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Effect of flunixin meglumine or prostaglandin E2 treatment 15 days after breeding on fertility in Saanen does

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ABSTRACT

The objective of this study was to determine the effects of timely injections of flunixin meglumine (FM) or vaginal application of prostaglandin E2 (PgE_2) on pregnancy, fertility, fecundity, and prolificacy rates in Saanen goats. One hundred and sixty-three nonlactating Saanen does were treated with a flugestone acetate (20 mg)-containing intravaginal sponge for 12 days. They also received eCG (400 IU) and a $PGF_{2\alpha}$ analogue (50 μg) 10 days after progestagen priming. Does detected in estrus were mated and assigned randomly to one of three treatment groups. The PgE_2 group (N = 40) received PgE_2 (2.5 mg) intravaginally 15 days after mating. The FM group (N = 54) received flunixin meglumine (total dose, 100 mg) intramuscularly 15 days after mating. Flunixin meglumine was administered at 9:00 AM. Animals in the control group (N = 69) received no treatment. Pregnancy was diagnosed using transrectal ultrasonography (B-mode at 8 MHz) 30 days after mating. The pregnancy rate was significantly greater ($P < 0.01$) after 30 days in goats treated with PgE_2 and also in the control group than in those treated with FM (67.5%, 59.4%, and 42.5%, respectively). The pregnancy rate did not differ between the PgE_2 and the control group. The pregnancy and fertility rate were lowest in the FM group compared with the other groups. There was no significant difference in the prolificacy rate among experimental groups. In conclusion, our results showed that FM administration during a late luteal phase is detrimental to early pregnancy in goats.

1. Introduction

Early pregnancy loss in dairy goats can negatively affect animal production. Nearly 40% of all pregnancy losses occur 15 to 17 days after estrus, a critical period during which the conceptus must produce sufficient quantities of IFN-τ (interferon-tau) to prevent pulsatile prostaglandin secretion and to maintain the corpus luteum (CL) [1,2]. In nonpregnant ruminants, the CL is broken down by a series of events initiated by the pulsatile release of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) from the uterine endometrium during the late luteal phase of the estrous cycle. The uterus has only a few days to recognize the presence of an embryo, and any factor affecting this synchrony could affect embryo survival and ultimately fertility [3].

Prostaglandin E_2 (PgE_2), a lipid mediator produced by most mammalian tissues, regulates multiple biological processes in normal and pathological conditions. In addition to being a key mediator of inflammation, PgE_2 was recently demonstrated to play an important role in the establishment of pregnancy. The embryo itself secretes and/or stimulates the endometrium to secrete PgE_2 to prevent luteolysis during early pregnancy [4]. It is generally

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accepted that PgE_2 and $PGF_{2\alpha}$ are involved in the life span of the CL but with opposite actions. In contrast to $PGF_{2\alpha}$, PgE_2 has a luteotrophic role in ruminant reproduction [5]. Endometrial production of the luteotropin PgE_2 in ewes increases during maternal recognition of pregnancy beginning on Day 13, thus increasing the ratio of PgE_2 to $PGF_{2\alpha}$ secreted by the endometrium [6]. In the uterine luminal epithelium, the biosynthesis of PgE_2 and $PGF_{2\alpha}$ is achieved by the sequential actions of three groups of enzymes. First, membrane-bound and secretory phospholipase A_2 isoforms convert phospholipids to arachidonic acid. Next, the cyclooxygenases (COXs) convert arachidonic acid into prostaglandin H_2, the substrate for specific isomerases that generate biologically active prostaglandins. Finally, terminal PgE_2 synthase or prostaglandin F synthase enzymes isomerize prostaglandin H_2 into PgE_2 or $PGF_{2\alpha}$, respectively. Numerous studies have demonstrated the existence of two distinct genes encoding isoforms of COX, namely COX-1 and COX-2 [2,7].

Currently there are several strategies, such as lengthening the life span of the CL, being used to prevent early embryonic loss. One of these strategies involves the use of flunixin meglumine (FM), a potent nonsteroidal anti-inflammatory drug that inhibits the synthesis of the COX enzyme [8]. The rationale for administering FM is to inhibit the activity of prostaglandin G/H synthase-2 and to reduce uterine synthesis of $PGF_{2\alpha}$, which both contribute to antiluteolysis during early pregnancy. Previous reports showed FM to inhibit $PGF_{2\alpha}$ secretion by bovine [9], porcine [10], mare [11], and goat [12] uteri. Guzeloglu et al. [13] reported that timely injections of FM to heifers increase pregnancy rates.

