May Deslorelinacetate be used safely in bitches for contraception? A retrospective clinical study

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Material and methods

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Dog population in Switzerland

Privately owned dogs: 0.5 millions (1 dog/16 habitants)
- Females: 62% spayed, males 35% neutered
- No dog over-population
  - No stray dogs
  - Dog population in shelters constant
- Strict laws (obedience training, microchip, registration)

Need for

Alternative to spaying (in dogs with a high risk for side effects of spaying)

Fully reversible contraceptive for future breeding bitches
Trigg et al., 2001: Use of a GnRH analogue implant to produce reversible long-term suppression of reproductive function in male and female domestic dogs

- Deslorelin at all doses increased duration of the mean interestrus interval and suppressed estrus for periods of up to 27 months
- 6/9 bitches became pregnant in first heat after recovery
  * 4 gave birth to healthy litters
  * 2 were necropsied close to parturition
  → treatment-induced effect on fertility is reversible
- No inflammation at site of implantation

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GnRH implant: How to prevent estrus induction?

In 2009 release of Suprelorin® (Deslorelinacetate)
- Temporary suppression of fertility in male dogs
- Off-label use in bitches:
  - To prevent induction of estrus, first application during diestrus (progesterone influence)

Effectiveness of Deslorelin Acetate for the Suppression of Heat in the Bitch?
Material and methods

Retrospective study
- Inclusion criteria:
  - Intact bitch
  - At least one Suprelorin® implant to suppress estrus
  - Telephone interview with the owner (questionnaire)
  - Interview with the veterinarian of the patient
- History of the dog
  - Time of first implantation
  - Stage of estrus cycle, weight of the dog
  - Implant size and number of retreatments
- Success of treatment
  - Side effects
  - Failure of estrus suppression

Bitches

n=102
- Patients from our clinic (n=31)
- Patients from 20 other veterinary clinics/practices (n=71)
- 47 different pure breeds and 7 mongrels: Eurasier, Boxer, Cocker Spaniel...
- Median weight 26 kg

Implantation
- Time of first implantation: median age 21 months
- P4 in 54 bitches (values above 5 ng/ml)
- Dosage/dog: 4.7 mg, 2 x 4.7 mg, 9.4 mg
- Frequency of implantation: 1 to 5 times
- Median observation period of 316 d

Material and methods

Def: Failure of estrus suppression

Estrus signs
A: Major criteria
- Mating observed
- Acceptance for mating
- Estrogen level increased
- Superficial cells in vaginal smear
B: Minor criteria
- Attractiveness to males
- Enlarged vulva
- Bloody vaginal discharge
- Bilateral alopecia

One major criteria, two minor criteria

Results

- 48% neither signs of estrus nor metropathy
- 29% signs of estrus
- 16% signs of estrus and metropathy
- 6% metropathy
- 6% persistent heat and metropathy
- 4% persistent heat
Results: Failure of estrus suppression

47 bitches out of 102 (46.1%)
- 26 with a confirmed P4>5ng/ml

Risk factors?
- Age: Bitches were older (31 months) than unaffected ones (19 months), P=0.003
- Frequency of implantation: 0.0026
- (Body weight: P=0.9)
- (Dosage / kg: P=0.167)
- (Progesterone >5ng/ mL: P=0.9)

Dogs with estrous signs
- FSH 0.4 – 12.5 ng/mL
- LH 0.8 – 3.0 ng/mL

Failure of estrus suppression

Application of implant during diestrus does not prevent E2 increase: prospective study (Körber et al. 2013)
- 18 bitches implanted with 4.7mg Suprelorin
  - 3 groups (diestrus, anestrus, estrus)
  - In diestrus (n=8): increase of estradiol-17β

- Application in anestrus: induced heat
- Application in estrus: prolonged heat

Are there possibilities to avoid induced estrus?

- Pretreatment with Osaterone acetate 0.5mg/kg for 2 days prevented estrus signs and ovulation in 68.7% of the bitches
- Pretreatment with progestins: No consistent data
- GnRH-Antagonists only delay, but do not prevent the initial flare-up effect of GnRH-Agonists
- No effect with
  - Aromatase inhibitor anastrozole 0.1mg/kg
  - Anti-estrogen clomiphene acetate

Wright 2001
Corrada 2006
Sung 2006
Hermo 2006
Valente 2009
Fontaine 2011
Anjolras 2011
Prepubertal bitches

Trigg 2006:
- 9.4mg deslorelin at 4 mo of age (n=6)
- 9.4mg deslorelin at 7 mo of age (n=6)
- Placebo at 4 mo of age (n=6)

⇒ All bitches implanted at 7 mo of age showed estrus signs - 1-2 wk p.imp.
⇒ No bitch implanted at 4 mo showed estrus signs during observation period (36 wk)
⇒ Control group: 5 showed first estrus 12-28 wk p.imp.

Schäfer-Somi 2012
• 10 bitches (mean age 4 months) 4.7mg deslorelin
• No signs of estrus but increase in superficial cell index
• Body development unaffected

Six prepubertal bitches in our study

Effectiveness
5 dogs (6-8 months) showed for 1-21days signs of heat
(2-13d after GnRH-treatment)
1 bitch (5.5 months) no signs of heat
Retreatments
• Once n=2,
• Twice n=3
• Three times n=1
All owners are satisfied (n=1) or very satisfied (n=5)

Results: Persistent estrus

Persistent estrus: estrus signs lasted at least 7 d longer than in the regular cycle of the bitch (before implantation)

n=11
- Treatment required n=7
- OHE n=5, implant removal n=2

Results: Persistent estrus

Persistent estrus: Noblesse, Borzoi, female, 7 years old
Results: Uterine disease

16 out of 102

Reduced general condition: n=6
Treatment: OHE (n=14)
  Implant removal and conservative treatment (n=2)

Affected bitches are older (62 months) than unaffected ones (21 months), (P<0.0001)

Other side effects

- Urinary incontinence: n=4
- Body weight changes
  - Weight gain: n=28
  - Weight loss: n=2
- Pseudopregnancy: n=32 (+15)
- Coat changes: n=29

Similar side effects are described in other studies
  - Induced lactation
  - Persistent estrus
  - Ovarian cysts, depression and cystitis
  - Behavioural changes
  - Cystitis, Vomiting, allergic reaction

Owners

- satisfied n=57
- unsatisfied n=37
- no comment n=8

Retreatment:
  - yes n=53
  - no n=46
  - not decided n=3
Conclusion

Deslorelin is an alternative to spaying
- in young bitches
- in bitches with high risk of side effects due to spaying

Owner should be advised about
- possibility of failure of estrus suppression despite application during diestrus
- possible necessity of implant removal or spaying

Application at the umbilical region

Further studies are needed!

Thank you for your attention!