

1-1-2012

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AKAR, YAŞAR; KIZIL, ÖMER; SAAT, NEVZAT; and YÜKSEL, MURAT (2012) "The effect of oxytocin and cloprostenol application via umbilical artery immediately after dystocia on time and rate of fetal membrane removal in cows," *Turkish Journal of Veterinary & Animal Sciences*: Vol. 36: No. 3, Article 9. <https://doi.org/10.3906/vet-1102-785>

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The effect of oxytocin and cloprostenol application via umbilical artery immediately after dystocia on time and rate of fetal membrane removal in cows

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Received: 18.02.2011

Abstract: The aim of this clinical study was to investigate the effects of oxytocin and cloprostenol application via umbilical artery on the time and rate of fetal membrane removal in cows with dystocia immediately after parturition. Metabolic profiles indicated certain serum biochemical parameters that were also determined in the cows. The study was performed on 60 cows with dystocia. All of the cows were randomly divided into 3 equal subgroups. The first group was injected with 100 IU oxytocin, while the second group was treated with 0.15 mg cloprostenol and the third group (the control group) received 10 mL 0.9% NaCl via intraumbilical artery. Blood samples were randomly taken from the jugular veins of 10 cows from each group. No significant differences were determined between the groups with regard to the values of aspartate aminotransferase, alkaline phosphatase, creatine kinase, total protein and bilirubin, albumin, glucose, Ca, Na, or K ($P > 0.05$). The lactate dehydrogenase level in the oxytocin group was determined to be significantly lower when compared to the cloprostenol and control groups ($P < 0.05$). The value of gamma-glutamyl transferase in the oxytocin group was significantly higher than in the other groups ($P < 0.05$). The time and rate of fetal membrane removal were not different among the groups ($P > 0.05$). In conclusion, the administration of combinations of other uterotonics and enzymes together with these agents should be investigated to determine the effects on cows with retained placenta prophylaxis. Future applications may also study the effects of these agents on fertility and time and rate of fetal membrane removal in cows with normal parturition and dystocia at the herd level.

Key words: Cloprostenol, cow, dystocia, fetal membrane, oxytocin, umbilical cord

İneklerde güç doğum sonrası göbek kordonu arteri yoluyla oksitosin ve kloprostenol uygulamasının yavru zarlarının atılım süresi ve oranı üzerine etkisi

Özet: Bu çalışmanın amacı, güç doğumdan hemen sonra ineklere göbek kordonu arteri yoluyla verilen oksitosin ve kloprostenol'un, yavru zarlarının atılımı oranı ve süresi üzerine etkilerini araştırmaktır. İneklerin bazı biokimyasal parametreleri de tespit edilerek, metabolik profilleri ortaya kondu. Çalışmada, güç doğum yapmış 60 adet inek kullanıldı. Tüm inekler, rastgele 3 eşit gruba ayrıldı. Birinci gruba 100 IU oksitosin, ikinci gruba 0,15 mg kloprostenol ve üçüncü gruba (kontrol) ise 10 mL % 0,9 NaCl göbek kordonu arteri yoluyla verildi. Her bir gruptaki rastgele 10'ar inekten, vena

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jugularisten kan alındı. Gruplar arasında, AST, ALP, CK, total protein, total bilirubin, albumin, glüköz, Ca, Na ve K değerleri yönüyle önemli bir farklılık ($P > 0,05$) yoktu. Oksitosin grubundaki LDH seviyesi, kloprostenol ve kontrol grubuna göre önemli oranda daha düşük ($P < 0,05$) tespit edildi. Diğer 2 gruba göre, oksitosin grubunda GGT miktarı önemli oranda yüksek ($P < 0,05$) bulundu. Gruplar arası, yavru zarlarının atılım süresi ve oranı yönünden farklılık yoktu. Sonuç olarak, bu maddeler ile birlikte diğer uterotonik ve enzim kombinasyonlarının kullanımının, ineklerin retensiyon sekondinarum profilaksisindeki etkileri araştırılmalıdır. Bu uygulamaların, gelecekte sürü seviyesinde normal ve güç doğumlu ineklerde yavru zarlarının atılım süresi ve oranı ile fertilité üzerine etkileri de çalışılabilir.

Anahtar sözcükler: Kloprostenol, inek, güç doğum, yavru zarları, oksitosin, göbek kordonu

Introduction

Fetal membranes are normally expelled within 3 to 8 h after parturition and their retention for more than 12 to 24 h is considered retained placenta (RP). The incidence of RP in cows ranges from 2% to 60%, with an average of approximately 10%. Dystocia increases the percentage of cows affected by RP. The economic impact of RP is reflected in loss of milk, impaired fertility, and a high culling rate. The consequences of RP are an increase in the calving to first service interval, a reduction in the pregnancy rate to first service, an increase in the number of services per conception, and a longer calving interval (1-3).

