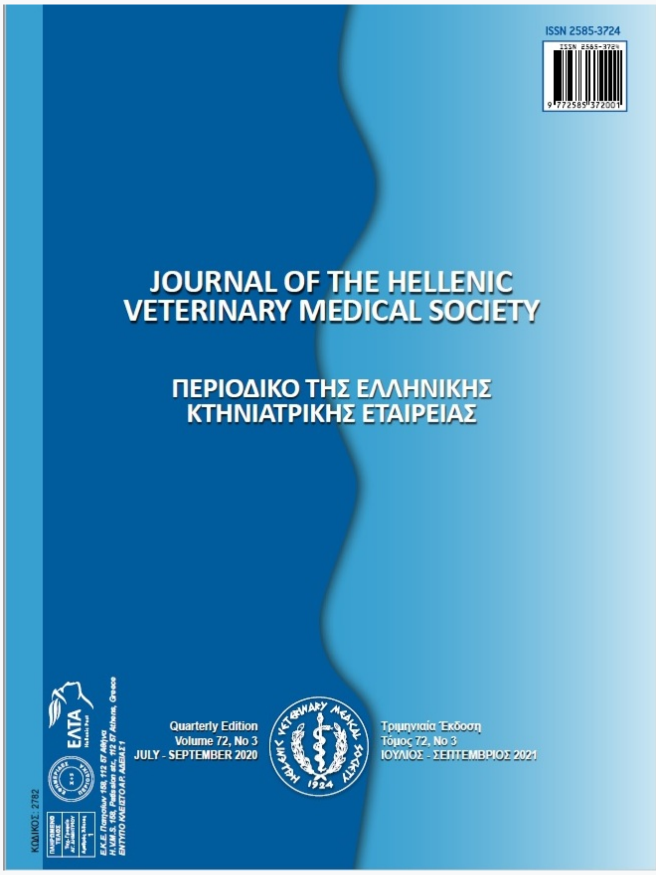
Journal of the Hellenic Veterinary Medical Society

Vol 72, No 3 (2021)

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doi: 10.12681/jhvms.28499

J HELLENIC VET MED SOC 2021, 72(3): 3101-3108
ΠΕΚΕ 2021, 72(3): 3101-3108

Research article
Ερευνητικό άρθρο

# Effects of carprofen and/or CIDR administration on pregnancies per artificial insemination around pregnancy recognition in lactating dairy cows

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**ABSTRACT:** Effect of carprofen and/or CIDR on pregnancies per AI (P/AI) 14 days after artificial insemination (AI) in lactating cows were investigated. Following detection of corpus luteum (CL) by ultrasonography (USG) 14 days after AI, cows (*n*=853) were randomly allocated to CARP (carprofen, 1.4 mg/kg; Rimadyl®XL), CIDR (progesterone, 1.38g, for seven days), CARP+CIDR and CONT (control) groups. CL was re-determined with USG 21 days after AI to monitored the maintenance of CL. Rates of maintenance of CL did not differed among CARP (79.6% [168/211]), CIDR (86.0% [196/228]), CARP+CIDR (80.0% [172/215]) and CONT (74.9% [149/199]) groups; however, the interaction effect of treatment by body condition score (BCS) at AI (P<0.05) were existed. In this matter, among cows with BCS≤2.5, chances of maintenance of CL was lower in CONT (70.7%, [111/157]) group compared to those in CARP (81.7%, [125/153]), CIDR (83.6%, [153/183]) and CARP+CIDR (80.1%, [129/161]) groups. Whereas, among cows with BCS>2.5, chances of maintenance of CL were lower in CARP (74.1%, [43/58]) and CARP+CIDR (79.6%, [43/54]) groups compared to those in CONT (90.5%, [38/42]) and CIDR (95.6%, [43/45]) groups. For the P/AI at 28-32 days after AI, there was no difference among CARP (48.8% [103/211]), CIDR (50.9 [116/228]), CARP+CIDR (47.4% [102/215]) and CONT (44.7% [89/199]) groups. Pregnancy losses between 28-32 and 55-60 days did not differ among CARP (3.9%, [4/103]), CIDR (4.3%, [5/116]), CARP+CIDR (5.9%, [6/102]) and CONT (6.7%, [6/89]) groups. However, there was a significant (P<0.05) interaction effect of treatment by the number of services on pregnancy losses. In this regard, pregnancy losses were higher in cows inseminated thrice and four or more times in CONT (11.8% and 16.7%) group compared to those in CARP (0% and 4.8%), CIDR (0% and 6.9%), CARP+CIDR (0% and 11.1%); respectively. Consequently, no effects of carprofen or CIDR around pregnancy recognition on P/AI were observed despite a higher maintenance rate of CL in lactating cattle. Furthermore, fewer pregnancy losses in cows following three or more services could indicate the beneficial carry-over effects of carprofen and/or CIDR administration around maternal recognition of pregnancy.

