Aetiology and Endocrinology of Pseudopregnancy in the Goat

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Contents

Pseudopregnancy in goats occurs when the corpus luteum (CL) persists in the absence of a viable conceptus. In this study, effects of active immunization against PGF₂α (prostaglandin F₂α) on the occurrence of pseudopregnancy were investigated. Does were either immunized against PGF₂α-ovalbumin (I-group; n=11), ovalbumin (CI-group; n=4) or remained untreated (C-group; n=8). Persistence of luteal function occurred in 7 animals of the I-group and one goat from the CI-group. Accumulation of fluid in the uterus of pseudopregnant goats was first detected between days 29 and 38 of the luteal phase. Immunization against PGF₂α therefore can induce persistence of the CL and leads to accumulation of fluid in the uterus. The lifespan of the persistent CL is slightly longer than the duration of a normal pregnancy.

Introduction

Pseudopregnancy is an anoestrous condition which occurs when the CL persists in the absence of a viable conceptus in the uterus. During pseudopregnancy aseptic fluid accumulates in the uterus and this pathological uterine condition is known as hydrometra (Pieterse and Taverne 1986). Presence of fluid in the uterus can be readily diagnosed by transcutaneous ultrasonographic scanning of the prepelvic area of the abdominal cavity. However, in animals which have been mated 20-30 days prior to such an investigation, the diagnosis of hydrometra is less easy because, at this early stage of gestation, a positive pregnancy diagnosis is also indicated by the recognition of uterine fluid (Hesseling and Taverne 1994).

From field studies it appeared that the incidence of hydrometra in herds of dairy goats varies between 3% and 21%, although hydrometra is rare in young goats (Mialot et al. 1991; Hesseling 1993a). The condition is usually diagnosed during routine pregnancy diagnosis of mated animals. However, it also occurs in unmated anoestrous does, both outside and during the breeding season. The uterine fluid is discharged (so-called "cloudburst") once the luteal phase spontaneously comes to an end. Lactogenesis occurs in conjunction with such a cloudburst.

Treatment of pseudopregnant goats with a luteolytic dose of PGF₂α will also cause discharge of the uterine fluid (Pieterse and Taverne 1986). It has been demonstrated under field conditions that a second treatment with PGF₂α, given 12 days after the induced cloud-burst, significantly improves the reproductive performance of the goats when they are mated during the oestrus induced by the second injection (Hesseling 1993b). Assuming that the accumulation of fluid in the uterine lumen is the result, rather than the cause of the persistence of the CL, disturbances in either the luteotrophic or luteolytic mechanism during the ovarian cycle can be expected to play a crucial role in the aetiology of hydrometra.

There are several reasons to suggest a role for prolactin in the pathogenesis of hydrometra in goats: first, prolactin forms part of the luteotrophic complex in cyclic does (Buttle 1983); secondly, udder development and lactogenesis take place during the last part of pseudopregnancy and around the cloudburst in non-lactating does; together with distension of the abdomen this provides the animals with a pregnant appearance; thirdly, a relatively short pseudopregnancy has been documented in goats in which ovulations had been induced during the anoestrous season; the final decline in progesterone levels in these animals coincided with the onset of the breeding season, when plasma prolactin can be expected to drop abruptly (Mizinga and Verma 1984); and finally, prolactin plays a role in the dynamics of fluid accumulation during pregnancy, especially at the interfaces of the endometrium and the fetal membranes (De Bakker 1986).

Conflicting results have been obtained from experiments which have been designed to demonstrate a role for prolactin. Suppression of prolactin release in pseudopregnant goats by daily treatment with bromocriptine during a period of 6-10 days resulted in a gradual but steady decline of plasma progesterone levels until a cloudburst occurred (Taverne et al. 1988). Partial or complete regression of the CL was also indicated by plasma progesterone profiles in pseudopregnant goats treated with bromocriptine for only 4 days (Taverne et al. 1994). The same was found in two hysterectomized does with persistent CL (unpublished data). In these experiments it was demonstrated that the effects on
luteal function could not be explained by a diminished luteotrophic support by LH (luteinizing hormone). It was therefore concluded from these data that prolactin plays a rather dominant role in the luteotrophic complex of pseudopregnant goats. However, measurements of prolactin in plasma samples from pseudopregnant goats in which hydrometra had been diagnosed on the farm, showed that prolactin levels were not different from those in normal reproducing herd mates. Also, prolactin levels in plasma collected from three goats during spontaneous prolongation of the luteal phase and subsequent development of hydrometra were within the normal range in two animals (Hesselink et al. 1995). This "prolactin enigma" can perhaps be clarified if it could be demonstrated that bromocriptine itself has a direct negative effect on luteal progesterone production (Hesselink 1994).

