Full Length Article

MEDICAL TERMINATION OF PREGNANCY IN THE CATS OF 30-35 DAYS OF GESTATION: EVALUATING THE EFFICACY OF CLOPROSTENOL AND CABERGOLINE

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ABSTRACT

Eighteen queen cats with a history of mis-mating were confirmed pregnant by ultrasound examination and were divided into three groups of six cats each; Group I: Normal pregnancy cats, group II: Cats treated with cloprostenol alone and Group III: Cats that underwent treatment with cloprostenol and cabergoline for medical termination of pregnancy (MTP). Haematobiochemical and ultrasonographic aspects associated with MTP as well as the efficacy of cloprostenol administration alone and its combination with cabergoline in inducing MTP were studied. Ultrasonographic evaluation showed a significant increase in mean heart rate and a decrease in mean gestational sac diameter ($p \leq 0.01$) values after 72 hours of initiation of the MTP treatment. Haematological parameters showed a significant reduction in RBC and PCV values; however, there was a significant increase in WBC and neutrophil values on post-hours treatment. Hence, the use of combined therapy (cloprostenol and cabergoline) can be considered a more effective protocol for MTP than single-drug therapy (cloprostenol) from 30- 35 days of pregnancy in cats.

Keywords: Cloprostenol, Cabergoline, MTP, Mis-mating, Queen cat

Received : 22.02.2024 Revised : 24.04.2024 Accepted : 27.05.2024

INTRODUCTION

Pregnancy termination is a growing concern and demand by many pet owners for various reasons, most commonly to eliminate an unwanted pregnancy or mis-mating. In queens, progesterone produced by corpora lutea(CL) starts increasing from 25–30 days of pregnancy and is necessary for the maintenance of pregnancy until 45–50 days, (Scott, 1970)

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while placenta takes part in the secretion of progesterone from 40-45 days of pregnancy (Malassine and Ferre, 1979). This was further evidenced by Verstegen *et al.* (1993) that bilateral ovariectomy performed before day 50 of pregnancy resulted in abortion in cats. Hence, progesterone sources can be removed from mid- and late-term pregnancy by medical approaches using prostaglandins, dopamine agonists, progesterone receptor antagonists and combinations thereof (Nachreiner and Marple, 1974; Onclin and Verstegen, 1997; Karakas *et al.,* 2019; Verstegen *et al.,* 1993). Further, most queen cats presented for mis-mating treatment might not be pregnant, hence pregnancy confirmation and prediction of gestational age should be done by ultrasound before administration of any abortion-inducing drugs. Hence, the present study was undertaken to investigate the efficacy of cloprostenol alone and its combination with cabergoline for the termination of unwanted pregnancy in queen cats and to study the ultrasonographic and haemato-biochemical changes during the medical termination of pregnancy (MTP).

MATERIALS AND METHODS

Queen cats of different breeds (1 to 5 years) which were presented to the Small Animal Gynaecology unit of Madras Veterinary College, Chennai from March to December 2023 for pregnancy diagnosis after 30-35 days of mis-mating were utilised for this study. The pregnancy was confirmed in queen cats by ultrasonography (EDAN) using a convex probe of 5-7.5 MHz. frequency. Following confirmation of pregnancy, measurements of either the gestational sac or fetal head (depending on the stage of pregnancy) were taken to calculate the gestational age (Nyland and Mattoon , 2002).

A total of 18 pregnant queen cats were selected, of which, 12 cats were subjected to MTP with the concern of the owners. They were randomly divided into three groups. Group I (n=6): Allowed for normal pregnancy without any treatment; Group II (n=6): Cats were subjected for MTP with Inj. Cloprostenol @ 5 microgram/kg, SC once daily and Group III (n=6): Cats were subjected for MTP with Inj. Cloprostenol (5 mcg/kg ; SC) in combination with Tab. Cabergoline @ 15 microgram/kg, orally twice daily. Group II and III cats received the treatment for MTP until complete resorption or expulsion of the foetus took place. In Group I, ultrasonographic monitoring of pregnancy was carried out on alternate days starting from the day of confirmation of pregnancy to 40 – 45 days and in treatment groups, from the day of initiation of treatment until abortion or resorption of foetuses. The efficacy of different treatment protocols was assessed by determining the percentage of resorption and /or expulsion of foetuses in Group II and III cats by the end of the MTP period.

