ABSTRACTS

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EFFECTS OF ANTIPROGESTIN ON THE MEDROXYPROGESTERONE ACETATE-EXPOSED UTERINE TISSUE OF CATS

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Objectives - Medroxyprogesterone acetate (MPA) is a synthetic progestin commonly used for temporary oestrus prevention in dogs and cats in which future breedings are desired. However, proliferations of endometrium and mammary glands, leading to developments of infertility and mammary hyperplasia are the adverse effects of the exogenous progestins [1, 4]. A single administration of depot MPA (at least 10 mg/kg) has shown to develop fibroadenomatous mammary hyperplasia in the cats [5]. However, the hyperplasia of the mammary tissue can be subsided after treatment with aglepristone, a progesterone receptor blocker (10 mg/kg twice at an interval of 24 hours) [3]. In addition, the aglepristone in combination with cloprostenol has been shown to reduce uterine diameter in the bitches with pyometra [2] but studies in cats with uterine pathology are scarce. The purpose of this study was to evaluate the efficacy of aglepristone at the recommended dose for treatment of endometrial hyperplasia induced by MPA administration in cats.

Materials and methods - Eighteen pubertal nulliparous domestic cats of mixed breed, 7-18 months of age and weight 2.9 ± 0.4 kg were divided into three groups; control (n=6), MPA (n=6) and MPA + aglepristone (n=6). Samples were collected from the mid part of the uterine horn after ovariohysterectomy. Uteri of cats in the interoestrous stage were used as controls (Control group). In 12 cats, endometrial hyperplasia was induced by administration of MPA (Depo-gestin, A.N.B.Lab, Thailand) 50 mg/cat during interoestrus. Three weeks after the MPA administration, six of the 12 cats were ovariohysterectomised (MPA group) whereas the remaining cats were given 10 mg/kg aglepristone (Alizine, Virbac, France) subcutaneously twice at an interval of 24 hours and the uterine samples were obtained at two weeks later (MPA+aglepristone group). Uterine samples were fixed in 4% (w/v) paraformaldehyde in PBS and embedded in paraffin wax. Endometrial and myometrial thickness was measured at x100 magnification using an ocular micrometer. A standard avidin-biotin immunoperoxidase technique using monoclonal mouse anti-PCNA antibody (Dako, Glostrup, Denmark) and monoclonal mouse anti-human progesterone receptor antibody (Clone 10A9, Immunotech, France) was performed for detection of proliferative activity and progesterone receptor (PR) expression, respectively, in luminal and glandular epithelium. The immunostainings were evaluated by counting 500 cells of each category in five random areas of a uterine section. Means of positive stained cells in three tissue sections were calculated and defined as percentage of positive cells for PCNA index and PR score. The PR scores were calculated as $P_1 + (2 \times P_2) + (3 \times P_3)$ where $P_1$, $P_2$ and $P_3$ were the estimated percentages of positive nuclei with low ($P_1$), medium ($P_2$) and high ($P_3$) intensity of immunostaining colour. The data were compared using ANOVA. Least square means were obtained and compared using Tukey’s adjustment for multiple comparisons. The level of significance was set at $P < 0.05$.

Results -The myometrial thickness, E/M ratio and PCNA index in the MPA-treated uteri were greater than the controls ($P < 0.05$) (Table 1 and 2). The PR scores were lower in the MPA-treated group than the controls ($P < 0.05$). Differences of all parameters were not observed between the MPA and MPA + aglepristone groups ($P > 0.05$).
Table 1 Measurement of endometrial and myometrial thickness in uterine tissue sections of cats in various groups (mean ± SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>Endometrial (E) (µm)</th>
<th>Myometrial (M) (µm)</th>
<th>E/M ratio</th>
</tr>
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<tbody>
<tr>
<td>Control (n=6)</td>
<td>208.9 ± 40.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>129.0 ± 3.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.7 ± 0.3&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>MPA (n=6)</td>
<td>325.8 ± 139.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>360.2 ± 141.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.0 ± 0.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>MPA + aglepristone (n=6)</td>
<td>331.4 ± 98.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>341.4 ± 141.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.1 ± 0.4&lt;sup&gt;b&lt;/sup&gt;</td>
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</tbody>
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Values within columns with different superscripts are significantly different (P<0.05).

Table 2 PCNA and PR immunochemical staining in uterine of cats in various groups (mean ± SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>PCNA index (%)</th>
<th>PR score (%)</th>
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<tbody>
<tr>
<td></td>
<td>Luminal epithelium</td>
<td>Glandular epithelium</td>
</tr>
<tr>
<td>Control (n=6)</td>
<td>28.7 ± 17.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>38.7 ± 13.5&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MPA (n=6)</td>
<td>56.1 ± 19.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>73.0 ± 7.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>MPA + aglepristone (n=6)</td>
<td>48.6 ± 16.3&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>56.3 ± 24.5&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
</tbody>
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Values within columns with different superscripts are significantly different (P<0.05).

Conclusions - The proliferation of endometrium induced by the MPA could not be reversed using aglepristone at the dosage of 10 mg/kg body weight twice at an interval of 24 hours in the cats. Increase dosage and frequency of treatment may improve the success since the effects of MPA on proliferation of the endometrium are long-acting.

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References