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Review Article

THERAPEUTIC APPROACHES FOR UNWANTED PREGNANCY IN CANINE- A REVIEW

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Abstract: Several pharmacological intervention are there for termination of pregnancy in canine species. Each and every method have its own advantages and disadvantages in their action on termination of pregnancy associated with changes in the general clinical status. Combination of abortifacient drugs gives better results when compared to single drug alone. The present review analyzed different pharmacological drug (abortifacient) and their combination effective on termination of pregnancy. The review provides the reader an overview of the various protocols available for preventing the birth of puppies following unwanted mating (or) pregnancy.

INTRODUCTION

Mismating is a common clinical problem in canine veterinary practice which may arise because dog owners are not aware of the Oestrus status of bitches. Several methods are followed by the veterinarian for termination of unwanted pregnancy in bitches in recent years. Wanke *et al.,* 2002 reported that delay the termination approaches until confirmation of pregnancy, as over half of the animals are unwantedly being treated. Srinivas *et al.,* 2008 reported that termination of pregnancy should be initiated after confirmation of pregnancy by trans-abdominal ultrasonography to avoid treatment of non pregnant bitches with abortifacient agents that cause severe systemic side effects. Ovariohysterectomy (OHE) would be the choice to prevent the birth of puppies following unwanted mating, but for breeding bitches, a need arises to maintain future fertility. So medical termination of pregnancy becomes imperative (Sridevi, 2015).

STAGE OF PREGNANCY PERIOD

Stage 1: *Fertilization to implantation (days 20 to 22 from LH peak)*

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Stage 2: *Implantation to foetal skeletal ossification (40 - 42 days)*

Stage 3: *Foetal skeleton ossification to parturition (42 - 65 days)*

Feldman and Nelson (2004) opined that canine corpora lutea are relatively unresponsive to luteolytic agent during the first 14 -28 days of pregnancy. Stage 2 is considered to be appropriate choice of stage for the veterinarians to perform medical termination of pregnancy effectively.

DIAGNOSIS OF MISMATING

Most of the cases presented to the clinics with the history of coital lock observed by the owner, however many mismated bitches are not always pregnant. Recent reports suggests that among such cases, 90 - 95 percent are positive for pregnancy (Feldman and Nelson, 2004).

The diagnosis is mainly based on Vaginal Exfoliative Cytology (VEC) where in sperm head are present along with superficial and cornified (anuclear) cells for a time period of 24-48 hour post-coital lock, thus confirming the occurrence of mismating. However VEC with the presence of sperm head need not be positive for pregnancy at 30 days of post-breeding. Veterinarians involved in canine practice need a very safe and cost effective method of protocol for termination of an unwanted pregnancy. In ancient days oestrogen compounds are used to terminate the unwanted pregnancy at pre implantation stage itself, but estrogenic compounds produce severe reproductive as well as systemic illness (Bowen et al., 1985) like pyometra, bone marrow destruction, and extend the oestrus when administrated in early luteal diestrual period. On the other way therapy with initial dose doses of prostaglandins compounds in the bitches have to be hospitalized as the severe systemic side effects includes respiratory embracement (respiratory distress and abnormal respiratory movement), panting, excessive salivation, tachycardia, vomiting and reflex defecation. So, the best time to start the treatment for termination of pregnancy was about 30 days post-breeding. Obviously at 30 days post-breeding, there is presence of mature Corpus Luteum (CL) which responds to exogenous abortifacient hormones.

Methods of Termination of Pregnancy:

The desirable properties of exogenous abortifacients that can be used for medical termination of pregnancy includes:

- Interference with implantation process
- Alter the endocrine environment
- Induce resorption / abortion
- Direct embryotoxicity

- Hinder the trans-oviductal movement of embryo
- Stimulate the uterine contraction & Expulsion of foetus.

The methods can be classified as:

A. Termination of pregnancy before implantation (Table.1)

B. Termination of pregnancy after implantation (Table. 2)

In canine species the embryo hatched out and implantation occur on the day 13-15 of post LH surge. That indicate fertilized embryo travels in the oviduct up to 8 cells stage. Probably ovulation and fertilization occur during a 6-7 day period during oestrus. So, within a week of post-breeding blocking the embryo at the oviduct level may prevent the implantation process following fertilization of ova. The only compound use for termination before implantation is estrogenic compounds. They possess excellent action on the oviductal closure at the level of utero-tubular junction (UTJ) but side effects are more weighed when compared to their beneficial action. Commonly used Estrogen compounds are Estradiol cypionate, Estradiol valerate, Estradiol benzoate. Now a day's oestrogen compounds are not used clinically in small and large animal for termination of pregnancy; More over it cause cystic ovarian condition culminate future fertility. This type of hormones are contraindicated in immuno-suppressed bitches because it further aggravate the condition due to bone marrow suppression effect in long bones.

