ABSTRACTS

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LOCAL EFFECTS OF CLOPROSTENOL AND AGLEPRISTONE ON THE CORPORA LUTEA IN PREGNANT BITCHES

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Introduction - Termination of pregnancy, which is mostly required in mismated bitches, can be induced for example by luteolysis or blockade progesterone receptors. Clinical application of such treatment protocols has been not always successful, while in some cases one or more embryos survived the medication. It is assumed that local mechanisms in the ovaries and uterus are involved in pregnancy maintenance. Therefore, the aim of the present study was to examine local effects of cloprostenol/cabergoline (CLO/CAB) and aglepristone (AGL) on the corpora lutea (CL) of pregnant bitches.

Materials and methods - Seven pregnant beagle bitches were divided into 3 groups: CLO/CAB (n=2), AGL (n=3), and control (C, n=2). In the CLO/CAB group, cloprostenol (1 µg/kg sc, Estrumate®, Essex Tierarznei, München, Germany) was given on days 24 and 27 after ovulation combined with daily oral application of cabergoline (5 µg/kg, Galastop®, CEVA Tiergesundheit GmbH, Düsseldorf, Germany) from day 24 to 30. Bitches in the AGL-group received aglepristone (10 mg/kg sc, Alizin®, Virbac, Germany) on days 24 and 25 after ovulation. Two pregnant bitches served as untreated controls. Pregnancies were monitored by ultrasound and endocrine effects of the medications on luteal function by analysis of progesterone concentrations in peripheral blood serum.

Ovariohysterectomy was carried out in all bitches between day 30 and 33 of gestation. The ovaries were fixed in paraformaldehyde and imbedded in paraffin. Histological slides were stained with Hematoxylin–Eosin (H.–E.) and for apoptosis (IN SITU CELL DEATH DETECTION KIT Boehringer). Relaxin (RLX), its receptor (RXFP-1), enzymes of the steroidbiosynthesis (3β hydroxysteroid dehydrogenase (3βHSD)), 17β hydroxysteroid dehydrogenase (17βHSD) and Macrophage Marker (MAC387; Dakocytomation) were analysed by immunohistochemistry.

Results - The control group showed physiological patterns of progesterone corresponding with morphologically intact luteal cells of the analysed CL. These luteal cells were characterized by strong expression of the RLX-system and of enzymes of steroid biosynthesis, supporting the diagnosis of an intact pregnancy. Under the application of CLO/CAB, blood progesterone concentrations declined immediately after the start of treatment, while in the AGL treated bitches peripheral progesterone levels were about the same as in the control group. Luteal cells of the CLO/CAB group showed degeneration with apoptotic nucleus and vacuoles in the cytoplasm. Signs of apoptosis were also found in blood vessels from the CL. Compared to the AGL group, the luteal RLX-system and the enzymes of the steroid biosynthesis (3β HSD and 17 βHSD) were expressed less and more luteal cells with vacuoles were detected in the CLO/CAB-group. Maximum numbers of macrophages per CL were present in the AGL treated bitches (CLO/CAB: 4.8±1.2; AGL: 82.3±12.3; C: 23.8±8.3).

Summary - both treatments resulted in pregnancy termination at a similar time range. The local ovarian mechanisms were different. Direct or indirect luteolytic effects caused by the CLO/CAB treatment were characterized by immediate and rapid degeneration of luteal cells
and blood vessels. As known from the literature, the application of the anti-progestin AGL occupies partly the progesterone as well as the glucocorticoid receptor of the luteal cells. This mechanism seems to induce incomplete luteolysis (supported by our histology results) and secretion of local para/autocrine factors, which induced a massive invasion of macrophages propably by chemotaxis.