



Non-Surgical Contraception in Male Dogs and Cats: Mechanisms and Clinical Perspectives

Zehra Coşkun Bahçe¹ and Fikret Karaca²

¹Department of Reproduction and Artificial Insemination, Faculty of Veterinary Medicine, Bingöl University, Bingöl, Türkiye

²Department of Reproduction and Artificial Insemination, Faculty of Veterinary Medicine, Hatay Mustafa Kemal University, Hatay, Türkiye

*Corresponding author's Email: zehracoskun6328@gmail.com



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ABSTRACT

Surgical sterilization is widely used for population control and reproductive management in dogs and cats; however, its irreversible nature has increased interest in non-surgical contraceptive methods. Hormonal approaches, including progestins, GnRH agonists, and GnRH antagonists, as well as immunocontraceptive and chemical methods, have been investigated for fertility control in male dogs and cats. The present review summarizes the current literature on non-surgical contraceptive methods in male dogs and cats, focusing on their mechanisms of action, effectiveness, reversibility, duration of effect, and reported side effects. Non-surgical approaches include GnRH agonists and antagonists administered systemically or via implants, immunocontraceptive methods, and chemical castration agents administered by intratesticular or intraepididymal injection. GnRH agonists have been reported to provide prolonged and reversible suppression of reproductive function, whereas GnRH antagonists generally have a more rapid onset but a shorter duration of action. Immunocontraceptive methods can suppress testosterone concentrations and spermatogenesis, although their effects may vary among individuals. Chemical castration can impair spermatogenesis and semen quality, with outcomes depending on the chemical agent and administration technique. In conclusion, non-surgical contraceptive methods revealed potential for fertility control in male dogs and cats.

Keywords: Cat, Chemical castration, Dog, Gonadotropin-releasing hormone, Immunocontraception

INTRODUCTION

Contraception is the prevention of reproduction through surgical or medical interventions; non-surgical (pharmacological) methods, including progestins, androgens, and GnRH analogs, act either by directly blocking reproductive hormone receptor-mediated events or by indirectly suppressing gonadotropin secretion through negative feedback (Kutzler and Wood, 2006). Interest in non-surgical methods as alternatives to surgical procedures for population control and reproductive management in domestic cats and dogs has increased, particularly since the 1970s (Rhodes, 2017). Historically, the lack of safe anesthetics, together with limited surgical equipment and instruments, increased surgical risks, making sterilization of dogs and cats uncommon until the latter half of the twentieth century (Brent, 2019). Although opinions on the risks, benefits, and appropriate age for surgical sterilization in dogs vary in the literature, the number of studies on medical contraceptive methods aimed at reversible or permanent fertility suppression has increased significantly in recent years (Tez et al., 2019). Progestins have been investigated as hormonal approaches for fertility control in male dogs (England, 1997). Gonadotropin-releasing hormone (GnRH) analogs, particularly GnRH agonists, have been widely investigated for fertility control in dogs and cats (Lucas, 2014). Different medical contraceptive methods, including GnRH antagonists, immunocontraceptive vaccines, and chemical sterilization approaches, have been developed, and research in this field remains active (Kutzler and Wood, 2006).

The present review aimed to examine non-surgical contraceptive methods in male cats and dogs, including GnRH agonists and antagonists, progestins, immunocontraceptive approaches, and intratesticular and intraepididymal administration of chemical agents, and to compare them in terms of efficacy, duration of effect, reversibility, safety, and clinical applicability.

METHOD

The present narrative review was based on a literature search conducted using Google Scholar and PubMed. Publications from 1997 to 2026 were considered. The search terms included “male dog”, “male cat”, “non-surgical contraception”, “GnRH agonist”, “GnRH antagonist”, “progestin”, “immunocontraception”, “chemical castration”, “intratesticular

injection”, and “intraepididymal injection”. Relevant studies on non-surgical contraceptive methods in male dogs and cats were selected and evaluated based on their mechanisms of action, efficacy, duration of effect, reversibility, safety, and clinical applicability. Among non-surgical approaches for suppressing fertility in male cats and dogs, immunocontraception has emerged as an important area of research. A summary of the included studies were presented in Table 1.