We hypothesized that support of the CL with vaginal application of PgE_2 or indirect inhibition of $PGF_{2\alpha}$ synthesis using FM treatment can increase the pregnancy rate by reducing embryonic loss in Saanen goats. To the best of our knowledge, there is no previous report on the effect of PgE_2 on the pregnancy rate in goats.

2. Materials and methods

This study was carried out at a commercial dairy goat farm located in Isparta, Turkey. The climate in the region is continental, with an average annual temperature of 12.1 °C and an average annual rainfall of 498 kg/m^2. These experiments were approved by the Animal Ethics Committee of the Faculty of Veterinary Medicine.

2.1. Animals

One hundred and sixty-three multiparous, nonlactating Saanen does 2 to 4 years of age (2.8 ± 0.05, mean ± SEM) and weighing between 45 and 75 kg (55.2 ± 0.7) with good body condition score (BCS) (3.0 ± 0.05) were used in this study. The BCS was assessed on a 1 to 5 scale at the time of enrollment. All animals were maintained in paddocks and allowed access to a mixture of oats and alfalfa, water, and a mineral lick ad libitum. Animals also received a commercial supplement (250 g) containing 14% crude protein daily.

2.2. Estrus synchronization

All does were treated with 20 mg flugestone acetate sponges (Chronogest CR, Intervet, Turkey) for 12 days. They also received 400 IU of eCG (Intervet) and 50 μg of a $PGF_{2\alpha}$ analogue (d-cloprostenol; Dalmazin, Vetaş, Turkey) 10 days after progestagen priming. Does in estrus were mated (hand mating) and the dates of mating were registered. Does that showed no estrus after sponge removal were excluded from the study.

2.3. Treatments

The mated does were divided randomly into three groups. The groups were approximately equal with regard to average BCS and body weight. One group, the PgE_2 group (N = 40) received 2.5 mg PgE_2 (one-quarter of a silicone implant, Propess; Controlled Therapeutics) intravaginally 15 days after mating. The second group, the FM group (N = 54), received 100 mg flunixin meglumine (Finadyne; Schering-Plough) intramuscularly 15 days after mating. The FM group was administered only one dose at 9:00 AM. Animals in the control group (N = 69) received no treatment. Pregnancy was diagnosed using transrectal ultrasonography (B-mode at 8 MHz) 30 days after mating.

2.4. Statistical analysis

Pregnancy rate (goats pregnant/goats presented to bucks), fertility (goats kidding/goats presented to bucks), prolificacy (kids born/number of kiddings), and fecundity (kids born/goats presented to bucks) were determined. The difference between two population proportions, p1 and p2, was compared by using the *z* test. All analyses were performed using the SAS statistical package (Version 8.1, Cary, NC, USA).

3. Results

All results are shown in Table 1. There was no statistical difference in the age, BCS, and body weight among groups. The pregnancy rate was significantly greater ($P < 0.01$) in goats treated with PgE_2 than in those receiving FM (67.5%

Table 1
Pregnancy, fertility, prolificacy, and fecundity rates in PgE_2 or FM treated goats compared with untreated goats.

Group	N	Age, mean ± SEM	BCS, mean ± SEM	BW, mean ± SEM	PR, % (N)	Fertility, % (N)	Prolificacy	Fecundity
PgE_2	40	2.70 ± 0.11	2.95 ± 0.09	53.6 ± 1.38	67.5^{a} (27/40)	57.5^{d} (23/40)	1.95^{g} (45/23)	1.12^{h} (45/40)
FM	54	2.85 ± 0.11	3.00 ± 0.09	54.0 ± 1.30	42.5^{b} (23/54)	38.8^{e} (21/54)	1.95^{g} (41/21)	0.75^{j} (41/54)
Control	69	2.95 ± 0.07	3.21 ± 0.08*	57.3 ± 1.19	59.4^{a,c} (41/69)	56.5^{d,f} (39/69)	1.79^{g} (70/39)	1.01^{k} (70/69)

Within a column, means without a common superscript letter differ significantly. a,b; j,k; h,j = $P < 0.01$; b,c; d,e; e,f; h,k = $P < 0.05$.
Abbreviations: BCS, body condition score; BW, body weight; FM, flunixin meglumine; PgE_2, prostaglandin E_2; PR, pregnancy rate.