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Parturition induction in ewes by a progesterone receptor blocker, aglepristone, and subsequent neonatal survival: Preliminary results

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ABSTRACT

The clinical effects of aglepristone treatment to induce parturition in ewes and their newborns were reported. Three experimental groups were defined: group AG5 (n = 5), group AG10 (n = 5), and group CG (n = 5) in which ewes were injected twice with 5, 10 mg/kg of aglepristone, and saline solution of ewes, respectively. Different parameters associated with parturition in ewes and their newborns were investigated. Serum progesterone, oxytocin, and free and conjugated total estrogens were measured after treatments until parturition. No statistical difference was found from first aglepristone administration to onset of lambing between AG5 and AG10 (23.90 ± 6.20, 40.00 ± 6.71 hours). Parturition induction in two groups shortened the gestational length significantly compared with the control group (P = 0.003). Dystocia was observed in two ewes in group AG10. The placental weight showed statistically significant difference only between the AG10 and CG (P = 0.039), but no difference was observed in the placental expulsion period between the groups. Decrease in food consumption 24 to 36 hours after parturition in all ewes and skin necrosis in an ewe in group AG5 were observed. Progesterone concentration was significantly lower in AG5 than that in ewes in group AG10 and CG (P < 0.05). No difference was observed in concentrations of free total estrogens and oxytocin between groups. The body temperature of lambs was significantly different between AG10 and CG groups both right after (P = 0.011) and 12 hours after parturition (P = 0.014). The lambs in CG had the highest mean birth weight (4.29 ± 0.28 kg), which was significantly different from the induced groups. No significant difference of blood pH and blood gases values between groups was identified both at birth and 12 hours after parturition for lambs. Significant differences could clearly be observed in total protein and blood urea nitrogen and total protein findings 12 hours after parturition (P < 0.05), whereas no difference was found in blood glucose, albumin, inorganic phosphor, triglyceride, or total cholesterol parameters. The results of this study show that the administration of aglepristone to induce parturition can precisely control lambing time without any side effects in either mothers or lambs.

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1. Introduction

Estrus and breeding period synchronizations and parturition induction are useful methods in animal reproduction. Especially on large farms, programmed lambing systems offer organizational advantages such as spending less time on estrus detection and observing animals for parturition problems, vaccination of newborns at proper intervals, and increased uniformity in parturition and weaning time. Although parturition induction is an uncommon procedure in sheep reproduction, synchronized lambing has significant advantages in terms of the assistance of pregnancy pathologies, treatment of diseases in periparturient ewes, immediate care of lambs, and the concurrent weaning period [1–3]. Effective parturition induction, thereby increasing lamb survival, in ewes can be managed only if the breeding date is known [1]. The survival rate for newborns decreases and most lambs are either born dead or die soon after parturition, as they are unable to breathe due to pulmonary immaturity and a lack of surfactant production. Moreover, uterine blood flow is negatively affected by uterotonic substances and uterine contractions; fetal acidosis occurs in parturition induction, and this may influence the vitality of newborns [4,5]. No information about neonatal survival, including biochemical parameters, was reported after parturition induction by aglepristone in ewes.

The administration of dexamethasone, estradiol benzoate, and prostaglandin $F_{2\alpha}$ was tested at different gestational periods with different doses, alone or in combination for parturition induction in ewes [3–10]. Dexamethasone at a dose of 10 to 20 mg is the most common method of inducing parturition, but the lambing interval changes according to the treated gestational day. Administration of dexamethasone from Day 137 to 144 results in lambing between 34 and 50 hours [1,3,10–13]. Lamb viability, the rapid effect in terminating a pregnancy, and minimal adverse effects are valuable parameters in assessment of parturition induction success. Uremia linked to increased protein catabolism was reported as a poor outcome after administration of dexamethasone [14,15].

