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# Comparison of the Efficacy of the Administration Route of D-Cloprostenol to Induce Abortion in Undesirable Pregnancy

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**Abstract:** This experiment deals with the efficacy of the administration route of D-cloprostenol in termination of pregnancy. After blocking according to parity and attaining the gestation stage, beef heifers were assigned to one of two routes of D-cloprostenol administration. D-Cloprostenol was injected either intramuscularly (150 μg, n = 45) or submucosally between distal of *Commisura labiorum* of vulva and clitoris (75 μg, n = 30). Abortion and retained placenta cases were monitored within a week after administration of D-cloprostenol. The percentage of aborted heifers was 73.33 and 90 and of heifers with retained placenta among aborted ones was 36.36 and 0 in response to the administration of D-cloprostenol intramuscularly and submucosally, respectively. In conclusion, intravulvo-submucosal administration of D-cloprostenol is economically more feasible and reliable than its intramuscular administration to terminate gestation when parturition is indicated.

**Key words:** D-Cloprostenol, abortion induction, intravulvo-submucosal injection, feedlot heifer

## INTRODUCTION

Abortion induction can be necessary in some cases, such as incompletion of maternal growth at the first gestation in heifers because of higher risk for dystocia and retained placenta (Bekyurek *et al*., 1998). Moreover, termination of gestation is necessary for eliminating low producing cows from herds and in cases of stillbirth and pathological developments including maceration and mummification of foetus, hydroamnion and hydroallantois during prenatal life (Roberts, 1971; Jackson and Cooper, 1977; Bekyurek *et al*., 1998). Surgical intervention of hardware disease occurring during late gestation may not be feasible to postpone postpartum and induction of parturition could be attempted (Aytug, 1989) to save the animal (Bekyurek *et al*., 1998).

Methods other than surgical attempt to induce abortion may directly and/or indirectly interfere with functions of tissues synthesizing progesterone and consequently may risk further gestations (Barth, 1986). However, indication of surgical intervention option may not be feasible due to economical constraints and prolonged postoperative recovery. Corpus Luteum (CL) is the major source of progesterone during the first 5 months of gestation and then both CL and placenta continue to release progesterone (Barth, 2006). Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and its analogues are used to terminate gestation. Mechanisms by which $PGF_{2\alpha}$ induces abortion include depressing peripheral progesterone level through luteolysis and stimulating abdominal contractions and partial cervical relaxation (Barth, 1986; Thomas, 1997). From fertilization to the last 2-4 weeks of gestation, level of progesterone is about 6-15 ng $mL^{-1}$, hence responsiveness of CL to $PGF_{2\alpha}$ is maximal from 5-7 days after ovulation to 150$^{th}$ day of gestation (Thomas, 1997). Several methods are available to induce abortion and include administration of $PGF_{2\alpha}$ to luteinise CL until day 150 of pregnancy (Bekyurek *et al*., 1998), of oestrogen during early gestation (Hartigan, 1995) and of tetracycline (2 g) and iodine (5%) within saline until day 90 of gestation (Thomas, 1997) and transrectal destruction of CL (enucleation) (Roberts, 1971). The latter is not suggested due to an increased risk for hemorrhage and adhesion in ovary and *Bursa ovarica*. Bursting amniotic sac via rectal palpation to induce abortion is not recommended (Roberts, 1971; Thomas, 1997).

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Prostaglandin $F_{2á}$ and its analogues are applied in different ways including intramuscular, intrauterine, intravenous, intraovarian, intracervical and intravulvo-submucosal routes (Mgongo, 1987; Duchens *et al*., 1993, Guler *et al*., 1993). Side effects of termination of gestation using these medications include retained placenta (80%) and foetal mummification (2-4%) and less frequently of metritis and pyometra (Refsal and Seguin, 1981; Grunert *et al*., 1984; Thomas, 1997; Bekyurek *et al*., 1998). It is not known if these adverse consequences are related to the administration route. This experiment was; therefore, conducted to evaluate efficacy of the administration route of D-Cloprostenol on abortion induction and follow-up reproductive problems.

## MATERIALS AND METHODS

**Animals and treatments:** Local breed beef cows culled for slaughter during Holy Sacrifice from the University Farm were examined for pregnancy. Due to ethical reasons, slaughtering pregnant ruminants is unacceptable. Day of pregnancy ranged from 45 days to 5.5 months in 75 culled pregnant heifers. Gestation was terminated by single injection of D-cloprostenol (Dalmazin®, Vetas Co., Istanbul, Turkey) either intramuscularly (150 μg, n = 45) or submucosally between distal *Commisura labiorum* of vulva and clitoris (75 μg, n = 30). A week after, heifers not aborted by the first injection of D-cloprostenol were subjected to the second injection. Day of pregnancy was 4-5.5 months in 8, 2.5-3.5 months in 5 and 1.5-2.5 months in 22 heifers in the former group and it was 4-5.5 months in 6, 2.5-3.5 months in 17 and 1.5-2.5 months in 7 heifers in the latter group, respectively. Within 5-7 days of the administrations, the rate of abortion and related clinical problems were recorded. In aborted foetuses, measurements weremadeto attain the actual day of gestation using formula described Richardson (Arthur *et al*., 2001).

**Statistical analysis:** Data were analyzed using the PROC FREQ (SAS, 1998). Significance of risk ratio among the groups ($p<0.05$) was attained by Chi-Square test.

