

COMBINATION OF ANTI-PROLACTIN AND LUTEOLYTIC DRUGS FOR MEDICAL TERMINATION OF MID-TERM PREGNANCY IN QUEEN CATS

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ABSTRACT

Twelve pregnant queen cats grouped under gestational age of 30-42 days of pregnancy (based on ultrasonography) were assigned to two treatments: Group I (n=6) with cabergoline (15µg/kg, daily, orally) combined with cloprostenol (5µg/kg, S/C) at 24 hours interval and Group II (n=6) with cabergoline (15µg/kg, daily, orally) combined with cloprostenol (5µg/kg, S/C) at 48 hours interval till complete resorption or expulsion of all the foetuses. The time taken for complete resorption of all the foetuses in both the groups were recorded as <3, 3 to <6 and 6 to 8 days. Results revealed that no queen cat had completed resorption within 3 days in both the groups but earlier completion of termination was noticed in the queens where PGF_{2α} was administered at 24 h when compared to 48 h interval. Medical termination of pregnancy has more demand in feline practice due to higher incidence of unwanted pregnancy in this species and use of combined therapy (cabergoline+cloprostenol) for the same is efficient in inducing complete foetal resorption.

Keywords: Anti prolactin, Medical termination, PGF_{2α}, Queen cat

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Mismating or unplanned mating is a common clinical problem in sexually matured queen cats because of their free roaming nature inspite of being domesticated. Hence, medical termination of pregnancy (MTP) becomes a frequent request from the cat owners (Eilts, 2002) to offload the unwanted pregnancy as ovariohysterectomy (OHE) becomes unethical during pregnancy. MTP in cats is more common during mid-gestation because the animal is usually presented for examination only when abdominal enlargement is noted after successful mating following estrus (Fieni *et al.*, 2006). Protocols to induce mid-pregnancy termination in cats are derived from those used for canine, including administration of prostaglandins (Nachreiner and Marple, 1974; Baldwin *et al.*, 2000) or anti-prolactin (Jöchle and Jöchle, 1988) or a combination of both (Onclin and Versteegen, 1997). The objective of this study was to demonstrate the effectiveness of PGF_{2α} at two different frequencies in mid-term pregnant cats with administration of same cabergoline dose in both the groups.

MATERIALS AND METHODS

The study utilized 12 non-descript cats aged between 8 months to 3 years. All cats were well-housed and maintained under both commercial and homemade food but had the habit of free roaming too. The queen cats were presented with the common history of abdominal distension and cessation of estrus. Before treatments were started, pregnancies were confirmed and their duration was calculated based on ultrasonographic examination. Criteria for positive pregnancy diagnosis were detection of echogenic gestational sacs and foetal heart beats. The

pregnant queens were falling under mid-term gestation (30-42 days) and were divided into two groups with six queen cats in each group.

The group I and II queen cats were administered with injection cloprostenol (@ 5µg/kg, S/C) at 24 and 48 h interval, respectively and apart from this, the queen cats of both the groups received Tab. Cabergoline (15µg/kg, P.O., BID) till complete resorption or expulsion of all the foetuses. To monitor the effect of treatment on pregnancy, periodical ultrasonographic examinations were performed once in every two days. The general condition along with the presence and character of vaginal discharge were recorded before performing ultrasonography.

Statistical analysis: Comparison between the duration of foetal resorption and the frequency of prostaglandin administration was achieved using Chi-square test since the sample size was less than 30. Since the values in the expected frequency table were less than 5, Yate's correction was applied. Results were considered non-significant at P>0.05.

RESULTS AND DISCUSSION

Ultrasonographic examination of all queen cats during mid-pregnancy showed that the foetuses were alive and the number ranged from 1 to 5 (mean 4.5). In both the groups, haemorrhagic-brown vaginal discharge was observed following treatment. Time taken for complete resorption of all the foetuses in both the groups were recorded as <3, 3 to <6 and 6 to 8 days. Results revealed that no queen cat has completed resorption within 3 days in both the groups. About 66.66 (4/6) and 50.00 (3/6) per cent

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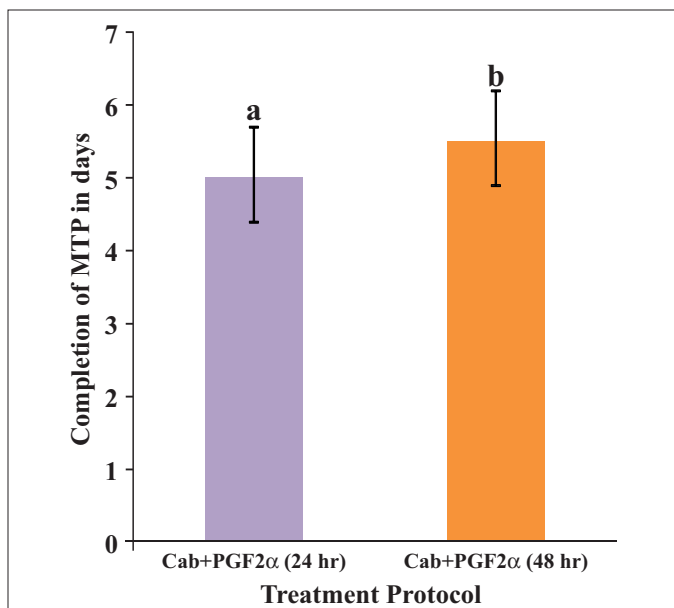


Fig. 1. Duration of complete foetal resorption between Group I and II queen cats of groups I and II, respectively, have completed resorption within 6 days and 33.33 (2/6) and 50.00 (3/3) per cent queen cats of groups I and II, respectively, have completed resorption between 6-8 days.