The foetal heart rate, foetal movements and gestational sac diameter were monitored by ultrasonographic examination to ascertain the foetal viability and growth. Blood samples were collected and evaluated for haematology and serum biochemistry parameters in

healthy pregnant cats (Group 1) on the day of confirming pregnancy and after queening and in MTP groups of cats before initiation and after completion of termination treatment. The data collected in the study were analysed using a paired t-test for haematological and serum biochemical parameters with SPSS (20.0 version) statistical software.

RESULTS AND DISCUSSION

Ultrasound examination

The ultrasound monitoring of foetal heart rate in normal pregnancy and MTP groups of cats were presented in Table 1. In the present study, no significant difference was noticed in foetal heart rate in the normal pregnancy group of cats from 30 -35 days of observation in concurrence with the findings of Verstegen *et al.* (1993). On the other hand, the foetal heart rate showed a highly significant ($p \leq 0.01$) increase in both the treatment groups after initiating pregnancy termination compared to the normal pregnancy group. This result was in concurrence with the observation of Blanco *et al.* (2016) in which they opined that acceleration in foetal heart rate could be attributed to increased plasma catecholamines concentration during foetal hypoxia. Further, decreased heart rate recorded 24- 48 hrs before complete abortion or expulsion of a foetus in the MTP group was in accordance with Gil *et al*. (2014)) who stated that foetal stress would have caused the decelerated heart rate. In cats undergoing MTP, a highly significant decrease in gestational sac diameter was observed after initiation of MTP treatment until termination of pregnancy. The reason for this could be due to the loss of foetal fluids and shrinkage of the gestational sac contents as the foetus was about to be expelled or resorbed.

Haematological evaluation

The haematological parameters of healthy pregnant cats (Group I) before and after parturition and MTP groups (Group II and III) before and after termination of pregnancy were presented in Table 2. In normal pregnancy cats, the haemoglobin parameter showed a highly significant ($P<0.01$) reduction in values after queening. The findings of the study showed agreement with Holst *et al.* (2019) who opined that the haemoglobin concentration decreased significantly with time in pregnant bitches due to an increase in plasma volume during pregnancy. However, no significant difference in the haemoglobin value was observed in both MTP groups of cats before and after the termination of pregnancy.

Similarly, values of red blood cells and packed cell volume showed a significant reduction in the normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. The result obtained was similar to the findings of Kaneko *et al.* (1993) where a reduction in RBC was observed in bitches as it approached late gestation and a reduction in PCV was observed due to haemodilution in pregnant women (Ahmed *et al*., 2018). The etiology of pregnancy-associated immune-mediated anaemia remains unclear and the only factor associated with haemolysis or anaemia is the gravid state.

A significant increase in platelet values was noticed in the normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. Kimura and Kotani (2018) also observed a significant increase in platelet count towards late gestation. However, the leucocyte count and neutrophils parameter showed a highly significant increase in values during normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. These changes were similar to the results obtained by Holst *et al* (2019) who explained that the change in WBC count was due to inflammatory changes that occurred during pregnancy.

Serum biochemical estimation

In the present study, a highly significant increase in alkaline phosphatase values was noticed in the normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. This observation was in agreement with Kimura and Kotani (2018) who observed a marked increase in ALP values during pregnancy and after parturition in bitches due to hepatic haematogenesis in canine foetuses. However, other serum biochemical parameters such as glucose, cholesterol, total protein, albumin, calcium, phosphorus, BUN, creatinine, alkaline aminotransferase, total bilirubin and direct bilirubin did not show any significant difference in the normal pregnancy group (G I) and MTP groups (G II and GIII) of cats (Table 3).

