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Medical termination of pregnancy in canines: A review

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ABSTRACT

Termination of pregnancy may be requested for a variety of reasons, most commonly unwanted mating. Several pharmacological interventions are available to terminate pregnancy in canines, each with distinct advantages and disadvantages with respect to their mechanism and efficacy. No single drug or drug combination currently available can be administered at any stage of gestation while being entirely free of clinical or haematological side effects, avoiding vaginal discharge, preserving future fertility, and remaining both easily available and inexpensive. This review integrates the pharmacological agents used for medical termination of pregnancy (MTP) in the bitch - estrogens, estrogenic compounds, prostaglandins, dopamine agonists, progesterone receptor antagonists, corticosteroids, progesterone synthesis inhibitors, GnRH antagonists, and combination protocols - along with their dosages, mechanisms of action, efficacy and associated side effects, and presents findings from a nationwide survey of canine practitioners in India regarding current clinical practice.

Keywords: Pregnancy termination, Bitch, Aglepristone, Cabergoline, Cloprostenol, Mifepristone, Prostaglandin F2 α

1. Introduction

Intentional interruption of gestation is termed as Medical Termination of Pregnancy (MTP) (Concannon, 2011) [1]. The most common cause for termination is unwanted mating, occurring with an inappropriate mate or at an inappropriate age (Kustritz, 2010) [2]; other indications include pre-existing medical conditions such as pregnancy-associated diabetes mellitus (Concannon, 2011) [1], non-viable pregnancies (England *et al.*, 1992) [3], shelter overpopulation and hereditary-disease prevention (Kutzler, 2005) [4], and owner-related constraints (Kustritz, 2010) [2]. Historically, only surgical removal of the uterus and ovaries was available; pharmacological interventions are now widely used.

Pregnancy must always be confirmed before termination, since administration of these compounds to a non-pregnant animal can cause serious adverse effects. Ultrasonography is the modality of choice, allowing assessment of fetal viability and biometry; radiography is useful only after fetal skeletal calcification, and hormonal assays (progesterone metabolites, relaxin) may also assist (Eilts, 2002) [5]. Canine pregnancy is divided into an early stage (fertilization to implantation, Day 20-22 from the LH peak), a mid stage (implantation to ossification, Day 22-42), and a late stage (ossification to parturition, Day 42-65); estrogens and estrogenic compounds are typically used before implantation, while prostaglandins, dopamine agonists, progesterone receptor antagonists, and corticosteroids are used after implantation (Thangamani *et al.*, 2018) [6].

This review is based on a narrative synthesis of peer-reviewed literature identified through PubMed, ScienceDirect, Google Scholar, and CAB Abstracts (1987-2024), using terms including "pregnancy termination," "mismatching," "abortifacient," and "canine," together with individual drug names. Studies reporting original experimental or clinical data on pregnancy prevention or termination in the domestic dog were included; studies addressing these agents for unrelated indications were excluded unless directly relevant to termination pharmacology.

2. Pharmacological methods for termination of pregnancy

2.1 Estrogens

Estradiol cypionate (ECP), estradiol benzoate (EDB), and diethylstilbestrol (DES) have been used for prevention of pregnancy (Wiebe *et al.*, 2009) [7], with ECP considered the most efficacious (Eilts, 2002) [5]. Estrogens tighten the uterotubal junction, altering oocyte transport and causing implantation failure (Pettersson *et al.*, 2009) [8]; ECP at 44 μ g/kg during estrus prevents pregnancy, but causes pyometra and bone marrow aplasia if given in diestrus (Bowen *et al.*, 1988) [9]. Owing to this toxicity, estrogens are not

longer recommended. Tsutsui *et al.* (2006) [10] showed a single post-ovulatory EDB injection (0.20 mg/kg) completely and dose-dependently prevented pregnancy.

Table 1. Estrogens used for prevention of pregnancy

Drug	Mechanism of Action	Dose & Duration	Results	Side Effects
Estradiol cypionate (ECP)	Tightens uterotubal junction, alters oocyte transport	44 µg/kg, single dose, IM	Prevents pregnancy; most efficacious estrogen	Pyometra, bone marrow aplasia (if given in diestrus)
Estradiol benzoate (EDB)	Same mechanism as ECP	0.20 mg/kg, single post-ovulatory, IM	Complete, dose-dependent prevention	Estrogen-related toxicity
Diethylstilbestrol (DES)	Same mechanism	75 µg/kg PO, 7 days	Historical use only	No longer recommended

2.2 Estrogenic compounds - Tamoxifen

Tamoxifen citrate, an antiestrogen in women, exhibits estrogenic activity in dogs at 1 mg/kg PO BID for 10 days. Given during proestrus, estrus, or early diestrus it completely prevents conception; on day 15 of diestrus it causes partial resorption/abortion, and on day 30 some pregnancies are carried to term (Bowen *et al.*, 1988) [9]. Prolonged use causes vulvar edema, purulent discharge, retinitis, and pyometra (Tavares *et al.*, 2010) [11], so despite its efficacy it is not recommended clinically.

