COMPARISON OF THE EFFICACY OF DIFFERENT METHODS ON THE MEDICAL TREATMENT OF CYSTIC ENDOMETRIAL HYPERPLASIA-PYOMETRA COMPLEX IN BITCHES

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Abstract

This study aimed to compare the effectiveness of ovariohysterectomy operations with aglepristone and aglepristone+PGF\(_{2\alpha}\) treatment protocols, preceded by clinical, gynaecological, and ultrasonographical examinations and total blood and hormone analyses in bitches. Furthermore, the influence of initial progesterone (P4) concentrations and uterine diameters on the efficacy of pyometra treatment was determined. Thirty bitches with pyometra were divided into three equal groups: the surgically treated group (OP) and groups treated pharmacologically aglepristone (AL) and with aglepristone+PGF\(_{2\alpha}\) (AP). A dose of 10 mg/kg of aglepristone was administered subcutaneously on days 1, 2, and 7 and if needed on day 14 (groups AL and AP). The bitches of the AP group received additionally 0.25 mg/kg of PGF\(_{2\alpha}\), dinoprost trometamin, once every 24 h between days 3 to 7. Eight bitches in the OP group (80%), five bitches (50%) in the AL group, and five bitches (50%) in the AP group recovered. The success rates we established, ignoring the criteria for treatment acceptance, increased to 60% in the AL group and 83.3% in the AP group when the bitches with P4>2 ng/mL and without ovarian cysts were evaluated and the difference between success ratios of the two groups was found to be insignificant. It has been found that carrying out frequently repeated examinations, pharmacological treatments using aglepristone or aglepristone+PGF\(_{2\alpha}\) constitutes a safe alternative to ovariohysterectomy in bitches in the dioestrus phase with P4>2 ng/mL and without ovarian cysts.

Key words: bitch, pyometra, treatment, aglepristone, PGF\(_{2\alpha}\).

Pyometra is a gynaecological disease, which can be frequently observed in intact bitches leading to an accumulation of purulent content and dilation in the uterine horns and needs urgent treatment (2). Although ovariohysterectomy is a permanent treatment option (13), pharmacological treatment carries an important role in cases of valuable breeding bitches in order to protect their breeding potential. Furthermore, surgical treatment carries a risk and the owner of the animal often rejects the suggestion.

In the treatment of pyometra, while the usage of oestrogen and oxytocin, testosterone and ergot alkaloids are generally unsuccessful, treatment with PGF\(_{2\alpha}\) and/or antiprogestins is inspiring (3, 6, 7, 9, 11).

PGF\(_{2\alpha}\) increasing myometrial contractions may enhance cervical relaxation and have a luteolytic effect (7). Antiprogestins bind to progesterone receptors with a strong affinity without showing any effect of progesterone (5, 10). Competitive blocking of progesterone receptors by aglepristone, a progesterone antagonist, leads to cervical opening, discharge of the uterine contents and distinctly lower uterine mass (2, 3).

The aim of the study was to compare the effectiveness of ovariohysterectomy operations and aglepristone and aglepristone+PGF\(_{2\alpha}\) treatment protocols on the basis of clinical and ultrasonographical examinations and total blood and hormone analyses. A further aim was to determine the influence of initial progesterone (P4) concentrations and uterine diameters on the efficacy of pyometra treatment in bitches.

Material and Method

Thirty bitches of different breeds and ages affected with pyometra were used in the study. The disease was diagnosed on the basis of clinical, ultrasonographical, haematological findings in addition to history data. The bitches were randomly allocated into three equivalent groups: the surgically treated group (OP group), group treated with aglepristone (AL group), and group treated with aglepristone and additionally with PGF\(_{2\alpha}\) (AP group). The mean age and weight of the bitches were: 9 ±2.05 years and 14.35 ±4.96 kg in OP group, 10.1 ±1.79 years and 7.8±2.29 kg in AL group, and 9.7±2.71 years and 8.35±0.9 kg in AP group. The day of the initial pharmacological treatment and that of surgical treatment was designed as the first day. Aglepristone (Alizine®, Virbac, France) was administered subcutaneously in a dose of 10 mg/kg on days 1, 2, and 7 and if necessary on day 14 (8, 9). The
AP group received subcutaneously 0.25 mg/kg of PGF$_{2\alpha}$ (Dinolytic$^\text{c}$, dinoprost trometamin, Pharmacia, Belgium), daily between days 3 to 7 in addition to the aglepristone protocol. Antibiotic therapy included amoxicillin and clavulanic acid (Synulox$^\text{c}$, Pfizer, Italy) for 7 d to all the bitches.

Among the pharmacologically treated groups, in cases where the conditions were deteriorating in their general status and even if no decrease in uterine diameter was determined, then ovariohysterectomy was performed. After that time, the evaluation data was not recorded among those animals. The determination of complete blood cell counts, ultrasonographical examinations, and analysis of blood concentration of oestrogen and progesterone were carried out on days 1, 2, 3, 7, 14, 21, and 28 before the drug applications. Progesterone and oestrogen assays were performed by the use of DSL-3900 RIA and DSL-4800 RIA kits (Diagnostic Systems Laboratories, INC. Webster, USA), respectively.

Statistical analyses were carried out by the use of SPSS 11.5 packet programme. One-Way Anova (one-way variance analyses) and Duncan (multiple comparison test) for comparison of progesterone, oestrogen and haemogram parameters, independent two models t-test for evaluating the uterus diameters, were used respectively. For all statistical analyses performed, the significance level was accepted as P<0.05. Mean values were expressed as X±SD.