The physiological delivery of the placenta after parturition requires adequate and regular uterine contractions. A deficiency in secretions of $\text{PGF}_{2\alpha}$, oxytocin, or serum Ca concentration, which maintain adequate contraction of the uterus, may cause RP, increase the risk of dystocia, and delay the involution of the uterus (4,5). High concentrations of $\text{PGF}_{2\alpha}$ and PGE_2 are produced by the uterus during the early postpartum period in cows and may play an important role in both placental separation and uterine involution (6). Many factors have been implicated in the production of RP and many of these are interrelated, such as uterine atony, abortion, delayed gestation, dystocia, high environmental temperatures, early parturition, infections, twin pregnancy, and vitamin and mineral deficiencies (1,4,7).

For the treatment and prevention of RP, injections of ecbolic drugs and enzymes such as oxytocin, prostaglandin, collagenase, and hyaluronidase have been administered within 24 h of parturition (2,3,8-11). Many investigators (8,9,12-14) have shown collagenase application via umbilical artery after parturition to reduce the time and increase the rate of fetal membrane removal in cows.

If RP is left untreated in women, there is high risk of maternal death. However, manual removal of the placenta is an invasive procedure with its own serious complications of hemorrhage, infection, or genital tract trauma (15). Therefore, the injection of oxytocin, ergometrine, or $\text{PGF}_{2\alpha}$ via the intraumbilical vein has been suggested as an alternative treatment for women experiencing RP. The method relies on the injected solution passing down the umbilical cord and through the placental bed to contract the myometrium behind the placenta, thereby causing its detachment (15-19).

Some investigators (15-18,20,21) suggest that intraumbilical vein injections of oxytocin or $\text{PGF}_{2\alpha}$ may be a beneficial, cheap, nonaggressive, nonsurgical method for treating RP in women. Others (22,23) indicate that intraumbilical vein injections of oxytocin are not effective for the removal of RP.

Kudlac et al. (24) investigated biochemical parameters in cows with and without RP and found that the values of these parameters (total protein, Ca, alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT)) mostly ranged within the interval of reference values. On the other hand, the cows with RP had significantly lower concentrations of glucose and higher bilirubin, aspartate aminotransferase (AST), and lactate dehydrogenase (LDH). Castillo et al. (25) evaluated some biochemical parameters (glucose, total protein, albumin, AST, and ALP) in cows after and before parturition with no significant differences.

In this study, a new application of oxytocin and cloprostenol in cows with dystocia via the intraumbilical artery was employed. Some biochemical parameters were also investigated, as were the effects of oxytocin and cloprostenol application via umbilical artery on the time and rate of fetal membrane removal in cows with dystocia.

Materials and methods

Hormonal drugs

Oxytocin (Vetaş Oksitosin, 10 IU/mL) and d-cloprostenol (Dalmazin Enj., 0.075 mg/mL) were purchased from Vetaş (İstanbul, Turkey).

Animals and location

The study was performed on 60 cows of differing breeds and ages (2-9 years) that had been brought to the Clinic of Obstetrics and Gynecology in the Faculty of Veterinary Medicine at Firat University. The study was carried out in Elazığ between 1 October and 30 December 2009.

Treatment schedule

All of the cows had dystocia and single-calf parturition. The cows were randomly divided into 3 equal subgroups. The first, second, and third groups (each group containing 20 cows) were administered 100 IU oxytocin, 0.15 mg d-cloprostenol, and 10 mL 0.9% NaCl, respectively, via intraumbilical artery immediately after expulsion of the fetus. All injections were applied to the umbilical cords, whose arteries and veins were massaged for 5 min for blood remnant removal. The injection to the umbilical cord artery was carried out as near as possible to the uterus using a spinal needle (22 G, 0.70 × 89 mm, Exelint International Co., Los Angeles, CA, USA). Additionally, in order to better introduce the injected substances (oxytocin, cloprostenol, or NaCl) to the uterus, the upward umbilical artery was massaged upwardly after each application and then the umbilical artery was clamped (Figures 1-4). All of the cows were observed at intervals of 10 min/h after parturition to determine the time of fetal membrane



Figure 1. The spinal needle and umbilical artery used in this study.

removal. No fetal membrane removal within 24 h of parturition was defined as RP.