**Key words:** Carprofen; cow; pregnancy; progesterone.

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*Date of initial submission: 10-04-2020*
*Date of revised submission: 18-04-2021*
*Date of acceptance: 24-05-2021*

## INTRODUCTION

Over decades, lower conception rates have been reported in lactating dairy cows(Lucy, 2001; Santos et al., 2004; Demetrio et al. 2007).In this matter, almost 40% embryonic losses have been reported between days 8 and 17 of pregnancy (Thatcher et al., 1994). Similarly, approximately 30% of pregnancy losses have been reported in lactating dairy cowsfrom days 8 to 27 of pregnancy during which embryo elongation and maternal recognition of pregnancy occur (Wiltbank et al., 2016).

Sufficient progesterone (P4) secretion via maintenance of CLis crucial to advance early pregnancy in cows (Mann and Lamming, 1995; Okuda et al., 2002). Embryos produce a trophoblastic protein, IFN-Ʈ, to prevent luteolysis caused by a pulsatile release of $PGF_{2\alpha}$ from the endometrium (Bazer, 1992;Demmers et al., 2001). In this matter, IFN-Ʈdiminishes the oxytocin-dependent pulsatile release of $PGF_{2\alpha}$ from the endometrium by suppressing oxytocin receptor expression; thereby, leading to maternal recognition of pregnancy between days 15 and 16 of pregnancy in cattle (Bazer et al., 1997; Farin et al., 1990; Thatcher et al., 1995).

Nonsteroidal anti-inflammatory drugs (NSAID), organic acids in the constitution, diminish the release of prostaglandins by blocking cyclooxygenase (COX) enzyme in the arachidonic acid cascade (Vane, 1971; Espinasse et al., 1994). As an NSAID, carprofen non-selectively inhibits COX-1 and COX-2 in cattle (Brentnall et al., 2012). In this regard, the effective suppression ofPGF2α release following a single dose of carprofen (0.7 mg/kg) administration has been reported in the postpartum cow (Thun et al., 1989).With regard to carprofen administration 15 days after artificial insemination (AI), no beneficial effect on conception rates to the first service was reported in lactating dairy cows (von Krueger and Heuwieser, 2010). Based on current literature, there were controversial results with regard to use of NSAID to increase pregnancies perartificial insemination (P/AI) in cattle. In this matter, Guzeloglu et al. (2007) reported higher P/AI following flunixin meglumine administration 15 and 16 days after AI in Holstein heifers. Similarly, flunixin meglumine administration approximately 14 days after AI just prior to transportation stress increased P/AIin beef cows regardless of transportation (Merrill et al., 2007). In contrast, no beneficial effects of two injections of flunixin meglumine 14/15 or 15/16 days (Von Krueger and Heuwieser, 2010), and 15.5 /16 days (Rabaglino et al., 2010) after inseminations on P/AIwere reported in Holstein heifers. Likewise, a single administration of flunixin meglumine approximately 13 days (10 to 15 days in range) after AI did not increase P/AI in beef cows and heifers (Geary et al., 2010). Moreover,Erdem and Guzeloglu (2010) reported lower P/AI upon meloxicam administration 15 days after AI in Holstein heifers.