A progesterone receptor blocker, aglepristone, has been licensed as an important abortifacient for small animal practice, and it is safely used in midgestation termination in queens, bitches, and rabbits [16–21]. In recent studies, the action of aglepristone has also been thoroughly investigated in parturition induction in dogs and farm animals [22–27]. Regarding antiprogesterone, only RU 486 was tested to control the time of parturition in ewes, and successful effects were reported without any side effects on parturition and postpartum processes [28]. However, no information has been reported about the clinical efficacy of aglepristone in parturition induction in ewes.

The placenta is the major source of progesterone and estrogen in the sheep [29,30]. Estrone sulfate is the major estrogen in peripheral plasma and starts to increase from around 70 days after conception in the pregnant ewe. Unconjugated estrogen concentrations such as estrone remain low until the last few days of pregnancy, and it rises dramatically [31]. The fall in progesterone production is inversely related to the increase in unconjugated and conjugated estrogen synthesis [29]. The estrogens increase the sensitivity of myometrium to oxytocin but it is not accompanied by a fall in progesterone production [32].

The objective of this investigation was to assess, for the first time, the clinical efficiency of aglepristone in parturition induction, by recording different parameters associated with parturition in ewes and newborns. In addition progesterone, oxytocin, and free and conjugated total estrogens changes were also evaluated between groups.

2. Material and methods

Fifteen healthy crossbreeds (Kivircik × Chios) ewes were included in the study. All of the ewes were subjected to estrus synchronization by inserting intravaginal sponges containing 30 mg of cronolone fluorogestone acetate (Chronogest CR, Intervet, Turkey) for 11 days and received 400 IU pregnant mare serum gonadotrophin (Chronogest/PMSG, Intervet, Turkey) intramuscularly when the sponge was withdrawn. On Days 12 to 14, the ewes were exposed to rams, and the breeding date was recorded. They were fed a totally mixed ration (alfalfa hay, whole corn, and barley straw) and were housed in a sheep farm in Görükle region in Bursa, Turkey, 40° N and 28° E at an altitude of 128 m above sea level. Approval from the ethics committee of the Uludag University to use the animals was obtained (2010-09/02). Pregnancy was confirmed by transrectal ultrasonographic examination 35 days after mating. Confirmed pregnant ewes were randomly assigned into three groups. The ewes in group AG5 ($n = 5$) and AG10 ($n = 5$) were treated with aglepristone (Alizin, Virbac, Germany) at a dose of 5 mg/kg and 10 mg/kg body weight subcutaneously once daily on 2 specific consecutive days (on Days 140 and 141 after mating). The ewes in the control group (CG; $n = 5$) received only 0.9% NaCl solution (Eczacibasi, Baxter, Turkey) subcutaneously.

The body temperature of ewes was recorded twice (every 12 hours) a day, starting from Day 139 of pregnancy and running up to 12 hours after parturition. Placental expulsion was controlled in terms of retention of fetal membranes and expelled fetal membranes were weighed. The pregnancy, treatment onset of lambing periods and placental expulsion periods were recorded.

The lamb weight and body temperatures were measured immediately after parturition. A jugular blood sample was taken with injection needles and blood gas syringes (0.70 × 32 mm, Ayset AŞ, Turkey), and the pH value was measured using a gas analyzing machine (IRMA TRUPOINT Blood Analyses System, ITC, Edison, NJ, USA). Twelve hours postnatum, blood pH determination and body temperature measurements of the lambs were repeated. For biochemical analysis, 10-mL blood samples were taken from vena jugularis, centrifuged for 10 minutes at 3000 × *g*, and the plasma samples were stored −80 °C until the analyses were carried out. Sera were analyzed with commercially available kits by means of the spectrophotometer (Shimadzu UV-1601). Total protein, albumin, triglyceride, total cholesterol, glucose (Ben Biochemical Enterprise), blood urea nitrogen (BUN), and inorganic phosphorus (TECO Diagnostics) were measured.