RELIABLE INDUCTION OF FERTILE OESTRUS IN DOGS

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Dog breeding has emerged as a lucrative venture in the animal husbandry sector. The aim of commercial dog breeding is to obtain maximum number of healthy pups during the breeding life of a female animal.

Dogs are monoestrous and polytocous species of animals with generally a non-seasonal breeding activity. They have prolonged follicular and luteal phases of oestrous cycle compared to other animals. After the end of diestrum, they have a physiologically normal anoestrus period of varying duration which creates problems in formulating an efficient breeding management regimen.

Fecundity could be increased by shortening the naturally long diestrous and/ or anoestrous phases. Clinically, a reliable method of induction of fertile oestrus can be used to treat a variety of infertility conditions, to treat delayed puberty and to treat animals which fail to exhibit overt signs of oestrus. It can be used in conjunction with routine breeding management when breeding opportunities are missed or following conception failure or if a particular mating must be timed around the availability of a valuable stud.

Several exogenous, natural and synthetic hormones have been used to induce oestrus in bitches. Gonadotrophin Releasing Hormones (GnRH) and its analogues, Gonadotrophins, Steroid hormones, prolactin inhibitors and various combinations of treatments are used with varying success rates for oestrus induction of canines.

Induction of oestrus using GnRH or its analogues

GnRH is a hypothalamic decapeptide hormone which stimulates the synthesis and release of gonadotrophins from pituitary. Treatments using short acting GnRH or its agonists are not clinically applicable due to the expensive pulsatile infusion pumps or need of hospitalization for continuous intravenous infusion. Prolonged administration may also result in pituitary overstimulation, down-regulation of GnRH receptors in pituitary, suppression of LH release, decreased progesterone secretion and subsequent pregnancy losses. Several GnRH analogues and their controlled release preparations are used successfully for induction of fertile oestrus in dogs.

No.	Protocols	Success rate	Reference
1	GnRH @0.096 – 0.139 µg/ Kg. IV every 90 min. 11 – 13days	87.5%	Cain *et al*., 1988
2	Lutrelin @ 0.6 – 2.4 µg/ Kg/ day SC for 12 – 14 days	88.9%	Concannon *et al*., 2006
3	Leuprolide @ 100 µg/ Kg SC once	78%	Inaba *et al*., 1998
4	Leuprolide @ 100 µg/ Kg IM once	83.3%	Becha and Ghosh, 2010
5	Deslorelin @ 2.1 mg SC once	43%	Kutzler *et al*., 2001
6	Deslorelin @ 2.1 mg vestibular submucosa once	70%	Volkmann *et al*., 2006

Induction of oestrus using Gonadotrophins

Several protocols are available with the use of exogenous pituitary gonadotrophins (FSH and LH), equine chorionic gonadotrophin (eCG/ PMSG) and human menopausal gonadotrophin (hMG) for oestrus induction in dogs. ECG is most widely and successfully used with protocols ranging from daily to weekly injections. Individual variations on the number of follicular development and allergic reaction make the ECG protocol unpredictable. Premature luteal regression with subsequent shortening of dioestrus and pregnancy losses in mid gestation in a frustration sequelae which reduces its use in canines. Some of the

successful protocols used are:

No.	Protocols	Success rate	Reference
1	FSH @ 0.77 – 1.1 mg IM once	20%	Shille *et al*., 1984
2	LH @ 0.1 IU/Kg TID for 7 days	37.5%	Verstegen *et al*., 1997
3	eCG @ 20IU/Kg SID IM for 10 days	35%	Arnold *et al.*, 1989
4	eCG @ 20IU/Kg SID IM for 5 days	50%	Arnold *et al.*, 1989
5	hMG @ 1.7 U/ Kg SID IM for 9 days	40%	Wanke *et al.*, 1997
6	eCG @ 20IU/Kg SID IM for 5 days	50%	Simon, 1997

Induction of oestrus using Steroid hormones

Approximately 30 days before the onset of proestrus, a significant increase in serum oestradiol concentration occurs in bitches. Similarly, the levels of mRNA encoding oestrogen receptors in hypothalamus, pituitary and ovaries increases during late anoestrus suggesting that oestradiol is involved in priming the hypothalamo- pituitary- gonadal axis in initiation of reproductive activity. Based on this, the following protocols were designed