2.3 Prostaglandins

Prostaglandins are luteolytic, uterotonic prostanoids typically given after day 30 of gestation (0.1 mg/kg SC q8h × 2 days, then 0.2 mg/kg q8h until complete), causing vasoconstriction/degeneration of the corpora lutea and conduct myometrial contraction (Lein *et al.*, 1989; Feldman *et al.*, 1993) [13, 12]. Fieni *et al.* (1997) [14] achieved complete termination in 67 bitches using cloprostenol (2.5 µg/kg SC × 3, 48 h apart, from day 30); Hubler *et al.* (1993) [15] described a gradual “25-50-100” µg/kg protocol over 7 days. Comparing agents, Wichtel *et al.* (1990) [16] found PGF_{2α} achieved 100% abortion versus 50% for bromocriptine, with side effects of panting and emesis.

Table 3. Prostaglandin (PGF) and PGF-analogue dosage

Drug	Dose(s)	Day of Pregnancy	Duration
PGF _{2α}	20-200 µg/kg, BID/TID	After Day 15-25	4-7 days or longer
Cloprostenol	2.5 µg/kg SC, TID, q48h	After Day 30	4 days or longer

(Wanke *et al.*, 2002) [17]

2.4 Dopamine agonists

Dopamine agonists suppress prolactin, removing its luteotrophic support and causing corpus luteum lysis (Concannon *et al.*, 1987). Bromocriptine (0.1 mg/kg PO/IM BID × 6 days, after day 30) crosses

the blood-brain barrier and causes aphagia, ataxia, and emesis, which can compromise efficacy. Cabergoline, more D2-selective, is effective at lower doses (5 µg/kg PO × 5 days, or 1.7 µg/kg SC q48h × 6 days, after day 40) with fewer, milder side effects (Onclin *et al.*, 1993, 1995; Post *et al.*, 1988) [18, 19].

Table 4. Comparison of bromocriptine and cabergoline

Feature	Bromocriptine	Cabergoline
Potency	Lower	Higher
D2 selectivity	Lower	Higher
Side effects	More frequent/severe (vomiting)	Fewer, milder
Dosing	BID	SID
Cost	Less expensive	More expensive

(Concannon & Verstegen, 1997; Verstegen *et al.*, 2001)

2.5 Progesterone receptor antagonists (Antiprogestins)

Antiprogestins bind the progesterone receptor, blocking endogenous progesterone and disrupting pregnancy maintenance (Galac *et al.*, 2000) [20]. Aglepristone is licensed in dogs; given before day 25 it prevents pregnancy, and between days 26-45 it terminates pregnancy

within 7 days (10 mg/kg SC, repeated once after 24 h) with 95-100% success and mild, transient side effects (Galac *et al.*, 2000; Pettersson *et al.*, 2009) [20, 8]. Mifepristone, not licensed for veterinary use but used off-label, achieves complete termination within 3-5 days at 2.5 mg/kg PO BID × 4-5 days with no adverse effects reported (Concannon *et al.*, 1990) [21].

Table 5. Antiprogestins used for termination of pregnancy

Drug	Mechanism	Dose & Duration	Result	Side Effects	Reference
Aglepristone	Binds progesterone receptor, blocks endogenous progesterone	10 mg/kg SC, repeat once at 24 h; day 26-45	Termination in 4-8 d; 95-100% success	Mild discharge, transient parturition signs, anorexia	(Galac <i>et al.</i> , 2000; Pettersson & Tidholm, 2009)
Mifepristone (RU-486)	Same mechanism; not vet-licensed	2.5 mg/kg PO BID × 4-5 d	Complete termination in 3-5 d (day 32)	No adverse effects reported	(Concannon <i>et al.</i> , 1990)

2.6 Corticosteroids

Dexamethasone, given orally in mid gestation, is an inexpensive termination option. Wanke *et al.* (1997) [22] terminated 58/62 pregnancies using a tapering BID protocol (200 to 10-20 µg/kg over 7.5-9.5 days). Its mechanism is not fully understood - progesterone decline

may be a direct effect or a consequence of abortion and it causes transient adrenal suppression, polyuria, polydipsia, and milk secretion (Wanke *et al.*, 2002) [17]. Zone *et al.* (1995) [23] confirmed termination in all 20 treated bitches (0.1-0.2 mg/kg BID/TID, tapered), with mild transient side effects.

Table 6. Dexamethasone dosing schedule (µg/kg, 9.5-day protocol)

Time	1	2	3	4	5	6	7	8	9	10
AM	200	200	200	200	200	200	200	120	40	10
PM	200	200	200	200	200	200	160	80	20	-

2.7 Progesterone synthesis inhibitors

Epostane inhibits 3β-hydroxysteroid dehydrogenase delta 6-5 isomerase, reducing progesterone synthesis by the corpus luteum (Kowalewski *et al.*, 2009) [24]. Given at 50 mg/kg/day PO for 7 days from the onset of diestrus, it offers a single-agent oral protocol, though with an increased chance of diestral disorders like mucometra (Thangamani *et al.*, 2018) [6].

