Slow release GnRH agonist implants- mode of action and their use as a contraceptive for dogs and cats

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Mode of action

Use in male dogs

Use in male cats

Use in queens

Principle of Downregulation

• Secretion of GnRH physiologically pulsatile => upregulation of GnRH receptors
• A higher and constant release of GnRH, e.g. by application of a slow release GnRH-implant, causes downregulation of the pituitary GnRH-receptors
• Efficacy is proven in male and female dog, cat and ferret

Use in male dogs

• Initial changes in testosterone concentrations:
  • stimulation after 40 min
  • peak after 60 min

Use in male dogs

• Long-term basal testosterone concentrations:
  • basal T after 21-27 days

Use in male dogs

Further changes as a consequence of testosterone withdrawal:
• significant decrease of testicular size to 35% of initial size after 14 weeks
• significant decrease of prostate volume
Use in male dogs

Further changes as a consequence of testosterone withdrawal:
- Changes in semen quality: initial decrease in semen concentration and motility and increase in pathomorphology (Junaidi et al. 2003) but initial increase in semen quality post-treatment (Romagnoli et al. 2012)
- Histological arrest of spermatogenesis on spermatogonia/spermatocytes (Junaidi et al. 2003; Goericke-Pesch et al. 2009)
- Complete sterility on days 23–84 (23, 40, 51, 60, 70, 84) (Romagnoli et al. 2012)

All effects are fully reversible:
- Testosterone increase, back to normal
- Increase of testicular and prostate volume
- Normal semen parameters and recovery of spermatogenesis (Riesenbeck et al. 2002; Junaidi et al. 2003; Goericke-Pesch et al. 2009)

Further indications:
- Androgen-related disorders: benign hyperplasia of the prostate, adenomas of the hepatoid glands
- Treatment of behavioral problems (hypersexuality, aggressiveness) => identify dogs where castration may not be beneficial
- Alopecia X (Goericke-Pesch et al. 2009; de Gier et al. 2012)

Use in tom cats

Initial changes in testosterone concentrations:
- 5 of 10 toms basal T after 20 days
- 9 of 10 toms basal T after 11 weeks (Goericke-Pesch et al. 2011)

Long-term changes in testosterone concentrations:
- Testosterone [ng/mL] over >15 months in all toms (Goericke-Pesch et al. 2011)

T<0.1 ng/mL over >15 months in all toms
Use in tom cats

As a consequence of testosterone withdrawal significant decrease of testicular volume:

As a consequence of testosterone withdrawal a loss of penile spines was observed:

Further changes as a consequence of testosterone withdrawal:
- initially increased sexual behaviour in 8/10 cats
- afterwards significantly decreased sexual behaviour from week 11/16 on
- no more urine marking
- temporary infertility: TSC ↓, motility ↓
- but: highly variable testicular histology

Full reversibility regarding all effects induced:
- rapid testosterone increase
- mean duration of efficacy: 551.9 ± 90.1 days; high variability

Reversible contraception and suppression of estrus:
- initial estrus induction possible: increase in fecal E2, clinical estrous signs
  - 10/10 Munson et al.
  - 20/21 Toydemir et al.
  - 4/10 Ackermann et al.: 1 ovulated, 3/6 without estrous signs, but ovulation
  - Significantly lower E2 after combined medroxyprogesterone treatment, but also
    estrus induction 6/7.
- induction of ovulation (100% in estrus, 40%) possible
- induced estrus may be fertile!
- possible influence on luteal function (early P4 decrease)

estrus during treatment possible (after 138 and 155 days, resp.)
- variable duration of efficacy (4.7 mg: 483 – 1025 days, 1x > 1102 days; 680.4 ± 62.0 days; 6 mg: 7.5 – 14 months; 9.4 mg: >18 months)
- reversibility of effects induced
  - estrus and ovulation induction possible
  - naturally occurring estrus
  - reversible infertility => 7/8 conceived in the first post-treatment estrus
  - litter size 1-5 kittens (3.3 ±1.5 kittens)
Conclusions

Male dog/Tom:
- reversible downregulation of endocrine and germinative testicular function
- Tom: high variability of the onset of endocrine downregulation, of the duration of efficacy and of the degree of germinative downregulation

Queen:
- initial estrus induction possible
- (short/long-term) suppression of estrus
- Full reversibility regarding estrus and fertility

For short-term treatment: treatment into umbilical area instead of neck. Repeated treatments possible for long-term/permanent contraception.

GnRH agonist implants offer a suitable alternative for contraception in male dogs and male and female cats!

Thank you for your attention!