MECHANISM OF IMMUNOCONTRACEPTION

Immunocontraception uses the immune response to suppress reproductive functions by inducing the formation of specific antibodies against reproduction-related protein antigens (Levy, 2004). Immunocontraception can, in principle, target different reproductive antigens, including gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), zona pellucida proteins, and sperm-associated antigens (Kutzler and Wood, 2006; Rhodes, 2017). However, some of these targets, particularly zona pellucida proteins, are specific to the female reproductive system (Kutzler and Wood, 2006). In male cats and dogs, GnRH-based immunocontraceptive approaches have been more widely investigated (Levy et al., 2004).

Based on the established role of immunological mechanisms in reproductive physiology, GnRH-based vaccines, in particular, have shown efficacy in suppressing gonadal function in males (Levy et al., 2004; Talwar et al., 2009; Munks, 2012). GnRH is a highly conserved decapeptide with a similar structure across mammalian species and is one of the key regulators of the hypothalamic-pituitary-gonadal axis (Padula, 2005). Antibodies produced against GnRH suppress reproductive function by interfering with GnRH activity, resulting in reduced testosterone concentrations and impaired spermatogenesis (Levy et al., 2004). To enhance immunogenicity, GnRH can be conjugated to carrier proteins and combined with adjuvants to induce a stronger immune response (Levy et al., 2004; Munks, 2012).

EXPERIMENTAL AND CLINICAL STUDIES

GnRH vaccines developed for immunocontraception have been reported to reduce testosterone levels and decrease sperm count and motility in male cats and dogs (Levy, 2004). The GonaCon™ (National Wildlife Research Center, Fort Collins, CO, USA) vaccine, developed for free-ranging animal populations, has been reported to produce effects lasting approximately one year after a single dose (Segura, 2023). In a study of male cats conducted by Levy et al. (2004), high antibody titers were observed following immunization with synthetic GnRH bound to a carrier protein, along with significant decreases in testosterone levels and spermatogenesis and the development of testicular atrophy. Histological examinations have revealed a reduction in interstitial cell numbers and atrophy of the seminiferous tubules (Levy, 2004). Similar studies have reported that GnRH-based vaccines can reduce testosterone concentrations in healthy male dogs (Sabeur et al., 2003; Walker et al., 2007). Antibody titers have been reported to peak within a few weeks after repeated subcutaneous injections of GnRH vaccines, leading to temporary infertility (Donovan et al., 2012; Siel et al., 2020). Immunocontraceptive methods are considered promising options in male cats and dogs due to their minimally invasive nature and potential reversibility (Kutzler and Wood, 2006; Munks, 2012). However, individual variability in antibody responses, uncertainty regarding the duration of contraceptive effects, and the relatively small sample sizes reported in available studies remain important limitations to the routine clinical use of this approach (Levy et al., 2004; Segura Ochoa et al., 2023).

GONADOTROPIN-RELEASING HORMONE ANTAGONISTS

Among non-surgical approaches to fertility suppression in male cats and dogs, GnRH antagonists are noteworthy because they directly inhibit the hypothalamic-pituitary-gonadal (HPG) axis (Gobello, 2007). GnRH antagonists bind to GnRH receptors in the anterior pituitary gland, thereby blocking the effects of endogenous GnRH and suppressing the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH; García Romero et al., 2009). The resulting decrease in LH and FSH secretion leads to reduced intratesticular testosterone levels and suppression of spermatogenesis (Baran et al., 2016). Unlike GnRH agonists, antagonists do not produce an initial transient stimulatory effect (Gobello, 2012). Unlike GnRH agonists, GnRH antagonists competitively block GnRH receptors in the anterior pituitary without initially activating them; therefore, directly suppress gonadotropin secretion without inducing an initial stimulatory flare (Gobello, 2012). The absence of an initial testosterone surge may represent a clinical advantage of GnRH antagonists by avoiding effects associated with the transient hormonal stimulation observed with GnRH agonists (Gobello, 2012). However, early GnRH antagonist formulations have been reported to cause adverse reactions associated with histamine release, significantly limiting their clinical use (Gobello, 2012). Although these side effects have been reported to occur less frequently with newer-generation GnRH antagonist analogs, their high cost limits their use in large-scale population control programs (Koechling et al., 2010). The effects of acyline, a third-generation GnRH antagonist, on fertility in male dogs have been experimentally investigated (Valiente et al., 2007; García Romero et al., 2009). A single