2.8 GnRH antagonists

GnRH antagonists rapidly inhibit the gonadal axis (Hull *et al.*, 1987) [25]. Valiente *et al.* (2009) [26] evaluated the third generation antagonist acylene in two different doses (low dose 110 µg/kg or and high dose 300 µg/kg, single SC dose, mid gestation) in 21 bitches at 25-35 days; all treated dogs aborted within 2-12 days, correlating with a marked progesterone decline, with no clinical or haematological side effects and only mild, transient discharge.

2.9 Combination therapies

Table 7. Combination protocols used for termination of pregnancy

Drug	Mechanism of Action	Dose & Duration	Result	Side Effects	Reference
Cabergoline + cloprostenol / alfaprostol	Dopamine agonist (prolactin suppression) + prostaglandin analog (luteolysis)	5-day protocol, starting day 25 or 32 post-LH peak	100% termination, primarily by fetal resorption within 7-8 days; progesterone < 1 ng/mL within 48 h	Severe with cabergoline + alfaprostol; moderate with high-dose cloprostenol; absent with low-dose cloprostenol	(Onclin <i>et al.</i> , 1995)
Cabergoline + double-dose cloprostenol	Dopamine agonist + prostaglandin analog	Cabergoline 5 µg/kg PO daily for 7 days; cloprostenol 1 µg/kg SC on days 1 and 3; 35-45 days post-mating	92.5% termination within 2-4 days	Mild vomiting, nausea, retching, and panting	(Corrada <i>et al.</i> , 2006)
Mifepristone + cabergoline	Antiprogesterin + dopamine agonist	Mifepristone 2.5 µg/kg PO BID for 4 days; cabergoline 5 µg/kg PO for 4 days; 30-35 days post-mating	100% termination within 4-6 days	No side effects	(Chaudhari <i>et al.</i> , 2020)
Cloprostenol + cabergoline	Prostaglandin analog + dopamine agonist	Cloprostenol 2 µg/kg SC; cabergoline 5 µg/kg PO; 3-5 days	100% termination within 3-4 days	Vomiting, mild anorexia, vocalization, tachypnea	(Parmar <i>et al.</i> , 2020)
Aglepristone + intravaginal misoprostol	Antiprogesterin + prostaglandin analog	Misoprostol 200-400 µg intravaginally with aglepristone	Rapid abortion and cervical dilation, 4.5 ± 1.1 days - most effective combination tested	No observable side effects	(Agaoglu <i>et al.</i> , 2011)
Mifepristone + misoprostol	Antiprogesterin + prostaglandin analog	Mifepristone 2.5 mg/kg PO BID; misoprostol 10 µg/kg PO after one mifepristone dose; 30-40 days of gestation	Successful termination in both treated dogs	No side effects	(Jyothi <i>et al.</i> , 2019)

3. Clinical considerations

Confirmation of complete termination is essential, since incomplete uterine evacuation predisposes to retained tissue, metritis, and pyometra; serial ultrasonography every 2-3 days is recommended until resorption/expulsion is confirmed, and owners should be advised to seek attention if discharge becomes purulent or systemic illness develops. Ovariohysterectomy remains the traditional alternative, offering single-procedure permanent sterilization but requiring anesthesia, surgery, and hospitalization while preventing future breeding; pharmacological termination preserves fertility and avoids surgery but requires accurate staging and repeated monitoring. The choice between the two should be individualized based on future breeding intent, owner's comfort, cost, and local availability of the agents discussed above.

4. Survey on MTP practices among Indian canine practitioners

A web-based survey of canine practitioners across states of India, circulated via Google Form, assessed case frequency, common reasons for termination, diagnostic preferences, drug choice, and protocol outcomes. Aglepristone emerged as the most preferred individual drug, and cloprostenol with cabergoline as the preferred combination; mifepristone with misoprostol is an increasingly used combination.

For initiating MTP, the most common indication recorded among various practitioners was "unwanted mating" (90.7%) and the preferred timing was "mid stage of gestation" (43.9%). Out of all diagnostic modalities, 82% of the practitioners preferred "ultrasonography". The effectiveness of the above mentioned protocols was rated as "very high" by the practitioners in their practice with 43.5% of complications and 29.7% systemic side effects.

5. Conclusion

Safe termination of pregnancy in bitches depends on accurate pregnancy diagnosis, appropriate drug selection, and close monitoring. The antiprogesterin aglepristone was the most consistently effective agent, with high reported success rates and minimal side effects, and mifepristone alone is also effective. Combinations of an antiprogesterin (mifepristone) or a prostaglandin (cloprostenol) with the dopamine agonist cabergoline may achieve successful termination with minimal side effects. Continued clinical and field-level research is warranted to identify a protocol effective at any stage of gestation while being free of side effects, preserving future fertility, and remaining affordable and widely accessible.

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