Blood sample collection and biochemical measurements

Blood samples (10 mL) were obtained at random by vein puncture from the jugular veins of 10 cows from each group immediately after parturition and before the intraumbilical artery injections. Serum was separated by centrifugation and stored at -20°C until analysis. Concentrations of serum biochemical parameters including ALP, AST, GGT, LDH, creatine kinase (CK), total protein, albumin, glucose, total bilirubin, calcium, sodium, and potassium were analyzed with a clinical chemistry analyzer (ADVIA 1200 Chemistry System, Bayer-Healthcare, Leverkusen, Germany).

Statistical analysis

All biochemical parameters and fetal membrane removal times were evaluated with Kruskal-Wallis variance analyses and the independent Student's t-test. Fetal membrane removal and nonremoval rates were evaluated by the chi-square test (26,27).



Figure 2. Injection of the tested drugs into the umbilical artery.



Figure 3. The clamped umbilical artery.

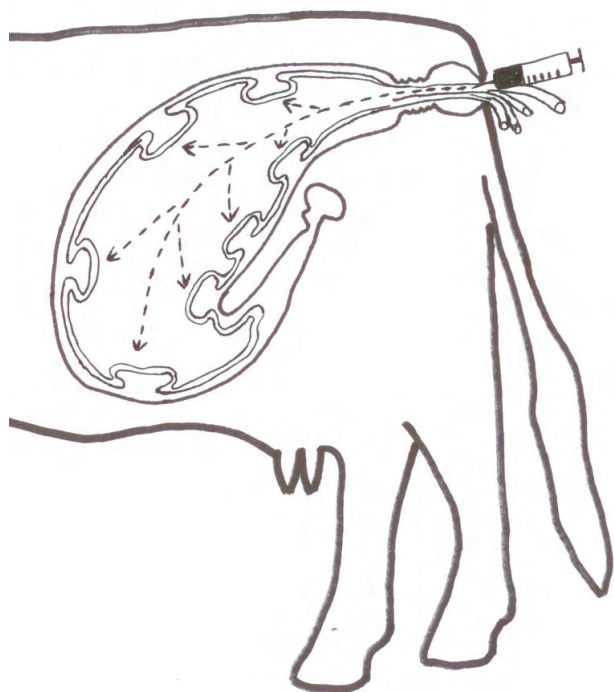


Figure 4. Diagram representing the injections used in the present study.

Results

The rates of fetal membrane removal and nonremoval and the time of fetal membrane removal between the groups were not different (Table 1).

Biochemical parameters of all of the cows are given in Table 2, which shows that the values of AST, ALP, CK, total protein, total bilirubin, albumin, glucose, Ca, Na, and K were not significantly different between the 3 groups. However, the level of LDH in the oxytocin group was determined to be significantly lower than that observed in the cloprostenol and

control groups ($P < 0.05$). The value of GGT was significantly higher in the oxytocin group when compared to the other groups ($P < 0.05$).

Discussion

The occurrence of RP should be prevented as much as possible (1,4,8,12), or the treatment and prevention of RP with injections of ecboic drugs and enzymes such as oxytocin, prostaglandin, collagenase, and hyaluronidase within 24 h after parturition must be applied (2,3,8-13). The rationale for their use is that they stimulate uterine contractions and thus physically aid the expulsion of the membranes (11).

Mollo et al. (2) showed that the intramuscular administration of 30 IU oxytocin immediately after delivery and again 2-4 h later reduced the incidence of RP significantly in Holstein cows and consequently reduced the occurrence of endometritis post-RP. Oxytocin treatment also improved the herd reproductive performance by shortening the average interval from calving to conception. Stocker and Waelchli (3) reported that intramuscular administration of 25 mg dinoprost immediately after parturition reduced the incidence of RP significantly in cows with dystocia. Miller and Lodge (10) reported no significant difference in the rate of RP in the cows treated intramuscularly with 100 IU oxytocin 3-6 h after calving. Haffner et al. (28) concluded that umbilical artery injections of collagenase were a safe and potentially effective treatment for RP in mares. Women given an intraumbilical injection of 20 IU oxytocin had a significant increase in spontaneous expulsion of the placenta within 45 min of delivery and experienced fewer manual removals of the placenta compared with women without treatment

Table 1. The rate and time of fetal membrane removal in the 3 groups.