subcutaneous dose of 330 µg/kg has been reported to induce short-term suppression of fertility, accompanied by decreased libido, reduced scrotal size, impaired semen parameters, and significant declines in circulating gonadotropin and testosterone concentrations (Valiente et al., 2007; García Romero et al., 2009). Similarly, reversible impairment of spermiogenesis, spermatocytogenesis, and sperm motility was reported in male cats following a single subcutaneous dose of acyline (330 µg/kg; García Romero et al., 2012). However, the short duration of action of GnRH antagonists and the need for repeated administration limit their use in clinical practice compared with long-acting GnRH agonist implants (Gobello, 2012). Therefore, the ability of GnRH antagonists to suppress fertility without inducing an initial transient hormonal stimulation is considered a potential advantage (García Romero et al., 2009).

GONADOTROPIN-RELEASING HORMONE AGONISTS

GnRH agonists are agents used to reversibly suppress fertility in male cats and dogs (Goericke-Pesch et al., 2011; Romagnoli et al., 2012). GnRH, the primary regulator of the HPG axis, controls the release of LH and FSH from the anterior lobe of the pituitary gland (Baran et al., 2016). In males, LH regulates testosterone synthesis, while FSH regulates spermatogenesis (Baran et al., 2016). By 2005, more than 2,000 GnRH analogs had been developed and experimentally tested (Padula, 2005). GnRH agonists mimic the effects of endogenous GnRH but generally have greater and longer-lasting biological activity (Padula, 2005). However, the continuous release of these potent GnRH agonists initially causes a temporary increase in gonadotropin secretion. Subsequently, GnRH receptor downregulation and desensitization occur in the pituitary gland (Gobello, 2007). As a result of this process, LH and FSH release is suppressed, testosterone levels decrease, and spermatogenesis is temporarily inhibited (Trigg et al., 2006). Because GnRH receptor desensitization is temporary, GnRH agonists provide reversible contraception, with reproductive function gradually returning after the implant's drug supply is depleted (Junaidi et al., 2003). GnRH agonists such as deslorelin have been formulated as slow-release subcutaneous implants to provide sustained drug delivery and prolonged suppression of reproductive function (Driancourt and Briggs, 2020). Slow-release subcutaneous implants cause a decrease in testosterone concentration and a significant reduction in motile sperm count (Driancourt and Briggs, 2020). The most commonly used GnRH agonist in clinical practice is deslorelin (Lucas, 2014). Deslorelin is reported to have biological activity approximately 100 times greater than that of endogenous GnRH (Padula, 2005). Deslorelin implants containing 6 mg of active ingredient, when administered subcutaneously, reduce plasma LH and testosterone concentrations to undetectable levels within approximately 4 weeks and cause infertility in male dogs within 6 weeks (Junaidi et al., 2003). The suppressive effects of the deslorelin implant were reversible, with LH and testosterone concentrations returning to normal ranges by approximately 52 weeks and semen characteristics fully recovering by 60 weeks after implantation (Junaidi et al., 2003). Deslorelin doses greater than 0.25 mg/kg have been reported to suppress spermatogenesis in male dogs (Trigg et al., 2001). However, reproductive function is not suppressed immediately after implant administration (Romagnoli et al., 2012). In a study by Romagnoli et al. (2012), six adult male dogs received a single 4.7 mg deslorelin implant (Suprelorin®), and sterility was achieved after a mean of 54 ± 21 days (Romagnoli et al., 2012). The delayed onset of sterility following deslorelin implantation is associated with the initial stimulatory effect of the GnRH agonist and the gradual decline in semen parameters (Romagnoli et al., 2012). Longer-acting formulations include implants containing 9.4 mg of deslorelin (Sirivaidyapong et al., 2012). Although reproductive recovery has been reported after approximately 60 weeks, considerable individual variability exists in the timing of recovery following deslorelin treatment (Morsink, 2009; Stempel et al., 2022). Although the Gonazon® implant containing 18.5 mg azagly-nafarelin was originally developed for use in female dogs, it has also been shown to suppress reproductive function in male dogs. In a study involving eight male Beagle dogs, administration of an 18.5 mg azagly-nafarelin implant reduced LH bioavailability by approximately 70% at 11 weeks, while testosterone concentrations decreased to basal levels within 17.5 ± 8.4 days (Ludwig et al., 2009). Following an initial increase lasting four days, testosterone concentrations were reported to return to baseline within three weeks, with azoospermia developing within 2 to 4 weeks (Ludwig et al., 2009). In a larger study, testosterone concentrations were found to fall below the threshold (< 0.35 nmol/L) in the vast majority of 53 dogs, and this suppression persisted for 6 to 22 months (Goericke-Pesch et al., 2010). Approximately 8 weeks after administration, reductions of 54% and 52% in testicular and prostate volumes, respectively, were observed. The reduction in prostate volume has been reported to be more pronounced in dogs with prostatic hyperplasia, and a decrease in aggressive behavior has also been observed (Goericke-Pesch et al., 2010). Implants containing 4.7 mg have been reported to cause a decrease in testosterone concentration, testicular atrophy, and a reduction in fertility. In cats, the efficacy of deslorelin implants has been evaluated. Implants containing 4.7 mg have been reported to cause decreases in testosterone concentration, testicular atrophy, and suppression of spermatogenesis (Novotny et al., 2012). Keratinized spines on the glans penis, considered clinical indicators of testosterone activity, have been reported to disappear within approximately nine weeks (Goericke-Pesch et al., 2011; Novotny et al., 2012). Histological evaluations in cats have shown the persistence of long spermatids in testicular tissue along with atrophy (Novotny et al., 2012). In addition,