Efficacy of different treatment protocols in MTP

The efficacy of different treatment protocols on MTP was presented in Table 4 and Fig. (1A and 1B). The present study revealed that complete termination of pregnancy took place at day 9 of treatment with cloprostenol alone (Group II) while it took a shorter period of day 7 in those cats that were treated with cloprostenol along with cabergoline (Group III). The results were in accordance with the study performed by Onclin and Verstegen (1997) where they observed 100 per cent success rate with cabergoline and cloprostenol from day 30 of pregnancy. Cats treated with cloprostenol for MTP showed a clear functional regression of CL with a sharp decline in progesterone production by fully developed CL (Nachreiner and Marple, 1974). Further, treatment with cabergoline, a dopamine agonist terminates pregnancies in cats by decreasing prolactin concentrations,a luteotropic factor for the maintenance of pregnancy during mid-gestation in queen cats (Maral *et al*., 2004).

RESULTS AND DISCUSSION

Ultrasound examination

The ultrasound monitoring of foetal heart rate in normal pregnancy and MTP groups of cats were presented in Table 1. In the present study, no significant difference was noticed in foetal heart rate in the normal pregnancy group of cats from 30 -35 days of observation in concurrence with the findings of Verstegen *et al.* (1993). On the other hand,

Table 1. Ultrasonography examination of foetal heart rate (Mean ± SE) in normal pregnancy and medical termination of pregnancy in cats

Period of ultrasound evaluation	Foetal Heart rate (Beats /min)			p value
	Normal pregnancy Group I (n=6)	MTP Group II (n=6)	MTP Group III (n=6)	
Day 1	236±6.19	240.33^{QR}±7.36	250.16^{Q}±4.30	**0.99^{NS}**
Day 3	239.00±3.94	248.50^{QR}±6.95	259.66^{R}±4.27	**0.94^{NS}**
Day 5	242.66^{bc}±3.05	253.50^{cbQR}±6.66	179.00^{aP}±5.61	**0.03***
Day 7	249.16^{b}±2.13	124.33^{aP}±55.63	-	**0.00****
Day 9	251.66±1.43	-	-	**-**
p value	**0.79^{NS}**	**0.00****	**0.00****	

^{NS} Non significant (p>0.05); *Significant (p ≤ 0 .05); **Significant (p ≤ 0.01)

Means bearing different smaller case superscript $^{(a,b,c)}$ in each row differ significantly between the groups

Means bearing different uppercase superscript $^{(P,Q,R,S)}$ in each column differ significantly within the groups

the foetal heart rate showed a highly significant (p ≤ 0.01) increase in both the treatment groups after initiating pregnancy termination compared to the normal pregnancy group. This result was in concurrence with the observation of Blanco *et al.* (2016) in which they opined that acceleration in foetal heart rate could be attributed to increased plasma catecholamines concentration during foetal hypoxia. Further, decreased heart rate recorded 24- 48 hrs before complete abortion or expulsion of a foetus in the MTP group was in accordance with Gil *et al*. (2014)) who stated that foetal stress would have caused the decelerated heart rate. In cats undergoing MTP, a highly significant decrease in gestational sac diameter was observed after initiation of MTP treatment until termination of pregnancy. The reason for this could be due to the loss of foetal fluids and shrinkage of the gestational sac contents as the foetus was about to be expelled or resorbed.

Haematological evaluation

The haematological parameters of healthy pregnant cats (Group I) before and after parturition and MTP groups (Group II and III) before and after termination of pregnancy were presented in Table 2. In normal pregnancy cats, the haemoglobin parameter showed a highly significant (P<0.01) reduction in values after queening. The findings of the study showed agreement with Holst *et al.* (2019) who opined that the haemoglobin concentration decreased significantly with time in pregnant bitches

Table 2. Haemogram (Mean ± SE) of normal pregnancy and medical termination of pregnancy in cats