No.	Protocols	Success rate	Reference
1	Oestradiol 17β @ 0.5 mg/Kg PO SID for 3 days, leuprolide @ 3.6µg intranasal spray for 14 days	71.4%	Hatoya *et al*., 2006
2	Estrone @ 100–600 µg IM every 24 – 48 h, eCG @ 200 – 400 IU	83.7%	Takeishi *et al*., 1976
3	DES @ 5 mg PO SID until Day 2 of proestrus, FSH @ 10 mg IM on Day 5, 9 and 10	30.8%	Bouchard *et al*., 1991
4	DES @ 5 mg PO SID for 6 – 9 days	100%	Bouchard *et al*., 1993
5	DES @ 0.1 – 0.2 mg/Kg SID PO for 14 days, FSH @ 0.2 – 0.4 mg/Kg IM on Day 5, 9 and 11	31%	Concannon *et al*., 1997
6	DES @ 0.2 mg/Kg SID PO for 9 days	50%	Becha and Ghosh, 2011

Short term oral treatment with oestradiol 17β or DES did not produce any side effect, but long term therapy may result in alopecia and bone marrow suppression.

Induction of oestrus using dopamine agonists or serotonin antagonists

Dopamine agonists are ergot derivatives that inhibit prolactin secretion by stimulating secretion of dopamine or suppressing secretion of serotonin. Administration of dopamine agonists shortens the duration of anoestrus or induces oestrus in prolonged anoestrus. The effectiveness of dopamine agonists depends upon the dose, duration of treatment and stage of anoestrus. Centrally acting dopamine agonists (eg. Bromocriptine) induce vomiting with 1 h of first treatment. Habituation to bromocriptine, beginning with lower doses eliminates this side effect. Prolonged treatment with cabergoline develops coat colour changes beginning with 2nd week and lasting till the next coat shedding. These groups of drugs are more successful for induction of fertile oestrus in dogs.

No.	Protocols	Success rate	Reference
1	Bromocriptine @ 0.3 mg/ bitch for 3 days, then 0.6 – 2.5 mg/ bitch PO SID for 3 – 6 days	83%	Zoldag *et al*., 2001
2	Cabergoline @ 5µg/Kg PO SID for 7 – 10 days	93.3%	Arbeiter *et al*., 1989
3	Cabergoline @ 6µg/Kg PO SID until Day 2 of proestrus	100%	Gobello *et al*., 2002
4	Cabergoline @ 5µg/Kg PO SID for Day 3–	100%	Verstegen *et al*., 1999

	8 of proestrus or 40 days		
5	Cabergoline @ 5µg/Kg PO SID until progression from proestrus to oestrus	83%	Rota *et al.*, 2003
6	Metergoline @ 0.56 – 1.2 mg/Kg IM every 3rd day until proestrus	75%	Kusuma *et al.*, 1993

Induction of oestrus using opiod antagonists

Neurotransmitters and neuropeptides increase GnRH secretion and initiates gonadal activity. Administrationof naloxone, an opiod antagonist, inhibits endogenous opiodergic tone and induces proestrus in bitches.

Induction of oestrus using miscellaneous or combination of drugs

Substances with oestrogenic properties such as bis(p-acetoxyphenyl)-cyclohexlidenemethane is used successfully induction of oestrus.

No.	Protocols	Success rate	Reference
1	Bis(p-acetoxyphenyl)-cyclohexlidenemethane (P006) @ 4 mg/Kg PO SID upto oestrus	71.4%	Jensen, 1967
2	Clomiphene citrate @ 75mg PO SID for 9 – 11 days	100%	Kodagali *et al*., 1985
3	Oestradiol @ 0.2 mg on alternate days; 100 IU of hCG and 400 IU eCG SC on Day 1	37.5%	Ishihara *et al*., 1982

Usually in case of induced oestrous cycle, the duration of proestrus and oestrus varies in different individuals. So exfoliative vaginal cytological studies, hormonal profile or other ovulation predicting methods can be adapted to assess the exact time of ovulation and thereby timing of mating to obtain optimum fertility.

Although many methods are available for oestrus induction in bitches, success rate vary among and within different protocols. Long acting preparations of GnRH are convenient for the owner and less stressful to the patient. Even though GnRH and its analogues or gonadotrophins can be used successfully for oestrus induction, pregnancy rates are not optimum due to premature luteal regression. Knowledge of the strengths and weakness of each regimen will assist the veterinarian in making a selection that will be best suited for each owner and patient.

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