GnRH stimulation tests using buserelin indicated an increase in testosterone concentrations before deslorelin treatment; however, after administration of a 4.7-mg deslorelin implant, four of the five tomcats had basal testosterone concentrations and revealed no further increase in response to buserelin from week 4 onward (Goericke-Pesch et al., 2013).

PROGESTINS

Progestins, which are synthetic analogs of progesterone, are widely used for contraception, especially in female dogs and cats (Kutzler and Wood, 2006). In male dogs, progestins may affect reproductive function through mechanisms other than gonadotropin suppression. Their effects on semen quality have been suggested to result primarily from direct effects on the epididymis, particularly during epididymal sperm maturation. However, significant suppression of libido has not been consistently demonstrated in male dogs (England, 1997). Oral administration of megestrol acetate (MA) at a dose of 2 mg/kg for seven days has been reported to cause no significant changes in sperm quality in male dogs, whereas secondary sperm abnormalities occurred at higher doses (4 mg/kg; England, 1997). Subcutaneous administration of medroxyprogesterone acetate (MPA) at a dose of 20 mg/kg resulted in rapid and significant reductions in sperm motility and output and deterioration in sperm morphology (England, 1997). The rapid changes in sperm motility, output, and morphology were considered to result primarily from the direct effects of MPA on epididymal sperm maturation and transport rather than from gonadotropin suppression, as plasma LH concentrations were not suppressed (England, 1997). No significant effects on libido were reported (England, 1997). The duration of action of progestins varies depending on the compound used and the route of administration. Megestrol acetate is a short-acting progestin with a half-life of several hours, whereas medroxyprogesterone acetate has a reported half-life of 12-17 hours after oral administration and 40-50 days after injection. No adverse effects have been reported following MPA treatment in dogs (Romagnoli et al., 2024). However, data regarding the duration and reversibility of progestin-induced fertility suppression in males remain limited. Compared with progestins, GnRH agonists have been more extensively studied for fertility control in male dogs, with more clearly characterized durations of action and reversibility (Romagnoli et al., 2024). In contrast, information regarding the duration of contraceptive efficacy, reversibility, and long-term safety of progestins in males remains limited (Vasetska, 2020; Romagnoli et al., 2024).