Haematological Parameters	Period of evaluation before and after queening/ MTP	Normal pregnancy	MTP		p value
		Group I (n=6)	Group II (n=6)	Group III (n=6)	
Haemoglobin (g/dl)	Before	10.10 ± 0.33	9.46 ± 0.37	10.60±0.65	0.60^{NS}
	After	8.95 ± 0.36	9.40 ± 0.39	10.03 ±0.55	0.77 ^{NS}
	p value	0.01**	0.96^{NS}	0.07 ^{NS}	
Red blood cells (mill/mm^3)	Before	5.11±0.13	4.98±0.11	5.40±0.28	0.87 ^{NS}
	After	4.53±0.17	4.75±0.12	5.09±0.25	0.68 ^{NS}
	p value	0.00**	0.02*	0.00**	
Packed cell volume (per cent)	Before	30.26±1.00	31.76 ± 1.39	31.58 ±1.71	0.77 ^{NS}
	After	27.78±1.64	29.70 ± 1.82	30.71± 1.69	0.66 ^{NS}
	p value	0.04*	0.03*	0.05*	
Platelet (cells/mm^3)	Before	167333.33 ± 12679.82	144333.33 ±18693.43	135500± 10468.21	1.30 ^{NS}
	After	166666.67 ± 14193.11	141500 ± 19004.82	140166.67± 10183.05	1.10 ^{NS}
	P value	0.12^{NS}	0.67^{NS}	2.36^{NS}	
White blood cells (cells/µl)	Before	8266.66 ± 1165.23	9450±1189.60	9683.33±558.22	0.64 ^{NS}
	After	11033±817.58	11566±991.85	11683±650.34	0.91 ^{NS}
	p value	0.01**	0.04*	0.05*	

NS Not Significant

due to an increase in plasma volume during pregnancy. However, no significant difference in the haemoglobin value was observed in both MTP groups of cats before and after the termination of pregnancy.

Similarly, values of red blood cells and packed cell volume showed a significant reduction in the normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. The result obtained was similar to the findings of Kaneko *et al.* (1993) where a reduction in RBC was observed in bitches as it approached late gestation and a reduction in PCV was observed due to haemodilution in pregnant women (Ahmed *et al*., 2018). The etiology of pregnancy-associated immune-mediated anaemia remains unclear and the only factor associated with haemolysis or anaemia is the gravid state.

A significant increase in platelet values was noticed in the normal pregnancy and MTP

Table 3. Serum Biochemistry parameters (Mean±SE) in normal pregnancy and Medical Termination of Pregnancy in cats

Serum Biochemistry Parameters before and after queening/ MTP		Normal pregnancy	MTP		p value
		Group I (n=6)	Group II (n=6)	Group III (n=6)	
Glucose (mg/dl)	Before	84.50±3.11	89.50±4.51	91.17±5.82	0.66^{NS}
	After	81.33±5.42	91.67±4.94	90.00±3.71	0.19^{NS}
	p value	0.93^{NS}	0.40^{NS}	0.56^{NS}	
Cholesterol (mg/dl)	Before	110.66±9.15	123±14.08	144.16±28.77	0.69^{NS}
	After	134.66±11.14	143.66±14.55	176.66±51.08	0.82^{NS}
	p value	1.24^{NS}	0.80^{NS}	0.73^{NS}	
Total protein (g/dl)	Before	7.17±0.41	6.48±0.29	7.30±0.36	0.25^{NS}
	After	6.8±0.29	6.47±0.21	6.97±0.42	0.54^{NS}
	p value	2.14^{NS}	0.06^{NS}	1.95^{NS}	
Albumin (g/dl)	Before	3.07±0.16	3.05±0.34	2.97±0.24	0.95^{NS}
	After	2.67±0.12	2.90±0.20	2.62±0.20	0.49^{NS}
	p value	3.38^{NS}	0.82^{NS}	1.81^{NS}	
Calcium (mg/dl)	Before	9.56±0.36	10.24±0.57	10.52±0.60	0.62^{NS}
	After	8.88±0.36	9.53±0.55	9.67±0.61	0.65^{NS}
	p value	0.98^{NS}	0.97^{NS}	0.96^{NS}	
Phosphorus (mg/dl)	Before	4.96±0.82	4.05±0.76	5.28±0.60	0.64^{NS}
	After	4.72±0.81	3.15±0.48	4.27±0.68	0.65^{NS}
	p value	0.99^{NS}	0.99^{NS}	0.96^{NS}	
Blood urea nitrogen (mg/dl)	Before	23.10^{b}±1.56	15.11^{b}±0.85	17.78^{a}±2.24	0.06^{NS}
	After	26.65±6.44	16.42±1.49	22.38±2.17	0.22^{NS}
	p value	0.61^{NS}	0.79^{NS}	3.61^{NS}	
Creatinine (mg/dl)	Before	1.08± 0.14	1.21± 0.13	1.22± 0.13	0.86^{NS}
	After	1.00±0.14	1.08±0.15	1.10±0.14	0.85^{NS}
	p value	0.97^{NS}	0.97^{NS}	0.94^{NS}	
Alanine amino transferase (IU/L)	Before	109.83±38.67	135.17±26.30	101.67±33.11	0.76^{NS}
	After	92.83±29.36	125.83±25.03	72.50±22.94	0.36^{NS}
	p value	1.65^{NS}	1.33^{NS}	2.46^{NS}	
Alkaline phosphatase (IU/L)	Before	75.33±9.54	133.6±30.06	84.00±25.33	0.99^{NS}
	After	55.83±8.07	54.20±5.76	60.67±10.63	0.12^{NS}
	p value	0.00**	0.00**	0.02*	

