

EFFECT OF SYNTHETIC PROSTAGLANDIN F_{2α} ANALOGUE (CLOPROSTENOL) ON LITTER SIZE AND WEIGHT IN A RABBIT LINE SELECTED BY GROWTH RATE

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ABSTRACT: The effect of a treatment with a synthetic analogue of prostaglandin F_{2α} (cloprostenol) administrated intramuscularly on day 28 of pregnancy in does belonging to a synthetic rabbit line selected by growth rate (line R) was studied. A reduction in gestation length was observed after treatment with prostaglandins (31.3±0.1 vs 32.4±0.1 days, for treated and control groups, respectively, P<0.05). Litter size at birth, and live-born pups were not affected by the treatment. Individual weight of young rabbits at birth was significantly different between treatment groups (52±1 vs 58±1 g, in treatment and control group respectively, P<0.05). In the control group, young rabbits born from multiparous does were

heavier than those from primiparous (53±2 vs 63±1 g, in primiparous and multiparous does respectively, P<0.05). There were not differences in birth weight of kits from treated multiparous and primiparous does. At weaning, individual weight was not affected by treatment (578±12 and 561±10 g, in control and treatment group respectively), and differences were observed in reproductive status (513±12 vs 626±9 g, in primiparous and multiparous does respectively, P<0.05). An increase in mortality was observed during lactation period after treatment with PGF_{2α} (48% vs 26%, in cloprostenol and control group respectively, P<0.01).

RESUMÉ: Effet d'un analogue synthétique de la prostaglandine PGF_{2α} (Cloprostenol) sur la taille et le poids de portée dans une lignée de lapins sélectionnés sur la vitesse de croissance.

L'objet de ce travail est d'étudier l'effet de l'injection intramusculaire d'un analogue synthétique de la prostaglandine PGF_{2α} (Cloprostenol) au 28^{ème} jour de gestation à des lapines appartenant à une lignée synthétique sélectionnée sur la vitesse de croissance (lignée R). La durée de gestation est réduite après traitement avec les prostaglandines (31.3±0.1 vs 32.4±0.1 jours, respectivement pour le lot traité et le lot témoin, P<0.05). La taille de portée à la naissance et le nombre de nés vivants ne sont pas modifiés par le traitement. Le poids individuel des jeunes lapereaux à la naissance est significativement différent entre les lots (52±1 vs 58±1g, respectivement pour le lot traité et le lot témoin, P<0.05). Dans le lot

témoin, les jeunes lapereaux nés de lapines multipares sont plus lourds que ceux issus de primipares (53±2 vs 63±1g, respectivement pour les primipares et les multipares, P<0.05). Dans le lot traité, le poids des lapereaux à la naissance ne varie pas selon qu'ils sont issus de lapines multipares ou primipares. Au sevrage, le poids individuel des lapereaux n'est pas modifié par le traitement (578±12 et 561±10g, respectivement pour le lot témoin et le lot traité) mais des différences sont observées selon la parité des lapines (513±12 vs 626±9g, respectivement pour les primipares et les multipares, P<0.05). Cependant, le traitement avec PGF_{2α} s'accompagne d'une augmentation de la mortalité pendant la lactation (48% vs 26%, respectivement pour le lot traité au Cloprostenol et le lot témoin, P<0.01).

INTRODUCTION

In rabbits, PGF_{2α} (and its synthetic analogues) is the hormone of choice for induction and synchronization of kindling (PARTRIDGE *et al.*, 1986; UBILLA and RODRIGUEZ 1989, 1990; MCNITT *et al.*, 1997; NEGATU *et al.*, 1998). Several authors have described the beneficial effects of PGF_{2α} on postpartum fertility (REBOLLAR *et al.*, 1989; MCNITT *et al.*, 1997) probably by modifying ovarian steroid hormones and LH levels (UBILLA *et al.*, 1992).

In rabbits, UBILLA and RODRIGUEZ (1989) observed that after prostaglandin treatment on day 29 of pregnancy the length of gestation decreased with a significantly greater proportion of does kindling between 24 and 60 hours after treatment; prolificacy and litter size at weaning were not affected by treatment and a decrease on neonatal mortality was observed. In other works, an increment in sexual

receptivity and fertility rate between 6 and 9 days post-partum has been reported, so the parturition-insemination interval was reduced (UBILLA and RODRIGUEZ, 1988). On the other hand, a favorable effect of PGF_{2α} on both masteokinetic and masteosecretory activities has been observed (RUFFINI-CASTROVILLI and NORDIO-BALDISSERA, 1980).