Mean duration of complete MTP, defined as the time span from first occurrence of vaginal bleeding to resorption of all foetuses, differed in both the groups though the difference was not statistically significant (Fig. 1 and Table 1).

Foetal resorption or abortion was monitored by ultrasonography in all the twelve queen cats. The process of foetal resorption was evident from indistinct appearance



Fig. 2. GA~32days



Fig. 3. GA~41days

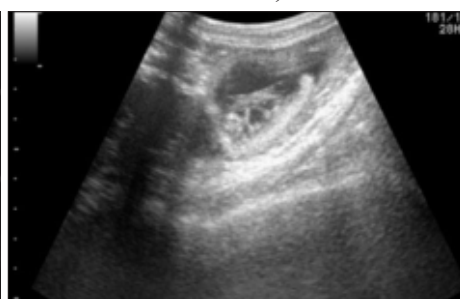


Fig. 4. Initiation of resorption



Fig. 5. Partially resorbed foetus

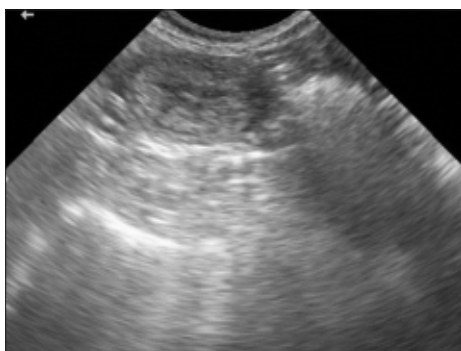


Fig. 6. Foetal remnants



Fig. 7. Empty gestational sac

Table 1
Fetal resorption in treatment groups

Groups	Duration of fetal resorption in days (% of queens showing MTP)			Completion of MTP in all queens (mean±SE)
	<3	3 to <6	6 to 8	
Group I	0	66.66 (4/6)	33.33 (2/6)	5.0±0.68 ^a
Group II	0	50.00 (3/6)	50.00 (3/6)	5.5±0.62 ^b

Values with different superscript differ significantly (P<0.05)
Values in parenthesis indicate number of animals

of foetuses, absence of heartbeats and disappearance of anechoic foetal sacs (Fig. 2 to 7). The primitive signs of foetal resorption often started in one or two foetuses which then subsequently spread to the remaining foetuses. Upon medication, adverse effects like vomiting, restlessness and diarrhoea were rarely exhibited by few cats.

The present study demonstrated that MTP was earlier in the queen cats where PGF_{2α} was administered at 24 h when compared to 48 h interval (Fig. 1) and complete resorption of all foetuses in both the groups has taken 6-8 days. Subramani *et al.* (2016) reported 100 per cent resorption of all the foetuses within 5 days using combination protocol for MTP. In the present report, the reduced percentage (66.66 and 50) of queens showing complete resorption of all the foetuses within 5 days of combination protocol might be because, most of the queen cats selected were in their advanced stages of gestation. The idea for use of combination protocol for MTP in this study was derived from many literatures where 100 per cent results have been achieved in termination of pregnancy (Onclin and Verstegen, 1997; Rangasamy *et al.*, 2016). As far as queen cats are concerned, maintenance of

pregnancy is dependent on ovarian or placental progesterone production. So any MTP protocol in cats must include those agents that directly or indirectly cause luteolysis thereby preventing normal attachment and development of the conceptus. The resulting alteration in the placental synthesis of progesterone causes evacuation of the uterine contents (Olson *et al.*, 1992).

The cascade of Corpus Luteum (CL) regression brought by PGF_{2α} includes both functional luteolysis and structural luteolysis. Structural luteolysis is caused by the shunting of blood flow away from CL along with membrane breakdown and decreased fluidity of the luteal cells. Functional luteolytic action of PGF_{2α} is its interference with the gonadotropin effect on the luteal cells. As a result, the ability of luteal cells to mobilise endogenous cholesterol for progesterone synthesis is blocked (Clark and Myatt, 2008; Jonczyk *et al.*, 2019). The uterotonic effect of PGF_{2α} involves initiation of myometrial contractions by acting as calcium ionophores. These contractions are also brought about by formation of gap junctions and through enhancement of electrical conductivity (Egarter and Husslein, 1992).

According to Jöchle (1997), prolactin serves as the essential luteotropic factor for pregnancy maintenance during second trimester in queen cats. Hence, anti-prolactin agents/drugs play a major role in case of MTP in cats during mid-gestation. Commonly used anti-prolactin agents for this purpose are dopamine agonists like bromocriptine and cabergoline. Among the dopamine agonists, cabergoline is highly preferred than bromocriptine because of its longer half-life, lower affinity for D1 receptors and stronger stimulation of 5HT_{2B} receptors. Cabergoline is also found to produce minimal side effects when compared with bromocriptine which may be due to selective affinity for D2 receptors (Krysiak and Okopien, 2015).

Since both progesterone and prolactin were found to be at their peaks at 30-45 days of pregnancy, a combination protocol aiming at the blockage of these two hormones have found to produce high success rates in small animals as far as MTP is concerned (Rangasamy *et al.*, 2016). In addition to the above fact, the present study also insists on the effectiveness of synthetic PGF_{2α} usage at 24hr interval.

However, further study with large experimental group is warranted for conclusive results.

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