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Non surgical contraception in cats: what's new ?

Contracepção não-cirúrgica em gatos: o que há de novo?

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Abstract

In the feline species, progestins, GnRH agonist implants and melatonin implants are the three main non-surgical contraceptive approaches that are important to discuss today. When available, those can actually come handy in many clinical situations when surgery cannot be performed or should be avoided. To date though, those only offer short to medium term options. Research using gene therapy is however on its way, with encouraging preliminary results. A long term alternative using this technology might become available in the future, changing how we approach contraception in cats in our veterinary clinics.

Keywords : *contraception, GnRH agonist, progestin, melatonin, queen, tomcat. spaying, neutering*

Introduction

There is no doubt that, in 2021, surgical contraception remains THE norm in cats. However, when it comes to this species, there are also now several non surgical options – like progestins, melatonin and GnRH agonists. Those can actually come handy in many situations, whether it is about finding alternatives to manage a feral cat population, to temporally pause the reproductive activity in breeding catteries or even if it is just an owner's preference. We will here review the most common molecules, as well as their protocols and indications, that are currently described in the veterinary literature, and discuss how veterinarians can implement them in their everyday practice.

Progestins

Progestins : how do they work ?

Progestins are synthetic derivatives of progesterone and bind to the progesterone receptor on target organs, therefore producing the same biological effect as endogenous progesterone. These molecules have been commonly used to control the reproductive cycle of female domestic animals and achiever their main contraceptive effect by suppressing estrus as well as preventing ovulation.

Chemical sterilization in queens

In 2021, one might be surprised to read about progestins as an alternative to consider for feline non surgical contraception. Those molecules have indeed been around for more than 50 years now and, have historically been used to efficiently suppress estrus activity in queens.

They are however well-known as well for their potential side effects on the uterus and the mammary glands – which is why we tend not to consider them anymore as a valuable alternative for feline contraception.

Why bringing them up here then ?

Because in a 2015 paper, Pr Stefano Romagnoli offered a new perspective on the use of those molecules in feline reproduction [1].

While he acknowledges that progestins should be used with caution in queens, he however mentions that side effects that have been described over the years might be related to the use of high doses and that low doses can actually offer a safe alternative that is worth considering.

In his paper, he mainly discusses the use of megestrol acetate and medroxyprogesterone acetate (levonorgestrel, chlormadinone acetate, delmadinone acetate, proligestone and altrenogest are also discussed – although he writes the efficacy and safety of these need to be further investigated).

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Megestrol acetate at 0.02mg/kg q24h and medroxyprogesterone acetate at 0.05mg/kg q24h seem to be appropriate dosages to be administered orally in queens.

For long term effect, injectable formulations of medroxyprogesterone acetate at 2-5.5mg/kg IM every 5 months or as low as 3mg/cat (equivalent to 0.75mg/kg in a 4kg cat) are also reported effective and likely to be devoid of any long term health risks. Since there is no scientific information on what is a safe length of progestin treatment using these low doses, he writes that a healthy young adult queen can probably be safely treated for longer than a year, while an adult female that is more likely to have undergone age-related changes of the uterus and/or mammary glands should not be treated for longer than a year.

Queens treated with progestins should be healthy and in post-estrus or anestrus. They should not be treated during estrus or diestrus.

Chemical castration in male cats

While of interest in the female, progestins are not recommend for chemical contraception in males and do not represent an interesting clinical option there.

When should they be considered ?

Whether it is for helping in the management of a feral cat colony (so that queens do not get pregnant while waiting to be surgically spayed) or to temporarily stop the reproductive activity in purebred queens in catteries, low dose progestins could be an option to consider therefore, based on this recent publication on the topic.

GnRH agonists implants

GnRH agonist implants have been available to veterinarians in Europe since 2009. While their primary indication is chemical sterilization in male dogs, several studies have also been carried out on their use in cats [2]. Indeed, this still raises lots of questions among practitioners.

GnRH agonists: how do they work?

