Group 4 (n=6) bitches which had a normal whelping were kept as untreated control.

Bitches selected for induction of whelping protocols were monitored at six hours intervals until the appearance of signs of whelping and thereafter continuously monitored until the completion of whelping. Side effects of the treatment, whelping signs and delivery time of the pups were recorded; numbers of fetuses delivered were counted. Duration of parturition was calculated for polytocous bitches only, as the time interval from the delivery of first pup to delivery of last pup. Inter pup interval was calculated by dividing the duration of parturition with number of pups born minus one and it is expressed in hours.

If parturition did not precede a standard intervention protocol like vaginal exploration, manual traction, injection of oxytocin, calcium borogluconate and dextrose 25% administration was applied as reported by Baan et al., (2005). Water consumption was monitored in all the four groups from beginning of treatment to until completion of whelping. Duration of lochia, colour and smell of lochia was observed after whelping. The data collected were subjected to statistical analysis by ANOVA (Snedecor and Cocheron, 1989).

In this study, whelping was induced in all (100%) bitches. The time required from the start of treatment to beginning of whelping, duration of whelping and inter pup intervals are shown in Table. Statistical analysis revealed that there was no significant difference among the three treatment groups ($P > 0.05$). In mifepristone plus cloprostenol group, three out of seven bitches delivered within 24 hours of administration of mifepristone alone. Four bitches which did not whelp with mifepristone alone were administered cloprostenol.

Mean interval from treatment to induction was longer in dinoprostone plus cloprostenol group followed by cloprostenol group and mifepristone plus cloprostenol group. Statistical analysis revealed that dinoprostone plus cloprostenol group has taken significantly ($P<0.05$) short whelping duration followed by mifepristone plus cloprostenol group. Cloprostenol group had similar whelping duration as in control group (Table). Procedures for the induction of whelping in the bitch in contrast to other domestic species have not been well documented. The drugs used to induce whelping in bitches should be able to cause regression of the corpus luteum, so that the progesterone level decreased to basal levels as in normal parturition. In this study, cloprostenol was used either alone or in combination with mifepristone or dinoprostone to induce whelping in bitches, so that it will regress the corpus luteum and decrease the

progesterone level as a result parturition was initiated in treated bitches.

In cloprostenol group, the mean interval between treatment and induction of whelping was in agreement with the findings of Tsutsui et al. (1989) and Meier and Wright (2000) who recorded 32 to 38 hrs intervals from starting of treatment to induction of whelping. Whereas, Williams et al. (1999) observed longer interval between treatment and induction (i.e. 47.6 hrs) than the present study with administering the cloprostenol using mini osmotic pump until the end of whelping, it might have down regulated prostaglandin receptors. In natural whelping, increase of prostaglandin concentration was only for a short period before whelping. Similarly Merier and Wright (2000) also reported longer duration of whelping (15±2.2 hrs) than the present study.

In dinoprostone plus cloprostenol group with the combination of these two drugs facilitated whelping like a normal whelping. $PGE_2$ plays an important role in the complex set of biochemical and structural alterations involved in cervical ripening. In contrast to the findings of this study Tan et al (2007) and Perry and Leaphart (2007) reported 41.9 to 93 per cent of vaginal delivery in women within 11.5 to 24 hrs after starting of treatment with dinoprostone gel or pessary alone. This may be due to variation in specie, size of the fetus and presence of multiple fetuses in bitch, when compared to the single fetus in women.

Results of mifepristone plus cloprostenol group were in accordance with the findings of Vander Weyden et al. (1989). Nohr et al. (1993) who reported induction of whelping in bitches after 56 days of pregnancy with mifepristone, the induction interval was between 26 and 76 hrs. similar findings also recorded by Fieni et al. (2001) and Meier and Wright (2000). Font Bonne et al. (2008) induced parturition in bitches with two doses of aglepristone at 24 hrs interval, the induction interval was 25 to 32 hrs, the mean expulsion duration was 4.5 to 9.6 hrs and the mean inter pup interval ranged from 1 to 2 hrs. Mifepristone is a progesterone receptor blocker, this will block the progesterone receptors of the uterus, it will remove the progesterone blocking effect on the uterus as a result uterine contractions are initiated and parturition takes place in bitch.

The inter pup interval in the cloprostenol group was significantly ($P<0.05$) longer than the control group. But there was no significant difference between dinoprostone plus cloprostenol group, mifepristone plus cloprostenol group and control group (Table). No significant difference was observed between the therapeutic group and control groups with regarding duration of lochial discharge. The mean number of obstetrical assistances required during the delivery was 1.5, 0.8, 0.86 and 1.5 times in treatment and control groups, respectively. Similar types of obstetrical interventions were used by Baan et al. (2005). The incidence of monotocous, bitocous, and polytocus bitches in treatment groups were 21.7, 13.04 and 65.22 per cent respectively. The monotocous and bitocous pregnancies may responsible for prolonged gestation.

More quantity of water consumption was observed in cloprostenol group followed by dinoprostone plus cloprostenol group, it was statistically significant ($P< 0.05$). Where, control and mifepristone plus cloprostenol group had no significant difference in water consumption. Polydypsia in bitches as observed in the present investigation was similar to the findings of Meier and Wright (2000) during the administration of $PGF_{2\alpha}$. Polydypsia was most likely due to renal effect of $PGF_{2\alpha}$ (Zook and Strandhoy, 1981). Prostaglandin affect kidney function by inhibiting vasopressin mediated water reabsorption, which result in formation of isotonic urine (Anderson et al., 1975).

The present study concluded that the induction of whelping protocols such as dinoprostone plus cloprostenol group and followed by mifepristone plus cloprostenol group have better induction efficiency. The mean duration of whelping and mean interval was better in these groups. Hence, dinoprostone plus cloprostenol followed by mifepristone plus cloprostenol combinations were found to be better choice for induction of whelping in bitches.

**TABLE. THERAPEUTIC EFFICACY OF VARIOUS PROTOCOLS FOR INDUCTION OF WHELPING IN BITCHES**

| S.No | Parameters | Therapeutic groups | | | |
|---|---|---|---|---|---|
| | | Cloprostenol | Dinoprostone + Cloprostenol | Mifepristone + Cloprostenol | Control |
| 1 | Interval between treatment and induction (hrs) | 34.46 ± 4.7 (6) | 40.48 ± 6.47 (10) | 26.98 ± 4.51 (7) | - |
| 2 | Duration of whelping (hrs) | 8.17± 1.52 $^{c}$ (5) | 4.22 ± 0.80 $^{a}$ (8) | 5.9 ±1.43 $^{b}$ (5) | 8.34± 0.40$^{c}$ (6) |
| 3 | Inter pup interval | 3.20± 1.04$^{b}$ | 1.13±0.18 $^{a}$ | 1.02±0.16 $^{a}$ | 1.31±0.13$^{a}$ |

Means bearing different superscripts row wise differed significantly. (P<0.05); Figures in parenthesis indicate number of bitches selected for treatment.

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