

Utilizarea și eficacitatea implantului cu deslorelină la animalele de companie

The use and effectiveness of deslorelin implant in companion animals

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Abstract

Control of reproduction in companion animals is ensured both by surgical sterilization and by the administration of contraceptive medication. Since most progestogens have frequent severe adverse effects, long-acting gonadotropin-releasing hormone (GnRH) agonists, such as deslorelin, are now more commonly used. The advantages of the deslorelin implant are easy administration, increased efficiency over a long period of time, safety of use and reversibility of sterilization. Apart from using the implant as a contraceptive method, it can be administered in the therapy of conditions such as benign prostatic hyperplasia or in the treatment of behavioral disorders (aggression, excessive marking). The purpose of this short review is to present the advantages of using the deslorelin implant in pets and to highlight its effectiveness in controlling their reproduction.

Rezumat

Controlul reproducerii la animalele de companie este asigurat atât prin sterilizarea chirurgicală, cât și prin administrarea medicației contraceptive. Întrucât majoritatea progestativelor prezintă frecvente efecte adverse severe, în prezent sunt mai des utilizați agonistii cu acțiune prelungită ai hormonului de eliberare a gonadotropinei (GnRH), precum deslorelina. Avantajele implantului cu deslorelină sunt administrarea ușoară, eficiența crescută pe o perioadă îndelungată, siguranța utilizării și reversibilitatea sterilizării. În afara utilizării implantului ca metodă contraceptivă, acesta poate fi administrat în terapia unor afecțiuni precum hiperplazia benignă a prostatei sau în tratamentul tulburărilor de comportament (agresivitate, marcarea excesivă). Scopul acestui scurt review este de a prezenta avantajele utilizării implantului cu deslorelină la animalele de companie și de a evidenția eficiența acestuia în controlul reproducerii acestora.

Introduction

Reproductive control in companion animals is becoming increasingly important today and is an active concern for owners.

Sterilization / castration is primarily resorted to in order to reduce or eliminate a series of conditions that may arise over time, such as mammary cancer, ovarian cancer, pyometra in females; testicular cancer, prostatic hyperplasia in males, or the spread of TVT

(transmissible venereal tumors), but also to significantly reduce the rate of abandonment of companion animals (12).

Over the years, several contraceptive medications have been developed for companion animals, but the frequency and severity of secondary adverse effects have limited their use.

Most types of progestives, oral or injectable, have been avoided both by owners and veterinarians, so surgical sterilization has

been the most widely used method, being safe and permanent (12, 25).

When surgical intervention was not possible, reproductive control was achieved using progestogens, until now, when new and challenging options have become available, such as long-acting agonists of gonadotropin-releasing hormone (GnRH).

A new therapeutic approach has been the development of analogs of gonadotropin-releasing hormone (GnRH). GnRH is a hypothalamic decapeptide hormone which has the same amino acid sequence in all mammals (12).

Modifications of the decapeptide structure of a GnRH agonist provide two types of analogs: GnRH antagonists and GnRH agonists. GnRH antagonists bind to the GnRH receptor (GnRHr) and completely block the secretion of LH/FSH and downstream signaling pathway activation that stimulates gonadotropin biosynthesis.

After cessation of GnRH agonist treatment, the animal becomes fertile, but the time period is unpredictable (12, 25, 26, 27).

The development of efficient implants with low doses, slow release, potent GnRH agonists such as deslorelin (Suprelorin, Virbac) (Figure 1) has allowed their use to become widespread in companion animals (12).



Figure 1. Deslorelin implant

The use of the deslorelin implant in dogs

The first study involving the administration of deslorelin to male dogs was conducted in 2001 by Trigg et al., using a 6 mg implant. Subsequently, several studies were conducted

(12, 25, 26, 27) using different concentrations (2.1, 4.7, 6, 9.4, and 12 mg/implant).

These studies reported that deslorelin implants represent a safe and well-tolerated sterilization method in dogs (12).

Moreover, repeated implantation is possible, and regardless of the concentration of deslorelin implant, following the loss of efficacy of these implants, all treated dogs reached physiological testosterone levels within 7-9 weeks, and semen quality returned completely.

Complete resumption of sexual function is a huge advantage in the case of valuable dogs used for breeding (9,10,11,17,18,19,22,25,26).

Typically, a rise in plasma levels can be detected as soon as 20 minutes following the implantation of deslorelin (10).

These levels drop to baseline values after 3 days and are not detectable at approximately 12 days post-implantation.

Regardless of size, all dogs treated with a 4.7 mg deslorelin implant show testosterone levels of <0.4 ng/ml from 22 to 33 days for at least 180 days (25).

