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Non-surgical methods of contraception and sterilization

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Abstract

The Humane Society of the United States estimates that each year between 8 and 10 million dogs and cats enter shelters and 4–5 million of these animals are euthanized due to lack of homes. Many veterinarians within the United States recommend surgical sterilization for population control in dogs and cats. However, there are non-surgical methods to control reproduction. Pharmacologic methods of contraception and sterilization can be safe, reliable and reversible. Hormonal treatments using progestins, androgens, or gonadotropin releasing hormone (GnRH) analogs act to either directly block reproductive hormone receptor-mediated events, or indirectly block conception via negative feedback mechanisms. Immunocontraception, via vaccination against GnRH, the luteinizing hormone receptor or zona pellucida proteins, is also possible. Intratesticular or intraepididymal injections provide a method for non-surgical sterilization of the male dog and cat. Additional methods have been employed for mechanical disruption of fertility including intravaginal and intrauterine devices and ultrasound testicular ablation. Alternative approaches to surgical sterilization will be reviewed.

Keywords: Contraception; Non-surgical; Sterilization; Canine; Feline

1. Introduction

Over half of all households in the United States own a dog or cat [1]. Although exact figures are unknown, the Humane Society of the United States estimates that each year between 8 and 10 million dogs and cats enter shelters and 4–5 million of these animals are euthanized [2]. Unwanted dogs and cats may be reservoirs or vectors of transmissible diseases to man and to economically valuable domestic species. In Great Britain, feral cats kill approximately 100 million birds and mammals each year [3]. There also are ethical implications of euthanizing millions of animals each year. The purpose of this review article is to present a 50-year perspective of research on non-surgical methods for limiting pet reproduction.

Traditional neutering of companion animals has been accomplished through surgical methods of sterilization, namely ovariohysterectomy (spaying) and orchidectomy (castration). However, for understandable reasons, not all owners have their pets surgically sterilized. For purpose-bred bitches and queens, the safest, most effective and least expensive method to prevent unwanted matings is indoor confinement and segregation from intact males. Even for those pets not intended for breeding, pet owners may still be reluctant to consider surgery. In a survey in Sao Paulo, Brazil, 56.5% of owners of adopted shelter dogs were against surgical sterilization, citing compassion (58.1%), unnecessary procedure (11.4%), cost (9.5%), and behavior change (4.8%) as reasons against this method of limiting pet reproduction [4]. In addition, when considering feral cat and dog populations where permanent sterilization is desired, surgical methods can

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be too time consuming and expensive to be performed on a large-scale.

Currently, several alternatives to surgical sterilization are being investigated. For the purposes of this discussion, contraception will be defined as a reversible method for blocking fertility (and will not include pregnancy termination). Pharmacologic methods of contraception and sterilization can be safe, reliable, and reversible. Hormonal treatments, including progestins, androgens, or analogs of gonadotropin releasing hormone (GnRH), act either directly to block reproductive hormone receptor-mediated events or indirectly block conception via negative feedback mechanisms. Immunocontraception via vaccination against GnRH, the luteinizing hormone (LH) receptor, or zona pellucida proteins are also possible. Intratesticular or intraepididymal injections provide a method for non-surgical sterilization of the male dog and cat. Additional methods have been employed for mechanical disruption of fertility, including intravaginal and intrauterine devices and ultrasound testicular ablation. Research investigating non-surgical approaches to contraception and sterilization will be reviewed.

2. Hormonal down-regulation

Hormonal down-regulation is an alternative for temporary suppression of fertility in breeding animals. Exogenous steroid hormones suppress fertility indirectly via inhibition of pituitary gonadotropin secretion and release (mainly LH) [5].

2.1. Progestins

2.1.1. Female dogs and cats

Megestrol acetate, a synthetic progestin, is a tasteless, odorless crystalline powder. Megestrol acetate is rapidly metabolized when given orally, with a half-life of 8 days in the dog [6]. Megestrol acetate has been used extensively for temporary estrus suppression in the bitch. When megestrol acetate was administered to bitches at a daily dose of 2.2 mg/kg body weight orally for 8 days (beginning in early proestrus), estrus was suppressed in 92% of cases [7]. Pyometra, a reported side effect of megestrol acetate treatment, developed in 0.8% of treated bitches [7]. Megestrol acetate was also effective at suppressing estrus in queens when given at a dose of 5 mg/cat orally for 5 days and then once weekly [6,8]. Reported side effects of prolonged megestrol acetate treatment in dogs included: increased appetite leading to weight gain; lethargy or restlessness [6,8]; marked mammary stimulation with hyperplastic and/or neoplastic changes; clinical and pathologic changes typical of diabetes mellitus [9,10]. Similar side effects have also been reported in queens [6,11,12].

Medroxyprogesterone acetate (MPA) is a long-acting injectable progestin that has been used to suppress estrus in the bitch and queen but to a more limited extent than megestrol acetate, due to the high incidence of side effects. Occurrence of uterine disease was common in MPA-treated animals. The prevalence of uterine lesions on histopathology (after ovariohysterectomy) was 45% for bitches treated with MPA for estrus suppression, compared to 5% for untreated animals [13]. In addition to uterine lesions, subcutaneous administration of MPA in dogs has resulted in clinical signs consistent with adrenocortical suppression (e.g. alopecia, hair discoloration, thinning of the skin and mobilization of subcutaneous fat) [14]. It is noteworthy that MPA is not recommended for use in cats [15].

Proligestone (14α,17α-propylidene-dioxy progesterone) is a unique progestin with weaker progestational activity than other synthetic progestins [16]. Proligestone is marketed in Europe (Delvosteron, Intervet) as an injectable canine contraceptive. The manufacturer claims that it is safe to use for prevention, delay or suppression of estrus when given to female dogs at an initial dose of 10–30 mg/kg SQ, with repeated administration 3 and 7 months later [17]. It can also be given to female cats (1 mL subcutaneously), causing estrus suppression for about 6.5 months [17]. In clinical trials, this regimen did not promote development of uterine disease or mammary tumors [16].

Canine and feline contraception through hormonal manipulation has been practiced for many decades, with the first report by Murray and Eden [18]. However, most of our understanding regarding the side effects of progestin administration in dogs comes from research on human contraceptives for which dogs served as animal models. In 1962, the U.S. Congress passed the Kefauver-Harris Amendment that mandated all drugs developed for use in humans must first be extensively tested in animals [19]. The current recommendations from the Food and Drug Administration are to administer new human contraceptives to dogs at doses 1, 10 and 25 times the anticipated clinical dose for humans [20]. Reported adverse effects depend upon the type of progestin administered, dose, time of treatment, treatment regimen, and age of the animal [21,22]. In beagles treated with doses of MPA 1–25 times the human contraceptive dose for 4 years, a dose-related increase in mammary dysplasia was reported [16,23]. However, it is important to note that the canine mammary gland undergoes pathologic changes following progestin administration in a way not