GnRH is a decapeptide synthetized at the hypothalamic level. Its pulsatile secretion modulate the secretion of pituitary gonadotrophins LH (Luteinizing Hormone) and FSH (Follicle Stimulating Hormone), both of them directly acting on the reproductive function. When such a treatment is initiated, the GnRH agonist implant's mode of action is a two-step process:

- First, it will stimulate the pituitary gonadal axis, and will lead to an increased secretion of FSH and LH, that will have for consequence the increased secretion of steroid sexual hormones.
- In the second time, their chronical use will lead to a desensitization of the pituitary and will provoke a stop in the gonadotrophin secretion, leading to a silencing of the reproductive function and chemical castration.

There are to date very few studies capitalizing on the initial GnRH agonist stimulating effect in cats. On the other hand, there is a growing body of literature on their use for chemical castration in this species.

The implants (4.7mg or 9.4mg) are inserted subcutaneously, whether between the shoulder blades or at the peri-umbilical area. The peri-umbilical area should be preferred for administration as it allows easier removal of the implant if this is required.

Chemical castration in tomcats.

Following the implant administration, an increase in sexual behavior (libido, mounting and mating) has been described in male cats. This usually lasts until day 16 following the treatment. After this though, the chronic effect of the GnRH agonist administration will kick in, progressively leading to chemical castration [3-4] :

- The penile spines, which represent the testosterone impregnation in male cats, will have completely disappeared around 9 weeks after treatment;
- The testicular volume will progressively decrease because of the spermatogenesis arrest ; 4 weeks following the implant administration it will be reduced by 25%, and by 60% at week 12 ;
- Sexual behavior & sperm production will be dramatically altered by week 16 following the

implant administration ;

Male cats treated with this implant will exhibit the same changes observed in surgically castrated male cats. Urine marking disappears within 10 weeks of treatment, and effects on behavior (decreased aggression towards the owner, reduction of vocalization) as well as the strong intact male cat smells were noted in average 19 days (range 10-35 days) post treatment with the GnRH agonist implant [5].
Those effects are fully reversible as soon as the deslorelin effect clears out. With a 4.7mg implant, normal testicular volumes & normal penile spines were noted 21 months after implant administration. Some of those cats were allowed to breed, confirming the return to fertility. A recent study using 9.4mg implants showed that their effect lasted in average 67 months [3].

Chemical sterilization in queens

In females, the primary stimulating effect can lead to estrus induction. In bitches this is the case for almost 100% of the females implanted in anestrus. When mature females are implanted though, the initial stimulation phase only led to visible clinical signs of estrus in 20-40% of the females treated. Typical estrous behavior started by 3.8 ± 2.2 days post-treatment and lasted for 3.5 ± 3.1 days [2].

Following administration of a 4.7mg implant, the first post-treatment estrus period appeared in 57 ± 2 months (range 16-37 months). We can expect this range to be longer when using a 9.4mg implant.

Resumption of fertility in females treated with a GnRH agonist implant was confirmed. In one study, 7 females became pregnant and delivered naturally and spontaneously. Litter size was 3.3 ± 1.5 kittens.

Chemical sterilization in cats using GnRH agonist implants : current challenges

The different studies that have been done so far confirmed that GnRH agonist implants can offer a safe & reversible chemical sterilization in male and female cats. However, some challenges still need to be addressed:

- As described in dogs, there is a large variability in terms of duration of efficacy in male and female cats ; it is therefore difficult to exactly assess the duration of the sterilizing effect and when to re-treat the animal if needed ;
- As in bitches, the stimulation phase in queens is potentially associated with an induced estrus ; this one can be fertile and it needs to be carefully managed to avoid unwanted pregnancies ; the use of progestogens at the time of administering the implant and/or implanting prepubertal queens have been investigated and sound like interesting options in order to prevent this potential problem ;

What are the advantages over surgery ?

The use of a deslorelin implant to chemically spay & neuter a cat has to be considered as an alternative to the surgery, whether it should be used for convenience or therapeutic purposes.