CHEMICAL CASTRATION

Chemical castration is a minimally invasive contraceptive method developed as an alternative to surgical orchiectomy in male cats and dogs (Oliveira et al., 2007; 2012). In chemical castration, chemical agents are administered directly into the testis, epididymis, or ductus deferens. Intratesticular injections may disrupt spermatogenesis through testicular tissue damage, whereas injections into the epididymis or ductus deferens may induce fibrosis and obstruction of sperm transport, potentially resulting in azoospermia and infertility (Oliveira et al., 2012; Hess et al., 2024).

Chemical castration has been proposed as a potential alternative to surgical castration in population control programs because it may reduce the need for surgical facilities and anesthesia; however, its suitability for large-scale use depends on the efficacy, safety, and practicality of the chemical agent used (Baran et al., 2010; Oliveira et al., 2013; Bahçe and Karaca, 2026). A recent study indicated that the mentioned method is a cost-effective and feasible alternative, although concerns remain regarding tissue damage and reversibility (Hess et al., 2024). The volume of the injected solution should be adjusted to the testicular size to ensure appropriate distribution within the testis (Leoci et al., 2014; Rafatmah et al., 2019). Intratesticular injection can be performed by advancing the needle along the long axis of the testis and depositing the solution gradually while withdrawing the needle (Leoci et al., 2014; Rafatmah et al., 2019). Alternatively, injection into the mediastinum testis has been investigated as a technique for controlled administration of chemical agents (Bahçe and Karaca, 2026). When determining the dose, testicular volume is taken into account, and the injection is performed without compromising anatomical integrity (Canpolat et al., 2016). Zeuterin® (Ark Sciences, USA), containing zinc gluconate, is a United States Food and Drug Administration approved preparation for use in male dogs and contains 0.2 M zinc gluconate (13.1 mg zinc/ml; Oliveira et al., 2013). The same active ingredient is used in Latin American countries under the name Esterilsol® for both dogs and cats (Kutzler, 2015). In a study conducted with Zeuterin, side effects were mostly limited to the injection site and were reported in 1.1% of 270 male dogs (Kutzler, 2015). Histological examinations revealed almost complete fibrosis of the seminiferous tubules and Leydig cells at 60 and 75 days after intratesticular injection (Tepsumethanon et al., 2005). With intraepididymal injections and injections into the ductus deferens, the primary mechanism is chemical obstruction and the development of secondary testicular atrophy. Azoospermia has been reported to develop within 90 days after intraepidermal administration of 50 mg of zinc arginine (Fahim et al., 1993). Histological examination revealed normal seminiferous tubules, atrophy of the rete testis, and an absence of spermatozoa in the epididymis and ductus deferens (Fahim et al., 1993). However, temporary

azoospermia or oligospermia has been reported following formalin administration (Bahçe and Karaca, 2026). In a study comparing formalin-induced chemical castration with surgical castration, a significant decrease in serum testosterone levels, deterioration in sperm parameters, and degenerative changes in testicular tissue were observed. Activation of the cellular stress response was also demonstrated (Moustafa et al., 2023). It has been emphasized that chemical castration may cause more pronounced local tissue damage than surgery and that dose and administration technique are key determinants of outcomes (Moustafa et al., 2023). Non-surgical sterilization methods based on the intratesticular administration of calcium chloride are being considered as alternative approaches to fertility control in male cats (Jana and Samanta, 2011). In a clinical study, a single intratesticular injection of a 20% calcium chloride solution was reported to substantially suppress spermatogenesis, cause degeneration and necrosis of testicular tissue, and lead to a substantial decrease in serum testosterone concentrations (Jana and Samanta, 2011). Biochemical analyses revealed increased testicular lipid peroxidation and malondialdehyde levels, together with decreased antioxidant enzyme activities, reduced glutathione/oxidized glutathione (GSH/GSSG) ratio, and mitochondrial membrane potential, supporting the involvement of oxidative stress in calcium chloride-induced testicular damage (Jana and Samanta, 2011).