## RESULTS AND DISCUSSION

Actual predicted foetal age confirmed by Richardson's formula (Arthur *et al*., 2001) was in agreement with day of gestation attained by rectal palpation. Suggested dose to activate luteolytic effect of D-cloprostenol is 150 μg for intramuscular injection and 75 μg for vulvo-vaginal submucosal injection (Thomas, 1997). However, Meira *et al*. (2006) reported that

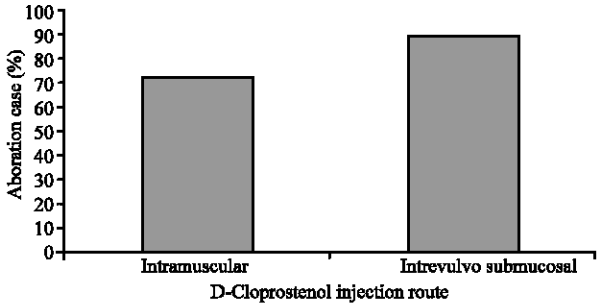


Fig. 1: The effect of D-cloprostenol administration route on the rate of abortion

administration of 50% of a conventional dose of Luprostiol IM or IVSM was the minimal dose for induction of a complete luteal regression efficiently and effectively as well as hastening the onset of oestrus. Administration of natural $PGF_{2\alpha}$ (25 mg, i.m.) or its analogues (Cloprostenol, 500 μg, i.m.; Dinoprost, 25-35 mg, i.m.; Fenprostalene, 1 mg, s.c.) alone to terminate gestation after day 150 may be ineffective (Jackson and Cooper, 1977; Johnson and Jackson, 1980; Refsal and Seguin, 1981; Grunert *et al*., 1984; Barth, 1986; Arthur *et al*., 2001) and it should be combined with glucocorticoids (Dexamethazone, 25 mg, i.m.) (Bekyurek *et al*., 1998). Abortion occurs within 5-7 days (2 days for hydroamnion and hydroallantois and 1-3 days for foetal mummification and maceration) upon administration of $PGF_{2\alpha}$ and/or its analogues alone or in combination with other agents (Thomas, 1997).

Figure 1 illustrates the incidence of abortion upon two-consecutive D-cloprostenol injections. The frequency of aborted heifers was 33.45 and 27.30 in groups injected with D-cloprostenol intramuscularly and submucosally, respectively. The odd ratio of inducing abortion in response to differences in administration route of D-cloprostenol was 2.67 ranging from (0.86-8.66; $p<0.08$). Intramuscular administration of $PGF_{2\alpha}$ is practiced throughout the gestation stages to terminate gestation through its luteolytic effect, with lessened effectiveness as gestation advances (>5 months) (Johnson and Jackson, 1980; Grunert *et al*., 1984; Hartigan, 1995; Bekyurek *et al*., 1998). In these studies, it was also shown that vulvo-vaginal submucosal administration of luteolytic agents was more effective. In late gestation (>5 months), the effectiveness of termination of gestation increased when $PGF_{2\alpha}$ administration was accompanied by glucocorticoids. Guler *et al*. (1993) administered luprostiol, a $PGF_{2\alpha}$ analogue (3.75 mg) and reported that ipsilateral vulva submucosal administration had more effective luteolytic effect than intraovarian administration. However, the administration route effect on gestation

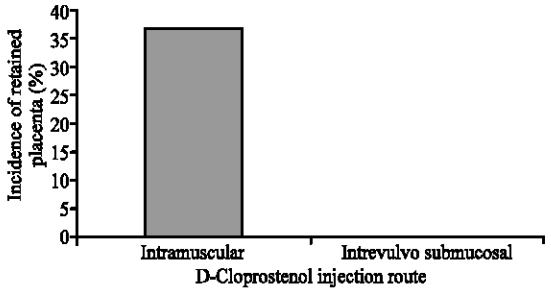


Fig. 2: Incidence of retained placenta in response to abortion resulting from different administration routes of D-cloprostenol

(Hooda *et al*., 1997) and other related hormones (Manalu *et al*., 1997) before and after abortion were not measured.

The incidence of retained placenta was 36.36 and 0% in aborted heifers resulting from intramuscular and submucosal injection of D-cloprostenol, respectively (Fig. 2). In the former group, 12 cases of retained placenta occurred among heifers pregnant for 2.5-3.5 months (n = 4) and 4-5.5 months (n = 8). No other contraindications were noted. Bekyurek *et al*. (1998) reported that frequency of retained placenta in aborted cows due to intramuscular administration of dinoprost tromethamine alone (25 mg, n = 8) or plus dexamethazone (24 mg) (n = 3) was 2 and 3, respectively.

## CONCLUSION

This experiment was conducted to evaluate the efficacy of the administration route of D-Cloprostenol on termination of gestation and follow-up consequences. Intramuscular administration was less effective to induce abortion with greater likelihood of occurrence of retained placenta than vulvo-vaginal submucosal administration. This could be related to vascular network around tissues (muscle vs. submucosa) and effective dose reaching target tissue. Consequences of unethical issues and clinical indications for undesirable gestation could be minimized by vulvo-vaginal submucosal administration of $PGF_{2\alpha}$ analogues during the early phase of gestation.

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