The main interest of these implants stays in their transient effect. Clinical observations showed that males and females that were implanted were the still fertile and had normal litters. This alternative can be of great interest for some owners, mainly breeders, who wants to breed their animals later.

This alternative is also of great interest when surgery is contraindicated, for example when the anesthetic risk is too important. Some owners of elder cats will appreciate this solution rather than going for surgery.

Melatonin implants

Melatonin is produced and secreted by the pineal gland of the central nervous system, the duration of melatonin secretion being proportional to the length of the night in cats. As a direct effect of the increasing light on the cerebral cortex, melatonin secretion is suppressed, consequently increasing the secretion of gonadotropins from the anterior hypophysis. This leads to an increase in sexual hormones which in felines potentially activates the reproductive function.

Melatonin implants : how do they work ?

Melatonin has been known to suppress estrus cycle in cats for decades now. The first studies

documenting this effect were however requiring whether daily intravenous injections or daily oral administrations. These however proved to be quite unpractical. Therefore, trials with long term release subcutaneous implants, as used in sheep for estrus induction, were performed [6-7]

The implant most commonly used in the different studies on the topic is a subcutaneous implant containing 18mg of melatonin (like Melovine, CEVA).

Chemical sterilization in queens

When the 18 mg implant is administered in interestrus in queens, estrus suppression is possible without initial estrus signs and lasts on average 3 months. Indeed, Schafer-Somi [6] reported that 22/27 queens treated this way, no estrus occurred for an average of 103.9 days. More recentlty, Furthner et al [8] reported also that 33/42 females had estrus inhibited following administration of a similar melatonin implant for a mean of 86 ± 50 days (range 21 -277 days).

However, there is a clear individual response to treatment. Schafer Somi mentioned one queen that started her season right after receiving the implant. The implant was not removed on this individual, the queen was bred, conceived and course and duration of pregnancy, parturition and lactation were normal in the end.

This is therefore something important to mention to the owners before initiating the treatment.

Surgical application by stitch incision with a scalpel blade after local anesthesia is the method of choice to administer the implant, rendering repeated treatment unattractive. The implant is mostly administered subcutaneously between the shoulder blades or behind the navel.

It is interesting to note that repeated use has not been investigated sufficiently to date. In her study, Schafer Somi [6] mentions that in one queen implanted twice, estrus suppression was not observed after the second implant administration ; this has also been observed in another study, where shorter inter-estrus intervals were noted on second application.

An explanation for this could be that the duration of suppression is relative to the prior melatonin pattern and not the absolute duration. This phenomenon, called photorefractoriness, occurs in mammals after prolonged light exposure when a sudden change to shortened light exposure occurs – although in cats, this remains yet to be proven.

From a practical point of view, as there was no effect in a rather high percentage of cats after single use, it is questionable whether investigations concerning repeated use make sense.

Chemical Castration in Male cats

Nunez Favre et al [9] looked at the effect of those melatonin implants in tomcats.

While they reported that the implant led to a reduction in sperm production and quality for approximately 120 +/-15 days after implant administration, it is important to note that treated animals actually kept their capacity to produce semen during this period.

Melatonin implants therefore do not appear as a valuable solution to consider when it comes to temporarily chemical castration in cats, as those cats might still have the capacity to sire litters.

Progestins, GnRH agonist & melatonin implants are the current medical solutions available to provide non surgical contraception in cats in veterinary clinics. Depending on the clinical case and availability of the product, veterinarians can pick and choose which one would fit their need best. They offer valuable alternatives to consider when non surgical contraception in cats is required. One limitating factor is that those treatments offer only short term contraception… but things could change in a near future. Indeed, as reported on the Alliance for Contraception in Cats & Dogs (www.acc-d.org), several initiatives are underway to provide long term solution. Some approaches leveraging gene therapy are well underway and preliminary results sound promising. It will be interesting to see what the future brings this way. Meanwhile though, the current solutions offer alternatives that are worth using in my opinion.

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