Reduced levels of gonadotropins and plasma concentrations of testosterone explain the significant reduction in testicular volume and azoospermia in dogs treated with deslorelin (12).

The dose-response relationship is not expressed in the degree of suppression of reproductive function but in the duration of suppression, with a slow-release 6 mg or 9.4 mg implant reducing testosterone and sperm production for up to a year (26).

Decreased testosterone levels are usually accompanied by a decrease in testicular volume (10, 12, 25, 26).

Complete recovery of semen quality was obtained for all dogs at all tested doses.

The recovery time of steroidogenesis has been reported to be variable, with smaller dogs (<10 kg) taking longer to recover than medium or large dogs (25).

Dogs are expected to remain sexually incompetent for up to an additional 9 weeks after discontinuing deslorelin treatment (21, 22, 24, 25).

In addition to contraception, GnRH agonists also cause significant contraction of

the prostate gland (11,16), which is clinically advantageous for dogs with benign prostatic hyperplasia (BPH), a common condition in intact male dogs (11, 16).

The effects of deslorelin on prostate volume in healthy dogs and clinically affected dogs with BPH have been evaluated by several authors (12), indicating the efficacy of deslorelin in BPH therapy.

A study by Nizański et al. in 2020 demonstrated that deslorelin acetate administration has longer-lasting efficacy compared to osaterone acetate in BPH (14).

According to a study by De Gier and Vinke (2010), another indication for using deslorelin in male dogs is the control of certain unacceptable behaviors related to testosterone action, such as aggression, fear/uncertainty, and sexual behavior in dogs (3).

Deslorelin implants are also used to delay puberty without affecting ovarian function and body development in both male and female dogs.

A study by Schäfer-Somi et al. in 2022 showed that in prepubertal bitches, both 4.7 mg and 9.4 mg implants delayed puberty until >2 years of age.

The local impact of deslorelin on ovarian suppression and resumption of ovarian activity has been highlighted, with no negative effects found on ovarian function after cyclicity recurrence (23).

Long-term reproductive data (up to two years after the first estrus) collected by Gontier et al. in 2022 support the hypothesis that females implanted with deslorelin have returned to fertility, exhibited regular heat cycles, were able to reproduce, and continued to conceive and give birth without major safety issues (8).

Thus, this implant offers a safe and highly effective alternative for reversible sterilization, with studies showing no evident side effects or health problems induced by repeated use of implants (8).

Initially, deslorelin implants were intended only for male contraception, being approved in the European Union only for administration to male dogs.

However, they are now being tested for use in females as well (2).

The use of the deslorelin implant in cats

In feline reproductive control, GnRH agonists are increasingly used.

The first study on chemical sterilization of male cats by administering deslorelin (4.7 mg implant) was conducted by Goericke-Pesch et al. (2010).

Just like in dogs,, the effect of chemical sterilization occurs through a decrease in testosterone levels (after an initial increase); however, in cats, the initial increase in testosterone was not significant, unlike findings in dogs.

Researchers found that testosterone levels rapidly decreased on day 20 post-implantation (<0.1 ng/ml) and remained at baseline concentrations for 11 weeks in most treated cats (6,7).

Similar to dogs, repeated implantation is possible, and after discontinuation of deslorelin implants, sexual function is resumed (4, 6, 7).

The main effect in male cats is on sexual behavior, and there is also a noticeable change in testicular size.

However, there is limited information about the effect of deslorelin on sperm quality and the return of sperm production in this species.

Histological studies have confirmed a rapid restoration of spermatogenesis at 1 month after implant removal, but more studies are needed on the return of sexual activity (5, 15).

A study by Amaral et al. in 2023 highlighted the effectiveness of deslorelin implants in reducing sexual behaviors in male cats, including reducing vocalization, urine marking, and aggression (1).

In female cats, the main use of deslorelin implants is to inhibit estrus.

A study by Munson et al. (2001) confirmed that deslorelin can be used to effectively suppress ovarian activity, but the duration of inhibition was highly variable (average of 14 months) (13, 20).

Conclusion

Chemical sterilization by administering deslorelin implants is a reliable option, offering a safe and effective reduction in fertility in males.

The main advantage of this implant is its reversibility, with full sexual function being resumed upon discontinuation.

At the same time, deslorelin helps decrease sexual behavior, providing an alternative therapy for behavioral disorders in pets due to testosterone. In males, deslorelin also represents a highly effective therapy option for benign prostatic hyperplasia.

Although deslorelin implants are currently widely administered only in males, more and more studies support their use in females.

The easy administration, long-lasting effectiveness of the implant, and its reversibility are just a few of the qualities supporting its use in pet reproductive control.

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