Nevertheless, BOSC *et al.*, (1975) and WETTENANN *et al.*, (1977) working with sows and CURRIE and THORBURN (1973) with goats; observed a negative effect on foetus weight and survival after prostaglandin administration.

In rabbits the PGF_{2α} treatment has been evaluated in crossbreed females from maternal races or lines (3.5 to 4 kg of adult weight) and no studies have been done on large-size races or lines selected for growth rate (5 to 7 kg of adult weight), whose males are normally

included in commercial rabbit selection programs as terminal sires. These races or selected lines habitually show more reproductive problems than those lines selected by maternal characteristics (46% vs 69% normal recovered embryos in a growth line (line R) and a maternal line, respectively LAVARA *et al.*, 2001) and lower live-born rates (line R, 10% mortality at birth, VICENTE *et al.*, 1995). The use of PGF_{2α} or its synthetic analogues could be a useful treatment to improve the reproductive results on this line.

The aim of this study was to evaluate the effect of a treatment with a synthetic analog of PGF_{2α} (cloprostenol) on the litter size and weight of the live-born pups using a rabbit line selected by high growth rate.

MATERIAL AND METHODS

Experimental animals

A synthetic rabbit breed selected by growth rate from weaning to slaughter (28-63 days) was used in this study. Selection methodologies were described by ESTANY *et al.*, (1992). Animals belonging to line R from two farms were assigned randomly to treatment groups and were housed in flat deck cages and fed (with a commercial diet) and watered *ad libitum*. The photoperiod employed was 16 hours light/day. Does were managed with a semi-extensive rhythm. The weaning was performed in all does the same day, being the average the day 28th after birth.

Semen collection and evaluation

Two ejaculates per male were collected each week using an artificial vagina. The percentage of motile sperm was evaluated subjectively after dilution (1:5) of the sperm with a Tris-citrate-glucose extender (250mM tris-hydroxymethylaminomethane, 83mM citric acid, 50mM glucose, pH 6.8-7.0); the evaluation was made under microscope, at a magnification of 400x. Only those ejaculates with more than 70% of motile sperm were used to perform the inseminations.

Insemination procedure

Receptive does were inseminated with 0.5 ml of extended semen using a curved plastic pipette (IMV, France). Immediately after insemination, ovulation was induced with 0.8 mg of busereline acetate (Hoescht). The reproductive status of the females at time of

insemination (multiparous or primiparous) was noted.

Induction and synchronization of kindling

Pregnant does were assigned randomly to the treatment groups; one group of does from each farm were treated with 0.2 ml of cloprostenol (17.5mg) injected intramuscularly in the morning (between 9 and 11h) on day 28 of gestation (cloprostenol group) and the second group was not treated (control group). At the moment of treatment, all does (treated and control group) were handled in their cages, randomizing the adverse effect of handling on birth. After treatment, the nests from both groups were opened.

In farm 1, birth day and litter size at birth (live and dead pups) were noted. In farm 2, birth day, litter size at birth, individual and litter weight at birth, litter size from each week of lactation period and individual weight at weaning were recorded.

Nest at birth were checked twice: at 8 am and 13 pm.

Statistical analysis

A general lineal model (PROC GLM, SAS Institute, 1996) was performed to assess the effect of treatment, farm, reproductive status (primiparous and multiparous) and their interactions on the gestation length and on the total number of young rabbits and live-born pups at birth. To evaluate the individual weight at weaning of the live-born rabbits, a mixed model analysis was performed (PROC MIXED, SAS Institute, 1996), including treatment and reproductive status as fixed effects, and as random effect common litter effect; total number of young rabbits at birth was included as a covariate in the model.

The percentages of mortality at birth and during lactation period were analyzed by a Chi-squared test with Yate's correction.

Table 1: Effect of treatment on litter size at birth (total and live-born young rabbits per doe).