	Oxytocin	Cloprostenol	Control
FMR %	70% (n: 14)	55% (n: 11)	60% (n: 12)
FMNR %	30% (n: 6)	45% (n: 9)	40% (n: 8)
	mean \pm std. error	mean \pm std. error	mean \pm std. error
FMRT (h)	5.20 \pm 0.39 (n: 14)	4.49 \pm 0.43 (n: 11)	6.02 \pm 0.56 (n: 12)

FMR: fetal membrane removal; FMNR: fetal membrane nonremoval; FMRT: fetal membrane removal time.

Table 2. Values recorded for various parameters in the 3 groups.

Parameters	Oxytocin mean \pm std. error	Cloprostenol mean \pm std. error	Control mean \pm std. error
AST (U/L)	109.0 \pm 6.9	100.7 \pm 3.4	90.4 \pm 2.5
ALP (U/L)	129.9 \pm 6.1	120.9 \pm 5.3	115.9 \pm 4.9
LDH (U/L)	797.4 \pm 23.7 ^a	848.2 \pm 45.5 ^{ab}	910.1 \pm 24.3 ^b
GGT (U/L)	9.5 \pm 0.4 ^b	7.4 \pm 0.4 ^a	8.4 \pm 0.6 ^{ab}
CK (U/L)	96.5 \pm 5.1	92.4 \pm 4.1	91.8 \pm 3.0
Total protein (g/dl)	6.92 \pm 0.04	6.93 \pm 0.04	7.03 \pm 0.06
Albumin (g/dl)	3.08 \pm 0.02	3.12 \pm 0.02	3.05 \pm 0.04
Glucose (mg/dl)	62.2 \pm 1.8	64.6 \pm 1.2	65.9 \pm 1.4
Tbilirubin (mg/dl)	0.71 \pm 0.06	0.70 \pm 0.05	0.67 \pm 0.08
Ca (mg/dl)	8.53 \pm 0.13	8.82 \pm 0.06	9.03 \pm 0.17
NA (mEq/L)	143.5 \pm 1.3	141.8 \pm 1.7	141.8 \pm 1.4
K (mEq/L)	4.5 \pm 0.1	4.4 \pm 0.1	4.6 \pm 0.1

^{a,b}: Different letters on the same line indicate significance ($P < 0.05$).

(20). Bider et al. (16) reported that intraumbilical vein injection of 20 mg PGF_{2 α} might be a beneficial method for treating RP. Although oxytocin and prostaglandin administration via intraumbilical artery, applied to cows with dystocia for the first time in this study, appeared to have a positive effect on the time and rate of removal of fetal membranes, this difference was not statistically significant when compared with the control group.

The blood serum parameters in cows from parturition to 45 days postpartum were at almost constant levels for AST, GGT, LDH, and bilirubin, but were low for glucose, total protein, and Ca levels at parturition. These parameters then increased until 20 days postpartum (29). It was observed that AST, GGT, and CK activities were significantly increased in the cow group with dystocia in comparison to the cows experiencing normal parturition, whereas the total bilirubin and glucose levels were not different (30). The concentration of serum albumin in cows immediately after parturition was significantly lower in cows with RP than those without RP, although Ca levels were not different (31). Blood serum levels of ALP and LDH in dairy cows with and without RP immediately after parturition were similar (32).

Doornenbal et al. (33) investigated the reference values of blood parameters in beef cattle of different ages and stages of lactation. Serum concentrations of total protein and bilirubin increased with age, as did the serum activities of AST and LDH; levels of Ca and ALP decreased with age from birth to 10 years of age. The cows had the highest levels of glucose at parturition, whereas levels of LDH and AST were lower at parturition according to the stages of lactation. The levels of AST, ALP, CK, total protein, total bilirubin, albumin, glucose, Ca, Na, and K determined in this study were not significantly different among the groups. The level of LDH in the oxytocin group was determined to be significantly lower than in other groups ($P < 0.05$), but the value of GGT in the same group was significantly higher than in the other 2 groups ($P < 0.05$). The metabolic profiles (except for LDH and GGT) between the groups before the administrations of oxytocin and cloprostenol were not significant, which indicates that this parameter would have no effect on the outcome of the treatment.

For the removal of fetal membranes from cows after parturition, uterus contractions should be maintained, and the role of oxytocin and

prostaglandin at this stage is important. In this study, the prophylactic effect of oxytocin and prostaglandin administered via intraumbilical artery on fetal membrane removal in cows with dystocia was investigated. The administration of oxytocin and prostaglandin via intraumbilical artery in cows with dystocia was determined to

produce no significant effect on the time or rate of fetal membrane removal. In conclusion, the study suggests that the administration of other uterotonic and enzyme combinations via umbilical cord should be investigated further with regard to their effects on reproductive performance and puerperal disorders in cows with and without dystocia at the herd level.

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