Another strategy for the maintenance of early pregnancy is P4 supplementation during maternal recognition of pregnancy. Garcia-Ispierto et al. (2016) reported improvement in conception rates following P4 supplementation around the time of pregnancy recognition after AI in high-producing dairy cows. Nevertheless, Alnimer and Lubbadeh (2008) reported that pregnancy rates (PR) on day 28 did not differ; however, pregnancy losses between days 28 and 45 tended to be lower in lactating dairy cows following administration of CIDR between 14 and 21 days after AI. Likewise, El-Zarkouny and Stevenson (2004) reported that PR on day 29 did not differ; however, pregnancy losses between days 29 and 57 were lower in lactating Holstein cows following insertion of used CIDR between 13 and 20 days after AI. Similarly, increased PR due to reduced pregnancy losses were reported following CIDR insertion between 14 and 21 days after AI in lactating dairy cows (Chebel et al. 2006). No effects of CIDR insertion fromday 14 to 23 (Bartolome et. al., 2009) or from day 14 to 21 (Galvao et al., 2007) after AI were reported on PR or pregnancy losses in lactating dairy cows.

In this study, it was aimed to use a single administration of carprofen due to its longer lasting effect and poorly excretion in milk in cows (Lohuis et al., 1991; Ludwig et al., 1989). Moreover, there is no study testing the potential additive effect of P4 supplementation and NSAID administration around the time of pregnancy recognition on P/AI in lactating dairy cows. Therefore, objective of this study was to investigate effect of carprofen and/or CIDR administration 14 days after AI onP/AI in lactating dairy cattle.

## MATERIAL AND METHODS

### Animals and Treatments

This study was approved by Local Ethical Committee for Animal Experiments of Erciyes University, Kayseri, TURKEY. In four commercial dairy farms, lactating Holstein dairy cows were housed in free stall barns, milked two or three times a day. Cows were fed a TMR prepared according to the National Research

Council (NRC) recommendations (NRC, 2001), and the cows were fed twice or thrice per day. In one of the dairy farm, AI was done following the detection of natural estrus; whereas, AI was performed following synchronization of estrus by $PGF_{2α}$ (Enzaprost-T®, Dinoprost tromethamine, 5 mL, Ceva Animal Health, Turkey) injection following detection of corpus luteum (CL) or Ovsynch protocol with the use of GnRH (Receptal®, Buserelin acetate, 2 mL, MSD Animal Health, Turkey) and $PGF_{2α}$ (Enzaprost®) in two farms (selective protocol), and AI was performed at detection of synchronized estrus following intravaginal P4 (CIDR®;1.38 g P4, Zoetis Animal Health, Turkey) insertion for seven days and $PGF_{2α}$(Dynolitic®, Dinoprost tromethamine, 5 mL, Zoetis Animal Health, Turkey) injection one day prior to CIDR removal or detection of natural estrus at the last farm. It means that this experiment was performed following either the first service or multiple services. After the last AI, no heat detection was performed during the study.

Following the detection of mature visible CL by ultrasonography (USG) 14 days after AI, lactating Holstein dairy cows (*n*=867)with CL and with/without postpartum health disorder prior to initiation of the study were randomly allocated to four groups in each farm. Due to missing data or health disorders including clinical mastitis, metritis, laminitis etc. during the study, 853 cows completed the experiment. In CARP group I (*n*=211), carprofen (1.4 mg/kg; Rimadyl®XL [5% carprofen], Zoetis Animal Health, TURKEY) was administered subcutaneously14 days after AI. In CIDR group (*n*=228), CIDR® was inserted intravaginally 14 days after AI and removed 21 days after AI for seven days. In the CARP+CIDR group (*n*=215), carprofen and CIDR were administered as in CARP and CIDR groups. No administration was done in CONT (*n*=199) as a control group. Cows were examined for the presence of visible CL by USG 21 days after AI to monitored the maintenance of CL. Pregnancies were diagnosed with USG and palpation per rectum 28-32, and 55-60 days after AI, respectively. Pregnancy losses between two pregnancy diagnosis by USG and rectal palpation were also determined. Body condition scores (BCS; 1-5 scale) were recorded at the last AI, 28-32 and 55-60 days after AI. BCS were accepted as poor if BCS <=2.5 or optimal if BCS is >2.5. Moreover, changes in BCS between AI and the first pregnancy diagnosis, and between two pregnancy diagnosis were calculated. Cows were classified as low (<=31.5 L) or high (>31.5 L) milk producer based on median value (31.5 L).

