



Misalliance and its Treatment- Medical Termination of Pregancy



Prepared by-

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Mis-mating in the Bitches

- The chances of mis-mating is high.
 - promiscuous behavior of bitches during estrus and longer estrus period.
- Roaming behavior of the estrus bitch, and the tendency to accept male partner increases the chances of mis-mating.
- Though there are several medications to nullify the mis-mating, none of them were found to be effective universally.

Indications

- Prevention of unintended mating at too young or old age.
- Reproductive management of valuable bitches
- Control of the pet overpopulation.
- Prevent birth of non-descript pups.
- Inability of the owner to bear expenses involved with rearing of pups

Therapeutics of mis-mating

A. Estrogens or synthetic estrogenic compounds

- Different preparations of estrogen are used for the treatment of mis-mating or misalliance detected early in bitches.
- Examples: **estradiol valerate, estradiol cypionate, estradiol benzoate, conjugated estrogen and diethyl stilbesterol.**
- **Estrogen interferes the transportation time in the oviduct and tightens the utero-tubal junction, resulting in implantation failure or embryonic death.**
- Estradiol cypionate augments the early transport of the embryo in the oviduct thereby preventing the implantation, and failure of establishment of pregnancy.

Sr. No.	Treatment	Dose and schedule	Advantage	Side effects:
1	Estradiol Valerate (Pregheat)	0.01 mg/kg IM or SC; on 0,3,5,7 day after mating	Early treatment of mis-mating	continuous estrus signs, anorexia, weight loss, Pyometra endometritis and Cystic endometrial hyperplasia,
2	Estradiol cypionate (Estradep, Depoestradiol)	0.02 mg/kg IM not exceeding 2 mg total dose; only once after mating		Prolonged estrogen therapy → Bone marrow depression leading to severe anemia, leucopenia, thrombocytopenia and death
3	Estradiol benzoate (Progynone Depot)	0.2 mg/kg 1msingle injection on 5th day of mating		
4	Conjugated estrogens (Premarin)	1.875mg total dose PO, daily for 3 days within 5 days of mating		

B. Progesterone synthesis inhibitors and Tamoxifen citrate

- The drugs like **Epostane** which inhibits the synthesis of progesterone by blocking the enzyme **β -hydroxy steroid dehydrogenase isomerase (β -HSD)** are also used for the management of mis-mating in the bitches.
- **Tamoxifen citrate** has estrogenic activity in bitches thereby interfering in zygote transport and/or implantation.

Sr. No.	Treatment	Dose and schedule	Advantage	Side effects:
1	Epostane	5 mg/kg body wt. PO for 7 days after mis-mating	Prevents the progesterone synthesis thereby inhibiting the establishment of pregnancy at early stage	Clinical efficacy is not proven
2	Tamoxifen citrate (Novadex, Oncomox, Oncotom)	1 mg/kg body wt. PO BID for 10 days starting on the day of mis-mating	Prevents the establishment of pregnancy at early stage	Ovarian cysts, endometritis, Longer treatment schedule Clinical efficacy is not proven

Advice to pet owners

- Identify the females in estrus early
 - sero-sanguinous vulvar discharge,
 - Increased roaming of the male dogs in the vicinity of the females in estrus.
- Don't loose bitch in estrous to prevent the occurrence of unwanted mating.
- In cases of unwillingness to rear pups then elective ovariohysterectomy at the pre-pubertal age.

Advice to pet owners...

- Provision of adequate nutritious food and fresh water *ad lib* to offset side effects of medication like weakness, or debility
- Follow up of hygienic measures to minimize side effects related to reproductive system.
- Owner may be requested to wait till the confirmation of pregnancy to avoid unnecessary cost and side effects.
- Following confirmation of pregnancy at 25-30 days, termination of pregnancy can be prescribed using **Cabergoline** and **Prostaglandins** combination which are much safer to use.

Medical termination of pregnancy (MTP)

- ✓ Different medications have been used for MTP. Confirmed pregnancy first then treat the bitch to avoid unnecessary cost and side effects.
- ✓ **40% of the mis-mating cases lead to establishment of pregnancy**
- ✓ **60% case remains non-pregnant.**
- ✓ Drugs used = estrogen, prostaglandins, dexamethasone, dopamine agonists, progesterone antagonists, GnRH antagonists, and their combinations have been used depending upon the stage of pregnancy

Indications

- For reproductive management of valuable bitches
- Control of pet over population
- Prevent birth of non-descript pups
- Bitches diagnosed with dead fetus or malformed fetus
- Medical emergency requiring termination of pregnancy in the bitch
- To avoid the unnecessary cost related to maintenance of pregnant bitch and the future pups

Therapeutics of MTP

Prostaglandin and its analogues

- Prostaglandins like Prostaglandins F₂α (**PGF₂α**) and its **synthetic analogues** are used commonly in the bitches for the premature induction of parturition between days 30-53 of the gestation.
- **Natural PGF₂α** is found highly effective for termination of pregnancy in bitches after day 30 of gestation