	Total young rabbits LSM±SE (n)		Live-born pups LSM±SE (n)	
	CONTROL	CLOPROSTENOL	CONTROL	CLOPROSTENOL
Farm 1	7.4±0.4 (106)	7.5±0.3 (149)	6.7± 0.4 (106)	6.2±0.3 (149)
Farm 2	8.4±0.5 (48)	7.6±0.4 (50)	7.4± 0.5 (48)	6.3±0.5 (50)
Total	7.8±0.3 (154)	7.5±0.3 (199)	6.8± 0.3 (154)	6.3±0.3 (199)

LSM±SE: Least-square means and standard errors.

Table 2: Effect of treatment and reproductive status of does on individual weight at birth (g) and individual weight at weaning (g).

	CONTROL GROUP		CLOPROSTENOL GROUP	
	Primiparous LSM±SE (n)	Multiparous LSM±SE (n)	Primiparous LSM±SE (n)	Multiparous LSM±SE (n)
Individual weight at birth (g)	53±2 ^b (85)	63±1 ^a (190)	51±2 ^b (97)	52±1 ^b (204)
Individual weight at weaning (g)	484±17 ^c (74)	637±11 ^a (185)	542±18 ^b (63)	614±15 ^a (96)

LSM±SE : Least-square means and standard errors.

^{abc} Values in the row with different superscripts are statistically different P<0.05.

RESULTS

A total of 352 pregnancies were controlled, 255 in farm one and 98 in farm two.

Gestation length was affected by prostaglandin treatment, the treated group showing lower gestation length than the control group (31.3±0.1 vs 32.4±0.1 days respectively, P<0.05). Neither reproductive status nor the treatment group*reproductive status interaction had any effect on gestation length.

Litter size at birth was similar between farms, reproductive status and treatment groups (Table 1), showing that line R had lower prolificacy (7.6±0.2 total young rabbits, 6.5±0.2 live-born pups, Table 1).

Individual weight at birth was significantly different between treatment groups, reproductive status and their interaction. Young rabbits from does treated with cloprostenol showed the lowest weight (52±1 vs 58±1 g, for treated and control groups, respectively, P<0.05) and no differences were observed in this group between primiparous and multiparous does (Table 2). In contrast, in the female control group, young rabbits born from multiparous does were heavier than those from primiparous ones (Table 2). Individual weight (of the litter) at weaning was not affected by treatment with cloprostenol (578±12 and 561±10 g, for treated and control group respectively). Differences were observed between individual weight (of the litter) at weaning and reproductive status, the

young rabbits from primiparous showing lower weight at weaning than those from multiparous (Table 2); the lowest weight was observed in the young rabbits from primiparous does belonging to the control group (Table 2).

When litter size was controlled from birth to weaning, a significant difference in mortality rate

was observed between the experimental groups, being higher in the group treated with prostaglandin (48%) than in the control group (26%). Since the mortality at birth was similar between groups (14.9% and 15.0% for control and treated group, respectively, Figure 1), the difference observed in mortality rate was mainly produced during the lactation period.

DISCUSSION

Line R usually has low litter size at birth and relatively high mortality rates in the perinatal period (Table 2 and Figure 1) than other lines selected by maternal characteristics (10.6±0.3 total young rabbits and 9.8±0.4 live-born pups in line V, selected on litter size at weaning, GARCÍA *et al.*, 2000). This could be due to its high growth rate (50-60g/day during growing period) and to its adult weight (5-6 kg), as well as to the large size of pups at birth (VICENTE *et al.* 1995).