TABLE 1. TERMINATION OF PREGNANCY BEFORE IMPLANTATION

DRUGS	DOSE	MECHANISM OF ACTION	SIDE-EFFECTS
(a) Estrogen compounds • Estradiol cypionate • Estradiol valerate • Estradiol benzoate	0.5 - 1 mg (once within 3 days post-breeding) 3 - 7 mg (once 4 - 10 days post-breeding) 0.5 - 3 mg every other day for total of 3 injections from 4 to 10 days post-breeding	• Closure of utero-tubular junction • Direct embryotoxicity (Herron *at al.*, 1974) • Delays oviductal transport of embryo	• Bone marrow suppression • Pyometra • Extended estrum • Vulvar enlargment • Hyper pigmentation of skin • Alopecia

TABLE 2. TERMINATION OF PREGNANCY AFTER IMPLANTATION

DRUGS	DOSE	MECHANISM OF ACTION	SIDE-EFFECTS
(a) Prostaglandin compounds • Dinoprost • Cloprostenol	100 to 250 mcg/kg BW BID until complete abortion 2.5 mcg/kg BW every 48 hours (4-7 days or until complete abortion)	• Lysis of CL • Reduced progesterone concentration • Smooth muscle contraction • Ecbolic effect • Dilation of cervix	• Vomiting • Defecation • Respiratory distress • Panting • Excessive salivation To mask Side-effects: Atropine Sulphate @ 0.04 mg/kg BW S/C administered (Lenin *et al.*, 1989).
(b) Dopamine Agonist • Bromocriptine • Cabergoline	0.1 mg/kg BW BID (until complete expulsion of foetus) 5 mcg/kg BW BID PO. until complete expulsion of foetus	• Suppress the hypothalamic prolactin hormone secretion	• Vomiting • Anorexia • Depression • Occasional Side-effects (Onclin *et al.,* 1995).
(c) Progesterone Receptor /Synthesis Antagonist • Mifepristone • Epostane • Aglepristone	2.5 mg/kg BW BID for 4.5 days 50mg/kg/day PO for 7days.Begining at the onset of diestrus 10mg/kg SC BID at day 0-25days of mating (prevention of pregnancy); whereas administered day 26 -45 days after mating (Resorption)	• Block the progesterone receptor and leads to decline in Progesterone concentration • Inhibits hydroxy steroid dehydrogenase delta 4-5 isomerase enzyme system.	• Pyometra • Cystic Endometrial Hyperplasia • Increased chances of diestral disorders No untoward side effect
(d) Corticosteroids	• 0.1- 0.2 mg BID PO for 5 - 10 days • 5 mg BID	• Mimic the parturition [7] • Induce stress to foetus	• Complete termination of pregnancy not achieved • Delivery of dead

	par enteral for 10 days	• Exogenous corticosteroids has an up-regulating effect on uterine or placental PG synthesis (Priyanka *et al.,* 2017).	foetus at near term

COMBINATION THERAPY

Combination treatments of dopamine agonist and PG analog reported to terminate pregnancy in pet animals (dog and cat) when administrated starting around day 25 to 28 days onwards. Action may be due to lysis of CL followed by withdrawal of prolactin support. Cabergoline at 5 mcg/kg BW daily and low dose of Cloprostenol injection @ 1 mcg/kg BW every 48 hours upto 9 days gives good results when compared to single drug. Cabergoline at 5 mcg/kg BW daily for 10 days and Cloprostenol injection @ 1 mcg/kg BW twice on days 1 and 5 of treatment. Low doses of Mifepristone and intra-vaginal applicable compounds like Prostaglandin E such as Misoprostol is currently used to terminate the pregnancy effectively (Cadepond *et al.,* 1997).

CONCLUSION

Several protocols exists for treatment of misalliance in canine species. Depending upon the time of presentation of cases, abortifacients are to be advised accordingly. Consent from the owner is necessary before attempting the treatment owing to the side effects of the drugs that are being used. Confirmation of pregnancy by using ultrasonography of fetal heartbeats and combination therapy provides very good efficacy in treating misalliance. Now a day's veterinarians are estimating serum *Relaxin* of bitches between day 26 and 30 to ascertain the gestational status and appropriately initiate medical termination of pregnancy. Most of the abortifacient drugs are prescribed via signed release form is important from legal standpoint. Veterinarians advice strongly recommended for any such termination of pregnancy.

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