**Statistical analyses**

The median value for milk production was determined by the univariate procedure of SAS (SAS, Software Version 9.3; 2002-2010 by SAS Institute Inc., Cary, NC, USA).Data were analyzed withthe logistic regression-stepwise selection procedure of SAS to obtain an estimated odds ratio with 95% confidence interval (CI).

The statistical model for risk of the presence of CL 21 days after AI included milk yield at AI,parity, BCS at AI, postpartum disorder, the season of enrollment, type of reproductive management at the last AI (heat detection versus synchronizations), the total previous number of AI services, treatment and two-way interactions. The statistical model for risk of pregnancy at 28-32 days after AI included milk yield at AI,parity, BCS at the first pregnancy diagnosis, changes in BCS between AI and the first pregnancy diagnosis, postpartum disorder,season of enrollment,type of reproductive management at the last AI, the total previous number of AI services, treatment and two-way interactions. The statistical model for risk of pregnancy losses between days 28-32 and 55-60 after AI included milk yield at AI, parity, BCS at the second pregnancy diagnosis,changes in BCS between two pregnancy diagnosis, postpartum disorder,the season of enrollment, type of reproductive management at the last AI, the total previous number of AI services, treatment and two-way interactions.

## RESULTS

Maintenance of of CL at 21 days after AI did not differ among CARP (79.6%, [168/211]), CIDR (86.0%, [196/228]), CARP+CIDR (80.0%, [172/215]) and CONT (74.9%, [149/199]) groups. For the maintenance of CL 21 days after AI, there are significant effects of type of reproductive management at the last AI (P<0.01), number of services ($P$<0.01), and interaction of treatment by BCS at AI ($P$<0.05). In this matter, rates of maintenance of CL 21 days after AI did not differ (odds ratio:1.96 [1.17-3.31]) between cows inseminated following CIDR and $PGF_{2α}$ based synchronization program (83.3% [170/204]) and those inseminated following the detection of estrus (83.3% [434/521]). Whereas, the rate of maintenance of CL 21 days after AI in cows inseminated following $PGF_{2α}$ or Ovsynch protocol (63.3% [81/128]) was 0.36 (0.23-0.57) times lower compared to those inseminated following the detection of estrus. Cows with only one service (74.7%, [280/375]) had 0.45 (0.26-0.78) times less chance for the maintenance of CL 21 days after AI than those with four or more services (84.0%, [152/181]). There were no differences for the maintenance of CL 21 days after AI in cows with two (85.7%, [156/182]) versus (odds ratio: 1.32 [0.72-2.42]) four or more services, or three (84.4%, [97/115]) versus (odds ratio: 1.14 [0.59-2.23]) four or more services. With regard to interaction effect of treatment by BCS at AI, among cows with BCS≤2.5, chances of maintenance of CL was lower (odds ratio:1.62 [1.10-2.40]) in CONT (70.7%, [111/157]) group compared to those in CARP (81.7%, [125/153]), CIDR (83.6%, [153/183]) and CARP+CIDR (80.1%, [129/161]) groups; whereas, among cows with BCS>2.5, chances of maintenance of CL were lower in CARP (74.1%, [43/58]) and CARP+CIDR (79.6%, [43/54]) groups compared to those in CONT (90.5%, [38/42]) and CIDR (95.6%, [43/45]) groups (Figure 1).