Total bilirubin (mg/dl)	Before	1.33±0.39	1.57±0.17	1.24±0.22	**0.68** ^{NS}
	After	1.45±0.19	1.93±0.22	1.62±0.26	**0.34** ^{NS}
	p value	**0.39**^{NS}	**4.40**^{NS}	**1.90**^{NS}	
Direct bilirubin (mg/dl)	Before	0.93±0.38	0.44±0.22	0.11±0.02	**0.10** ^{NS}
	After	0.10±0.02	0.27±0.15	0.12±0.02	**0.30** ^{NS}
	p value	**2.25**^{NS}	**0.83**^{NS}	**0.52**^{NS}	

^{NS} Non significant (p>0.05); *Significant (p ≤ 0 .05); **Significant (p ≤ 0.01)

Table 4. Outcome of medical termination of pregnancy in different treatment groups of queen cats

No. of days cats underwent treatment for MTP	Medical Treatment of Pregnancy in Queen Cats			
	Group II (n=6)		Group III (n=6)	
	Foetal resorption (%)	Foetal expulsion (%)	Foetal resorption (%)	Foetal expulsion (%)
Day 1	0	0	0	0
Day 3	0	0	0	0
Day 5	0	0	16.67	16.67
Day 7	16.67	33.33	0	66.67
Day 9	16.67	33.33	0	0
Total Percent	33.33	66.67	16.67	83.33

Fig. 1A: Representative image showing expelled foetus on 33 days of gestation in a group III cat

Fig. 1B: Representative image showing expelled foetus on 38 days of gestation in a group II cat

groups of cats after queening and termination of pregnancy, respectively. Kimura and Kotani (2018) also observed a significant increase in platelet count towards late gestation. However, the leucocyte count and neutrophils parameter showed a highly significant increase in values during normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. These changes were similar to the results obtained by Holst *et al* (2019) who explained that the change in WBC count was due to inflammatory changes that occurred during pregnancy.

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In the present study, a highly significant increase in alkaline phosphatase values was noticed in the normal pregnancy and MTP groups of cats after queening and termination of pregnancy, respectively. This observation was in agreement with Kimura and Kotani (2018) who observed a marked increase in ALP values during pregnancy and after parturition in bitches due to hepatic haematogenesis in canine foetuses. However, other serum biochemical parameters such as glucose, cholesterol, total protein, albumin, calcium, phosphorus, BUN, creatinine, alkaline aminotransferase, total bilirubin and direct bilirubin did not show any significant difference in the normal pregnancy group (G I) and MTP groups (G II and GIII) of cats (Table 3).

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Thus, it is concluded that the present study where the administration of cloprostenol, a synthetic prostaglandin in combination with cabergoline from 30 to 35 days of pregnancy was effective in inducing abortion or resorption within 7 days of treatment in cats.

ACKNOWLEDGEMENT

The authors thank The Dean, Madras Veterinary College and the Director of Clinics, Tamil Nadu Veterinary and Animal Sciences University, Chennai for facilitating the research work.

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