Results

From the OP group, eight bitches (80%) recovered and two bitches (20%) died. Five bitches (50%) from AL group and five bitches (50%) from AP group recovered within 28 d after the onset of the treatment (Figs 5, 6, and 7).

Out of the five bitches in the AL group with the initial progesterone concentration P4>2 ng/mL and with no ovarian cysts, three (60%) were recovered; out of the other five dogs in the AL group that did not match the latter criteria, only two recovered.

Out of the six bitches in the AP group with the initial progesterone concentration P4>2 ng/mL and with no ovarian cysts five (83.3%) were recovered, whereas the other four dogs that did not match those criteria did not recover.

Difference among the mean progesterone concentrations in bitches of the OP, AL, and AP groups was found to be insignificant on days 1, 2, 7, 21, and 28, whereas the differences between the OP and AL and OP and AP groups on day 3 were significant (P<0.05). On the 14 d, while the difference of mean progesterone concentrations between OP and AP groups was insignificant, the difference between the AL group and other two groups was significant (P<0.05) (Fig. 1). When the oestrogen concentrations were evaluated, the differences among all groups on days 1, 2, 3, 7, 14, 21, and 28 were insignificant (Fig. 2).

While the mean leukocyte concentrations in AL and AP groups increased from day 1 to day 3, after the 7 d they gradually decreased and on the 28 d, they were within physiological limits in all groups (Fig. 3).

In the ten animals in pharmacologically treated groups with closed-cervix pyometra, it was observed that the cervix opened and a great amount of vaginal fluid discharged following the first injection of aglepristone at least 16 and at most 48 h later with the mean time of 31.6±3.45 h. At physical examination on the second treatment day, the present vaginal discharge of the ten animals with open-cervix pyometra increased.

There was no significant difference between mean uterus diameters of AL and AP groups on days 1, 2, 3, 7, 14, and 28 (Fig. 4).
The diminishing ratios (%) of uterus diameters in bitches with or without recovery from day 1 to 7 or 1 to 14 were shown in Fig. 8. The variances of initial individual uterus diameters or the pharmacological treatment, whether with aglepristone or aglepristone+PGF$_2$$\alpha$, did not have an important effect on the diminishing ratios.

Discussion

In comparison to previous studies (8, 9, 12), although the success rate of 50% we achieved may seem to be low in general aspect, it could be explained by the fact that we ignored the treatment acceptance criteria, which were stated by Hoffmann et al., (9) and Lemmer (12) as P4>3.2 µmol/L, Breitkopf et al., (3) and Blendinger (1) as P4≥2 ng/mL, and Blendinger et al., (2) as P4>5 ng/mL, or the acceptance of the bitches without ovarian diseases or cyclic abnormalities.

High plasma progesterone levels in early and middle phases of the dioestrus in conjunction with the presence of reduced expression of progesterone receptors (4) may be related to the effectiveness of aglepristone. Besides, in the present study, a reduced recovery rate in bitches with pyometra that had P4<2 ng/mL, may be explained with insufficiency of aglepristone in the late term of dioestrus due to the decreased P4 levels and progesterone receptors increase.

Fieni et al., (6) found a global success rate of 87% and 63%, for aglepristone+cloprostenol and aglepristone alone, respectively. When we evaluated the recovery rate by ignoring the initial P4 level>2 ng/mL criteria and the presence of ovarian cyst in 5 bitches (50%) from both groups recovered; however, when we matched these criteria, 3 (60%) out of 5 bitches in AL group and 5 (83%) out of 6 bitches in AP group were recovered. The difference between these groups was insignificant (P<0.05).

Gobello et al., (7) in a previous study reported no relationship between the initial basal P4 levels and therapy success. In comparison, there was an increased success rate by matching the initial P4 level>2 ng/mL criteria in the present study. The statement of Gobello et al., (7) on the success achieved in the bitches within the P4 basal levels due to the uterotonic effect of cloprostenol and the fact that cloprostenol, a synthetic prostaglandin analogue, has stronger and longer efficacy (13) in contrast to the dinoprost, a natural prostaglandin used in this study, created the differences between the studies.

In the AL group, P4 concentration decreased gradually. Whether in AL or AP groups, the decrease we established was in line with the other researchers (2, 3, 7, 9, 12).

The increase of leukocyte concentrations in OP group on day 2 resulted in a difference in comparison with the other two groups. This was thought to be a
and effective solution. It has been determined that complex in bitches still maintains its success as a radical treatment for cystic endometrial hyperplasia-pyometra. As a conclusion, ovariohysterectomy as a pharmacological treated bitches were determined previously (7, 8, 14).

In this study both in AL or AP groups, leukocyte concentrations increased from day 1 to day 3, as mentioned (1-3), and then gradually decreased and reached the normal limits on days 21 and 28, as reported previously (7, 8, 14).

The uterus diameters in the successfully pharmacologically treated bitches were determined within the physiological limits on days 21 and 28, in line with other researchers (3, 7, 9).

As a conclusion, ovariohysterectomy as a treatment for cystic endometrial hyperplasia-pyometra complex in bitches still maintains its success as a radical and effective solution. It has been determined that carrying out pharmacological treatment with aglepristone or aglepristone+PGF2α, preceded by general, gynaecological, haematological, and ultrasonographical examinations, constitute a safe alternative for bitches in dioestrus, with progesterone concentrations higher than 2 ng/mL and without ovarian cysts. As for the pharmacological treatment performed in our study, it is believed that the decreases in the ratios of uterus diameters from day 1 to 7 and from day 1 to 14, give important clues about the prognostic value of the case. Consequently, this helps in deciding whether to perform an operation or to continue the pharmacological treatment, thus increasing the survival chance of the patient.

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References