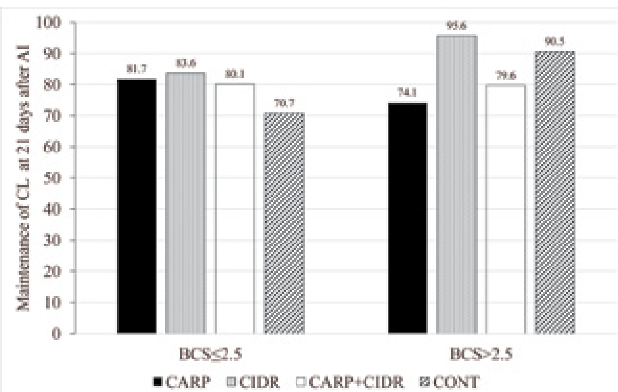


**Figure 1.** Interaction effect of treatment by BCS on maintenance of CL at 21 days following AI.

For the P/AI at 28-32 days after AI, there was no difference among CARP (48.8% [103/211]), CIDR (50.9 [116/228]), CARP+CIDR (47.4% [102/215]) and CONT (44.7% [89/199]) groups. For the P/AI at 28-32 days after AI, there were significant effects of milk production at AI (*P*<0.01) and the number of services (*P*<0.05). Low milk-producing cows (57.0%, [245/430]) had3.31 (1.73-6.36) times the higher chance for pregnancy at 28-32 days after AI compared to high milk producing cows (39.0%, [165/423]). Cows with two services (55.5%, [101/182]) had a 1.75 (1.17-2.80) times the higher chance for pregnancy than those with four or more services (47.5%, [86/181]). Based on odds ratios, there were no differences for the risk of pregnancy at 28-32 days after AI in cows with one service (42.9%, [161/375]) versus four or more services(odds ratio:0.81 [0.51-1.28]), or three services (53.9%, [62/115]) versus four or more services (odds ratio:1.51 [0.93-2.44]).

Pregnancy losses between 28-32 and 55-60 days did not differ among CARP (3.9%, [4/103]), CIDR (4.3%, [5/116]), CARP+CIDR (5.9%, [6/102]) and CONT (6.7%, [6/89]) groups. For the pregnancy losses between 28-32 and 55-60 days, there are significant effects of type of reproductive management at the last AI (P<0.01) and interaction of treatment by the number of services (P<0.05). Pregnancy losses in cows inseminated following $PGF_{2\alpha}$ or Ovsynch protocol (16.7% [10/60]) were 11.78 (3.03-45.82) times higher than those inseminated following the detection of estrus (3.2% [8/248]). Pregnancy losses between cows inseminated following CIDR and $PGF_{2\alpha}$ based synchronization program (2.9% [3/102]) and those inseminated following the detection of estrus did not differ (odds ratio: 1.39 [0.30-6.40]). With regard to the interaction effect of treatment by the number of services, pregnancy losses were higher in cows inseminated thrice and four or more times in CONT (11.8% and 16.7%) group compared to those in CARP (0% and 4.8%), CIDR (0% and 6.9%), CARP+CIDR (0% and 11.1%), respectively (Figure 2).

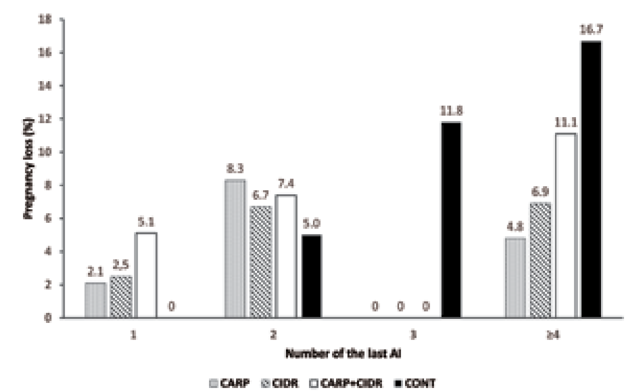


**Figure 2.** Interaction effect of treatment by number of the last AI on pregnancy loss between days 28-32- and 55-60-days following AI.