Pseudopregnancy in the goat forms an attractive pathophysiological model to study (1) processes involved in the persistence of the CL in the absence of embryonic signals; (2) the dynamics and contents of endometrial secretions under the influence of physiological plasma progesterone levels, but in the absence of a conceptus; (3) myometrial activity in a gradually enlarging uterus in the absence of a fetus; (4) myometrial activity during the demise of the CL and the following cloudburst.

Since pseudopregnant goats could only be obtained after ultrasonographic examinations of large groups of animals in the field, attempts were made to induce hydrometra in experimental animals by artificial prolongation of luteal function. Because PGF2α is known to play a final role in the luteolytic mechanism of the goat's oestrous cycle (Homeida and Cooke 1982), active immunization against PGF2α appeared to be an obvious method. A similar approach has been followed by others to control ovarian function in sheep (Scaramuzzi and Baird 1976; Ronayne et al. 1990; Bettencourt et al. 1993).

Animals, Material and Methods and Results

Experiments were performed with adult Saanen goats during the breeding season. All animals were kept indoors under natural light conditions and hay was fed ad libitum, with daily portions of a concentrate as a supplement. After they had completed at least one oestrous cycle, 11 does (I-group) were primary immunized by subcutaneous injections in both axillary regions with an emulsion of 5 mg PGF-ovalbumin conjugate in 0.5 ml saline and 1.5 ml Freund's complete adjuvant. Four does (CI-group) were similarly injected with an emulsion of only ovalbumin in saline and the adjuvant.

Booster injections with the conjugate or ovalbumin and incomplete Freund's adjuvant were given 6 weeks later. Eight goats from the same herd remained as untreated controls (C-group).

From October until April, jugular blood samples were taken by venipuncture twice a week. Thereafter, weekly samples were taken until the duration of the induced pseudopregnancy approached the duration of a normal pregnancy. At this stage, samples were taken twice a week again.

Plasma P₄ (progesterone) concentrations were measured on the day of blood collection by means of a direct solid phase radioimmunoassay (Coat-A-Count, TKPG, Diagnostic Products Corporation, Los Angeles, CA, USA). Separate vials of the plasma sample were stored for prolactin and 3HPGF₂α-binding and prolactin assays. Transcutaneous ultrasonographic examinations (Aloka SSD 500V, 3.5 MHz convex sector transducer) were performed in conjunction with the blood sampling, starting when a persistent CL was considered to be present (P₄ ≥ 1 ng/ml for more than 25 days). Images were stored on video-tape for evaluation and documentation. During the second half of pseudopregnancy samples of uterine fluid were obtained by transabdominal, ultrasound-guided puncture at about monthly intervals.

Mean (±SD) duration of the luteal phase (P₄ ≥ 1 ng/ml) in cyclic animals of the C-group was 17.0 ± 1.3 days (n=29). Before and immediately after immunization, the length of the luteal phase was 16.7 ± 1.6 days (n=39) and 17.8 ± 1.3 days in animals of groups I and C1 respectively. Persistence of luteal function occurred in 7 animals of the I-group (64%); each of these animals had developed an antibody titre. However, another 4 does remained cyclic, despite the fact that 3 of them produced PGF₂α antibodies. Antibody dilution curves from these latter animals were not different from those obtained from does with a prolonged luteal phase. One goat from the C1-group also developed a persistent CL which had a lifespan of 150 days. Accumulation of fluid in the uterus of the pseudopregnant animals of the I-group was first detected between days 29 and 38 of the prolonged luteal phase. Although the maximal volume of fluid could not be measured, it was estimated to vary from one to several litres. The animals showed a "cloudburst" at the end of their pseudopregnancy. In 3 goats this happened within a few days after transabdominal uterine puncture for collection of fluid. The duration of the lifespan of their corpora lutea was 103, 138 and 162 days. In three other goats the lifespan of the CL was 165, 166 and 168 days. Two animals developed a second pseudopregnancy immediately fol-
lollowing the cloudburst.

Conclusions
From these data it was concluded (Kornalijnsliper 1995) that (1) immunization against PGE
F2α is an effective method to induce persistence of the CL in goats; (2) induced or spontaneous Persistence of luteal function invariably leads to accumulation of fluid in the uterus; (3) it takes at least about 1 month of exposure to progesterone before accumulation of fluid becomes apparent; (4) the lifespan of the induced persistent CL is slightly longer than the duration of a normal pregnancy in goats.

Ongoing experiments are concentrating on the secretion and contents of the uterine fluids and on changes in plasma levels of prolactin, growth hormone, insulin-like growth factors and their binding proteins in intact pseudopregnant goats in comparison with plasma levels in hysterectomized pseudopregnant and normal pregnant animals.

References
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