Clinical use of hormones in the control of reproduction in bitches and queens
[Utilização de hormonas no controlo da reprodução em cadelas e gatas]

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Introduction

Synthetic analogues of progesterone, also termed progestins or progestogens (PG), are pharmaceutical compounds commonly used to control the reproductive cycle of domestic animals. The following PGs are commonly used in dogs and cats for temporary (starting the treatment shortly before proestrus onset) or prolonged (starting in anestrus) postponement of estrus, or for suppression of estrus (starting the treatment after proestrus onset): medroxyprogesterone acetate (MPA), megestrol acetate (MA), proligestone (PR), chlormadinone acetate (CMA), delmadinone acetate (DMA), norethisterone acetate (NTA) and melengestrol acetate (MGA). From the clinical point of view all these product act in the same way through a block of the production and/or release of GnRH from the hypothalamus. These compounds show a variety of action on the reproductive and endocrine system (such as hyperplasia of the endometrium, hyperplasia of the mammary parenchima, decreased production of adrenocorticosteroids, increased secretion of prolactin and growth hormone, insulin resistance) as well as some local skin reactions at the injection site and behavioral modification (increased appetite and weight, polydipsia, slight depression, decreased libido in males). In pregnant bitches and queens use of PGs may cause masculinization of female fetuses if administered early in pregnancy (during organogenesis) or delayed parturition if administered in the last decade of pregnancy.

Clinical considerations for a safe use of progestogens

All the above cited effects are reversible and do not generally cause problems in healthy young to adult animals treated for not too long and using the recommended dosage. In general, a treatment period of 6 months is considered adequate in most individuals, although longer treatments can also be safe provided that the female is given a rest of 1-2 months every 4-6 months. While most bitches and queens may tolerate well treatment periods of more than 6 months, animals with a pre-existing disease such as subclinical diabetes, microscopic mammary lesion/tumor or cystic endometrial hyperplasia may see their condition worsen rapidly as a result of the PG treatment. The following is a series of considerations on patient selection and type of presenting complaint for which a PG treatment should or should not be used.

* Do not use long acting compounds (such as MPA or PR or any other compound marketed for long term use) prior to puberty in felines, as this may cause the queen to develop a long-lasting mammary hypertrophy which could become a life-threatening situation. In prepuberal animals it is best to use initially a short acting compound (such as MA) per os for 1-2 weeks and then change to a long acting PG once potential side effects have been ruled out.

* Do not treat pregnant females, as this may cause fetal developmental defects as well as delayed parturition, thereby causing fetal death in utero due to placental ageing and detachment.

* Do not treat pseudopregnant bitches. During a PG treatment clinical signs of pseudopregnancy will disappear but will recur once treatment is discontinued, and the problem may worsen.

* Do not treat a female during diestrus. The stage of the reproductive cycle should always be identified using vaginal cytology and/or serum progesterone assay, and the bitch or queen should best be treated during anestrus. Diestrus should be ruled out in felines too, as approximately 30% of queens ovulate spontaneously, maintaining thereafter a 30-45 day-long diestrus.
* Do not treat females with uterine haemorrhage. Prolonged sanguineous vulvar discharge following parturition in the bitch can be a critical problem which should either be treated with a uterine contractive drug (i.e. as ergonovine) or sent to surgery. Milder bloody vulvar discharge can be caused by uterine neoplasia, cystic endometrial hyperplasia with superimposed endometrial inflammation, pyometra, metritis. None of these conditions will benefit from administration of a progestogen.

* Do not treat diabetic patients. Although not always necessary, it would be wise to measure blood glucose before and/or after a prolonged treatment to confirm health status with regard to glucose metabolism.

* Do not use PGs in females with prolonged heat. A prolonged heat may be due to ovarian cyst(s), a granulosa cell tumor, or may be due to a split heat (in the bitch) or to a misinterpretation of normal estrous signs by the owner. For none of these categories is a progestogen treatment indicated (although in some cases an ovarian cyst may benefit from administration of a progestogen). Therefore, bitches or queens with a prolonged heat should not be treated with a progestogen, unless a diagnosis of cystic ovarian disease has been carefully confirmed and surgery or administration of GnRH or hCG are not a valid therapeutic option.

Choosing the right candidate

The ideal candidate is an adult postpuberal female in anestrus. Prepuberal females should not be treated long acting compounds because of the risk of precipitating a subclinical uterine, endocrine or mammary condition (such as diabetes, cystic endometrial hyperplasia-pyometra in the bitch or mammary hyperplasia in the queen) which are rare but have been reported in young animals. If one of the above conditions is present the administration of a long acting progestogen prior to diagnosis may pose a serious health threat on the female. A minimum database of clinical information to be gathered prior to administering a long-acting compound should include:

- collecting a thorough reproductive history to rule out occurrence of estrus within the last 1-2 months (which would mean that the female is in diestrus);
- a complete clinical exam;
- palpation of the mammary gland to rule out presence of mammary nodules;
- a vaginal smear to rule out presence of oestrus.

Table n° 1 shows the suggested dosages of the most commonly used progestogen-based compounds in the bitch and queen.

<table>
<thead>
<tr>
<th>Suggested Dosage</th>
<th>Dog</th>
<th>Cat</th>
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<tbody>
<tr>
<td>Medroxyprogesterone Acetate</td>
<td>2.5-3.0 mg/kg IM every 5 months</td>
<td>2.0 mg/kg IM every 5 months for the feline</td>
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<tr>
<td>Megestrol Acetate</td>
<td>≤2.0 mg/kg administered for ≤2 weeks in proestrus, or ≤2.0 mg/kg administered for a longer duration of time in anestrus. A typical dosage for estrus suppression is 2.0 mg/kg/day for 8 consecutive days, while a typical dosage for temporary postponement is 0.5 mg/kg/day in late anestrus.</td>
<td>≤5.0 mg/cat administered every other day for ≤3 weeks or with a slower rate of administration.</td>
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<tr>
<td>Proligestone</td>
<td>10-33 mg/kg SC every 3,4,5,5 months</td>
<td>10 mg/kg SC every 3,4,5,5, months</td>
</tr>
</tbody>
</table>

Table n° 1 – Suggested dosages of the 3 most commonly used progestogen compounds in bitches and queen for the control of estrous.

References

Curtis EM, Grant RP – Masculinization of female pups by progestogens. JAVMA 144: 395-398, 1964


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