Sr. No.	Treatment	Dose and schedule	Advantage	Side effects/ Disadvantage
1	Natural PGF2a (Lutalyse)	0.1mg/kg S/CTID for 2 days followed by 0.2 mg S/C TID til termination of pregnancy	Highly effective in inducing whelping	Panting, respiratory distree, hyper salivation defecation, vomition urination
2	Cloprostenol Sodium (Synthetic) Vetmate, Clostenol, Pragma	2.5 mcg /kg IM every 12-24 h till parturition	More specific than natural PGF2a, greater luteolytic effect, low doses	Prolong treatment schedule

- To minimize these side effects related to natural as well as synthetic PGF2 α administration, observe the dog for 30 minutes for any side effects.
- Food should be given to the bitch 1-2 h after the administration of PGF2 α to avoid vomiting.
- To avoid the side effects associated with PGF2 α administration, **atropine sulphate @ 0.04 mg/kg S/C should be given 10-15 min before the administration of PGF2 α .**

Dexamethasone

- Dexamethasone is also used occasionally for the premature induction of parturition in bitches at the mid gestation.
- It results in the **production of estrogen and prostaglandins** in the body by feto-placental unit.

Dopamine agonists

- Prolactin and LH are required for luteotropic action in bitches where LH peak of estrus maintains CL function for approximately 4 weeks and prolactin becomes dominant luteotropic agent during 2nd half of gestation.
- Dopamine agonists are ergot derivative alkaloid compounds that exert anti-prolactinergic effects.

Combination of PGF2 α and dopamine agonists

- The combination of synthetic PGF2 α analogue i.e. **cloprostenol** and dopamine agonist like **Cabergoline** are found to be more effective in the premature termination of pregnancy with minimum or no side effects at all.
- This therapy can be started at day 28 of gestation after confirmation of the pregnancy.

Sr. No.	Treatment	Dose and schedule	Advantage	Side effects/ Disadvantage
1	Dexamethasone	200 mcg/kg body wt. PO for 7 days followed by tapering dose of 10-20 mcg /kg body wt for next 3 days	Less costly, can be administered orally	Long therapy period, immunosuppressive, polydipsia, panting, polyuria
2	Bromocriptine (Bromogen, Parlodel, proctinal)	30-100 mcg/kg b wt. BID PO for 5-6 days starting at 35-40 days		Vomition, inappetance, anorexia, depression, not 100% effective

Sr. No.	Treatment	Dose and schedule	Advantage	Side effects/Disadvantage
3	Cabergoline (cabegolin, Collete)	5 mcg/kg body wt. OD PO for 5-6 days	Few side effect, Long acting	
4	Cloprostenol + Cabergoline	Cloprostenol @ 1 mcg/kg body wt. SC on alternate days 3 times starting at day28 of gestation. Cabergolin @ 5 mcg /kg b wt. OD	Reduces side effect of PG given alone, Increases the efficacy of Dopamine agonists, almost 100% effective	Longer treatment schedule, Sanguinous vaginal discharge

Anti-progesterone therapy

- The application of synthetic steroids which are progesterone receptor antagonists blocking the action of progesterone, for the premature termination of pregnancy in bitches has increased considerably.

Sr. No.	Treatment	Dose and schedule	Advantage	Side effects/ Disadvantage
1	Mifepristone (Mtpill, Unwanted, Mifegest)	2.5 mcg/kg b wt. BID PO for 4-5 days affter day 30 of gestation	Termination occurs mainly by resorption, No major side effect	Effective in around 80% cases

Supportive therapy

- Many side effects associated with medication for mising and MTP.
- Decreased appetite, depression and prolonged therapy schedule leads to immunosuppression and stress on the animal.
- Broad spectrum antibiotics to prevent occurrence of secondary infections.
- Antihistamines like chlorpheniramine maleate
- Multivitamins and multiminerals should be given as supportive therapy
- Vitamin C as a part of anti-stress treatment with appetizers to increase the feed intake and for proper digestion
- Fluid therapy to prevent dehydration and compensate anorectic period of bitch.

Sl. No.	Medicament	Time of therapy	Effective period
1	Estrogen	On the day of mis-mating	5-7 days
2	Epostane	On the day of mis-mating	7 days
3	Tamoxifen citrate	On the day of mis-mating	10 days
4	Aglepristone	Anytime from day of mating to 45 days of gestation	5-7 days
5	PGF _{2α} and its analogues	At day 30 of gestation	5-7 days
6	Dexamethasone	At day 30 of gestation	10 days
7	Dopamine agonists	At 35-40 days of gestation	6-7 days
8	Combination of PGF _{2α} and dopamine agonists	At day 25 of gestation	9 days
9	Mifepristone	After day 30 of gestation	4-5 days
10	GnRH antagonist	After day 30 of gestation	6-7 days

Table 6 Time of therapy and effective period of different treatment regimen used for management of mis-mating and MTP

MTP, Medical termination of pregnancy; PGF_{2α}, Prostaglandin F_{2α}; GnRH, Gonadotropin releasing hormone



THANK YOU