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Long-term effects of GnRH agonists on fertility and behaviour

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Slow release GnRH agonist implants (SRI) are widely accepted as an alternative to surgical neutering. An implant containing either 4.7 or 9.4 mg deslorelin is licensed in Europe to induce temporary infertility in healthy, intact, adult male dogs and ferrets (9.4 mg only). It is well known that application in the male dog results in a reversible downregulation of endocrine and germinative testicular function. This means that, following an initial stimulation (“flare-up”) that is possibly associated with an improved semen quality during the first month after treatment, spermatogenesis is subsequently downregulated to an arrest on the level of spermatogonia/spermatocytes. Following application of a 4.7 mg deslorelin implant, male dogs become sterile after 22-84 days for mean 400 days (<10kg) or for maximum 400 days (>25 kg). The duration of efficacy (DE) of the 9.4 mg implant has been described by the manufacturer to be about 12 months. A minimum of 9 weeks after implant removal/cessation of effect are considered necessary to re-obtain sexually competence and normal semen quality. Different to that, semen parameters were only within the reference values after in average 25 weeks using another implant, although first sperm were already found after 15 weeks. In tom cats, effects of treatment are highly individual with basal testosterone (T) concentrations obtained after 3-11 weeks in most toms (4.7 mg), azoospermia after 40-72 days (9.4 mg) and a mean DE 17.5 ± 2.9 months (4.7 mg); however, as time of downregulation and testicular histology during efficacy are extremely variable, time to infertility/azoospermia is likely even more individual than in the dog. Pretreatment T concentrations are obtained 3 weeks, normal libido in average 10 weeks after the end of efficacy. However, fertile matings had been described from 7 weeks after the end of efficacy. Deslorelin implants are also suitable for long-term contraception and suppression of estrus cycle and sexual behaviour in male and female ferrets with a DE of 1012 ± 38 days. In bitches, queens and jills, estrus induction has been observed under specific situations indicating a clear need of “control” of the animals within the first period after application to avoid unwanted matings and offspring as induced estrus has been shown to be fertile. The DE (4.7 mg) in bitches ranges from 2.1 to 23.3 months and normal fertility has been shown in a limited number of animals after the end of efficacy. Application in queens has been shown to reversibly suppress cyclicity and fertility for 680.4 ± 62.0 days (4.7 mg) and 768 ± 124 days (9.4 mg). Data about the effect on behaviour are mainly based on owner-observations and sexual behaviour. GnRH agonists have been shown to significantly reduce sexual behaviour and libido in male dogs, cats and ferrets. Additional behavioural traits that are obviously at least to some extent T-dependent and therefore significantly positively affected by treatment are hypersexuality, aggressive behaviour as intermale dominance and excessive territorial micturition/urine marking. The rates of animals with a marked improvement or ceasing of the respective behaviour are comparable to those after surgery. An initial worsening of the respective problem behaviour during the flare-up has been described in some animals. Besides, increased appetite (male and female dogs), increased anxiousness including typical defense reactions, increased playfulness (both male dogs), behavioural changes related to pseudopregnancy (bitch), decrease in/ceasing of urine spraying (surgically neutered cats) and calmer and friendlier behaviour (ferrets) during efficacy has been described. In conclusion, SRI are suitable for long-term contraception in several species and to predict castration-related effects on behaviour, making them a valuable option to test for if sex hormone-withdrawal results in the effects aimed for.