Table 1. The representative studies on non-surgical contraceptive methods in male dogs and cats

Study	Species	Contraceptive method	Application	Main findings
Levy et al. (2004)	Male cats	GnRH immunocontraception	GnRH vaccine	Anti-GnRH antibodies developed; serum testosterone declined, with testicular atrophy and suppressed spermatogenesis
Donovan et al. (2012)	Male dogs	GnRH immunocontraception	GnRH immunization	Reproductive and endocrine functions were suppressed
García Romero et al. (2009)	Male dogs	GnRH antagonist (acyline)	Subcutaneous injection	Gonadotropin (LH, FSH) and testosterone concentrations were temporarily reduced
Romagnoli et al. (2012)	Male dogs	GnRH agonist (deslorelin)	4.7-mg implant	Semen quality declined and temporary sterility developed
Goericke-Pesch et al. (2011)	Male cats	GnRH agonist (deslorelin)	4.7-mg implant	Testosterone and testicular volume decreased, and reproductive behaviour was suppressed
Oliveira et al. (2013)	Male cats	Zinc-based chemical contraception	Intratesticular injection	Azoospermia occurred in most treated cats, and testicular size decreased
Oliveira et al. (2012)	Male dogs	Zinc gluconate-based chemical contraception	Intratesticular injection	Azoospermia was observed in most treated dogs
Moustafa et al. (2023)	Male dogs	Chemical castration (formalin)	Intratesticular injection	Testosterone decreased, and degenerative changes in testicular tissue were observed
Bahçe and Karaca (2026)	Male dogs	Chemical castration (formalin and CaCl ₂)	Testicular mediastinum injection	Semen quality declined, and testicular tissue changes were observed

GnRH: Gonadotropin-releasing hormone; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone; CaCl₂: Calcium chloride.

CONCLUSION

In the present review, non-surgical contraceptive methods in male dogs and cats, including progestins, GnRH agonists and antagonists, immunocontraceptive approaches, and chemical castration methods, were evaluated in terms of their mechanisms of action, duration of effectiveness, reversibility, and clinical applicability. Surgical sterilization remains a widely used method today due to its high effectiveness and permanent effects. However, non-surgical approaches may provide reversible or permanent alternatives depending on the method used. GnRH agonists may provide long-term suppression of reproductive function; however, the duration of their effects and the time required for fertility to return may vary among individual animals and cannot be predicted with certainty. GnRH antagonists generally have a rapid onset of action, although their relatively short duration of effect may limit their clinical use. Immunocontraceptive methods may provide prolonged contraceptive effects, but variability in individual immune responses remains an important limitation. Chemical castration methods may represent a minimally invasive alternative to surgical castration; however, their efficacy and safety depend on the chemical agent and administration technique used.

The present review has some limitations that should be considered when interpreting the findings. The available evidence for some non-surgical contraceptive methods in male dogs and cats is based on a limited number of studies with relatively small sample sizes. In addition, differences in treatment protocols, doses, outcome measures, and follow-up periods make direct comparisons among the available methods difficult. The limited number of long-term and comparative studies also restricts definitive conclusions regarding their efficacy, reversibility, safety, and clinical applicability. Future studies should therefore focus on standardized treatment protocols, long-term safety, duration and predictability of contraceptive effects, recovery of fertility, and direct comparisons between different non-surgical contraceptive approaches.

DECLARATIONS

Author's contributions

Fikret Karaca conceived and determined the topic of the review. Zehra Coşkun Bahçe conducted the literature search, evaluated the relevant literature, and wrote the manuscript. All authors critically reviewed, checked, and approved the final version of the manuscript before publication.

Availability of data and materials

No new datasets were generated or analyzed in the present review. All information evaluated in this article was obtained from previously published studies cited in the manuscript.

Competing interests

The authors declare no conflict of interest.

Ethical consideration

Ethical issues, including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy, have been checked by all the authors. ChatGPT (OpenAI) was used solely to assist with language editing and improving the clarity and readability of the manuscript. All AI-assisted text was critically reviewed, revised, and verified by the authors to ensure scientific accuracy, appropriate academic language, and consistency with the original sources. The authors take full responsibility for the final content of the manuscript. The originality and accuracy of the information presented in the manuscript were checked and confirmed by the authors before submission and will be reconfirmed before acceptance and publication.

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