Review Article

EFFECT OF MEDROXYPROGESTRONE ACETATE "SANGINISUI" ON BITCH

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Introduction

A number of different synthetic progestational drugs have been used for temporary suppression of reproduction in dogs. Medroxyprogesterone Acetate (MPA) [e.g.Injectable Depo-Provera® (Pfizer)], long-acting depot preparations of progestins is an widely used contraceptives in bitches (Immegart, 2000). In Nepal, it is available in the brand name of Sangini (Nepal CRS Company) to be used as contraceptive in women. Effectiveness of MPA is based on interference in reproduction by both local actions in the reproductive tract, as well as effects on the brain, caused by negative feedback on GnRH release from the hypothalamus.

Progestins are used to suppress estrous cycle in intact females but the use of such compounds causes various health hazards in dogs including suppression of immune function, diabetes, mammary tumor promotion and pyometra. The side effect profiles are related to the type of progestational drug used, when during the estrus cycle they are given, and the dose and the duration of use. Progesterone induces changes in the uterus which prepare a suitable environment for early embryo development, including endometrial proliferation, increased uterine glandular secretions and decreased myometrial contractions, as well as a relaxation in normal uterine cellular immune defenses (Teunissen, 1952). They are in general effective for short term suppression of fertility, but most products and dosing regimens are accompanied by potentially serious side effects such as uterine and mammary tumors, as well as diabetes mellitus and acromegaly.

MPA has a relatively long duration of action, usually 6 weeks to 3 months, depending on the species and dose used. It is commercially available around the world as a contraceptive for women. However, human studies showed that MPA to have the disadvantage among the progestins of being one of the most androgenic (Labrie, 1987) and having the strongest suppressive effect on the immune system (Hapgood, 2004; Huijbregts, 2014). MPA is given to female dogs or cats by injection, usually every five to six months during anestrus or as tablets orally once a day. We can minimize the side effect if the precise dose is calculated on a weight basis (Bryan, 1973). The suggested dosage of Medroxyprogesterone Acetate for the bitch is 2.5-3.0 mg/kg IM every 5 months (Evans, 1989).The label directions indicate that the tablets should not be administered for more than two consecutive treatments, making this an impractical long-term solution for contraception. MGA exerts both progesterone and glucocorticoid activity. Its progestational activity was about 125 times greater than that of progesterone as measured by estrus cycle inhibition in cattle; anti-inflammatory assays in rats showed that its glucocorticoid activity was comparable with that of hydrocortisone. The anabolic mode of action of MPA is assumed to be due to stimulation of the ovarian synthesis of endogenous estradiol (Schiffer, 2001).

The pathology caused by progestins includes hyperstimulation of the endometrium, called cystic endometrial hyperplasia, which can be a precursor condition for pyometra, a potentially fatal uterine infection (Dow, 1960). The effect of progestins on endometrial growth was found to be exacerbated if the uterus had been sensitized by estrogen, either endogenous (as during proestrus) or exogenous administration (Dow, et.al.).Thus, if progestin contraception of dogs is considered, treatment should not be initiated when estradiol has been elevated, as during proestrus. Progestin effects are made worse when coupled with estrogen, as would happen if treatment begin during proestrus or estrus, initiating treatment during deep anestrus and using a lower dose may avoid serious side effects. Pyometra has

consistently been shown to predominantly affect middle-aged to older dogs, with mean age at presentation ranging from 6.4 to 9.5 years. The disease can occur from the time of the first season and has been reported in dogs as young as six months of age (Gibson, 2013).

Progestagens have been suggested to promote mammary tumorogenesis in the dog by their induction of the growth hormone overproduction (Rutteman, 1993) .Some progestins stimulate the pituitary glands production of growth hormone (GH) and possibly insulin-like growth factor (IGF-1) in dog mammary glands (Selman, 1994). Furthermore, tumor prevalence can simply be a function of dose; high but not low doses are more likely to result in mammary tumors, including carcinomas (Misdrop, 1991). Treatment with progesterone or MPA resulted in increased GH and altered glucose homeostasis, and MPA caused glucose intolerance (Rijnberk, 1997). High doses of MPA also have resulted in acromegaly, a condition due to chronically high GH concentrations that cause abnormal growth of head, paws and internal organs, as well as skin thickening and folding (Concannon, 1980). MPA have potency to suppress the adrenal (Briggs, 1973) glands involving suppression of the immune response potentially compromising the ability of the animal to respond to infection.

Therefore, long acting compounds such as MPA should not be used prior to puberty as this may cause development of long-lasting mammary hypertrophy. In prepuberal animals it is best to use initially a short acting compound such as megestrolacetate orally for 1-2 weeks and then change to long acting progestins once potential side effects have been ruled out. Use in pregnant female this may cause fetal developmental defects as well as delayed parturition, thereby causing fetal death in utero due to placental ageing and detachment. In case of pseudopregnancy clinical signs will disappear but will recur once treatment is discontinued. 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 is not a valid therapeutic option. The ideal candidate for the use of MPA 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 (Evans, 1989).

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