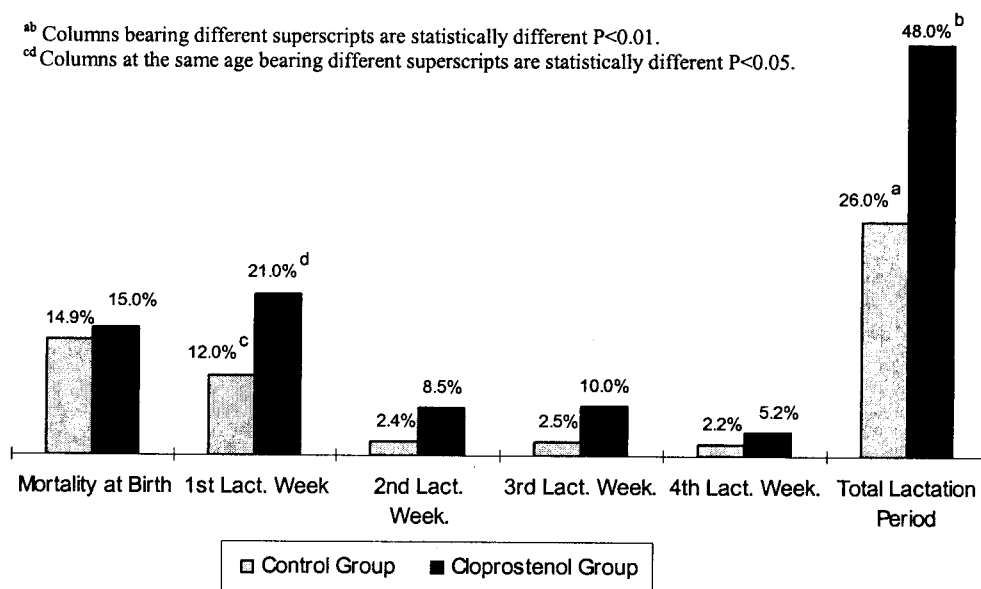


Figure 1: Mortality percentage (%) in young rabbits in the lactation period (0-28 days of age).

Gestation length was reduced after treatment of the females with cloprostenol, but perinatal mortality was not different between groups (15.0% of mortality at birth, 7.6 and 6.5 total and alive young rabbit at the birth, respectively). Due to the reduced on gestation length after prostaglandin treatment (about 1 day), the weight of live young rabbits born from treated females was lower than those from control does (52 ± 1 vs 58 ± 1 g, in treated and control group respectively, $P < 0.05$). Previous data on fetal weight were reported by CLIMENT *et al.* (1993), SANTACREU *et al.* (1994), GARCÍA *et al.* (1983) and VICENTE *et al.* (1995) showing that in the last gestation period (25th gestation day to birth) a foetus from a maternal line can increase the weight 23 g. (34 to 57 g, respectively). The reduction of weight observed in young rabbits born from treated females in this study could be explained by the fact that foetal growth rate is not linear and the growth rate is very high during the last gestation period. There was no difference observed between groups in the individual weight of young rabbits born from primiparous does, maybe due to the competition between the final development of the females and the growth of the fetuses (THEAU-CLÉMENT and ROUSTAN, 1992).

When individual weight at weaning was analyzed, it was observed that the rabbits born from primiparous females were smaller than those born from multiparous does, as has been reported by other authors (VICENTE and GARCÍA, 1992). No differences were observed between control and treated does, but an unexpected interaction was detected between the reproductive status of the female and the treatment, the weight at weaning of the young rabbits born from primiparous treated does being higher than that observed for the rabbits born from primiparous does belonging to the control group (Table 2); this difference could be due to a slight increase in milk production. In general, authors have not reported any effect on lactation when prostaglandins had been used to induce parturition, either in rabbit (PARTRIDGE *et al.*, 1986, UBILLA and RODRIGUEZ, 1988) or in other species (cattle, JIRAN *et al.*, 1981, goat, WALKER, 1983, or sows JÖCHLE *et al.*, 1982). However, RUFFINI-CASTROVILLI and NORDIO-BALDISERA (1980) observed a favorable effect on the weight of young rabbits at 21st day of age and suggested a favorable effect of prostaglandins on masteokinetic activity and, possibly, on masteosecretory action. This effect was dose-dependent and was only observed when using 5mg of a synthetic analogue of PGF_{2α}. The lower weight of primiparous does and higher sensitivity to PGF_{2α} treatment could have induced a favorable effect in masteosecretory activity in accordance with RUFFINI-CASTROVILLI and NORDIO-BALDISERA (1980), improving the weaning weight of young

rabbits from treated females.

On the other hand, the use of cloprostenol increased the mortality rate during the lactation phase. This negative effect was significant during the first week of lactation period (21% vs 12% in treated and control group, respectively, $P < 0.05$, Figure 1) and very important when considering the whole lactation period (48% vs 26% in treated and control group respectively, $P < 0.01$, Figure 1). So we can conclude that the maternal behavior of this line seemed to be affected by the dose of cloprostenol used in this study, increasing reproductive problems to an even greater degree.

Further studies are necessary to evaluate different doses and synthetic analogues of PGF_{2α} to try to improve the productivity of this selected line with high genetic value.

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