## DISCUSSION

Because cows had visible CL at 14 days after AI were included in the study, all cows were assumed to be ovulated after AI. Detection of visible and mature CL 21 days after AI could indicate maintenance of CL; however, some of the cows could have longer estrous cycles which may lead to overestimation of the maintenance of CL. In this matter, Remnant et al. (2015) reported longer range of interservice intervals in modern dairy cows and higher unexplained variation for cycle length within individual cows rather than between cows or herds. Therefore, some ofthe assumptions for the maintenance of CL based on the presence of CL could be overestimated due to longer estrous cycles at 21 days after AI in current study. However, differences in rates of CL maintenance based on the presence ofCL among treatment groups on day 21 after AI could not be solely attributed to longer estrous cycles because cows were randomly assigned for each treatment group in this study. Lower rates of maintenance of CL 21 days after AI in cows inseminated following $PGF_{2\alpha}$ or Ovsynch protocol compared to those inseminated following the detection of estrus or CIDR and $PGF_{2\alpha}$ based synchronization program could indicate lower ovarian stimulation following $PGF_{2\alpha}$ or Ovsynch protocol. Moreover, cows following the first service had lower rates of maintenance of CL 21 days after AI compared to those following subsequent inseminations. Probably, at the first service cows could not maintain the CL due to impotent embryonic development and its signal and/or impotent luteal development for the sake of lactation. The interaction effect of treatment by BCS at AI could indicate the beneficial effects of carprofen and/or progesterone treatments on maintenance of CL among cows with BCS≤2.5 could be due to ovarian stimulation among cows with poor BCS. In contrast, there were detrimental effects of carpofen treatment with or without progesterone supplementation among cows with BCS>2.5. Cows with optimal BCS could have better quality and larger embryos than those with poor BCS. In this matter, the effect of BCS on the quality of preimplantation embryos recovered from dairy cows was reported (Makarevich et al., 2016). Similarly, it has been reported that improvement of BCS at AI is required to increase embryonic survival in lactating dairy cows (Santos et al., 2009). In this case, carprofen administration with or without P4 supplementation could compromise $PGE_2$ secretion in cows with optimal BCS, and faster growing embryos could not be developed during attachment process.

With regard to P4 supplementation 14-21 days after AI in the current study, no beneficial effect was found on P/AI similar to no effects of CIDR insertion from day 14 to 23 (Bartolome et. al., 2009) or from day 14 to 21 (Galvao et al., 2007; Alnimer and Lubbadeh, 2008) and from day 13-20 days after AI (El-Zarkouny and Stevenson, 2004) after AI on PR in lactating dairy cows.In contrast, Garcia-Ispierto et al. (2016) reported an increase in PR following P4 supplementation from days 15 to 17 after AI in cows without retained placenta. In addition, a 1.4 times higher chance for pregnancy following P4 supplementation from days 15 to 17 following AI was reported by Garcia-Ispierto and Lopez-Gatius (2017). This discrepancy between current and previous studies could be due to the longer length of P4 supplementation following AI, and probably P4 supplementation could have been implemented just during maternal recognition of pregnancy but not further in current study. Perhaps, longer P4 supplementation could accelerate embryonic growth and cause asynchrony between embryo and uterus leading to no benefit for fertility. In this regard, slight reduction in PR was reported following CIDR insertion between 14 and 21 days after AI in lactating dairy cows (Chenault et al., 2003).

Current results could indicate that carprofen administration 14 days after AI had no effect on P/AI in lactating dairy cows similar to carprofen administration 15 days after AI in a study conducted by von Krueger and Heuwieser (2010). Therefore, the administration of carprofen as an NSAID one day prior to previous report could reveal neither beneficial nor detrimental effect on embryo survival in lactating dairy cows. However, in the current study and a previous study conducted by von Krueger and Heuwieser (2010) all experimental cows were healthy. If the same studies would perform on cows with subclinical health problems, these results would have been different, and this phenomenon warrants further research. Perhaps, lower pregnancy losses in repeat breeder cows in the CARP group could be attributable to the beneficial effect of carprofen in repeat breeder cows with subclinical or chronic disorders.

Unexpectedly, a combination of CIDR and carprofen did not have an additive effect on embryo survival. In this regard, CIDR supplementation could fasten embryonic growth and larger embryos could be dependent on $PGE_2$ secretion for embryonic development during carprofen administration in this study. Because carprofen administration could non-selectively suppress $PGE_2$ secretion, an additive effect of the combination of CIDR and carprofen applications could not be existed in current study. In this regard, it has been known that $PGE_2$ promotes luteal function (Kennedy, 1983; McCracken et al., 1999) and involves the establishment and maintenance of gestation in mammals (Bazer, 1992; Bazer et al., 1997). Moreover, it has been postulated that IFN-t could stimulate PG-endoperoxide synthase-2 expression leading to alteration of the prostaglandin production cascade from $PGF_{2\alpha}$ to $PGE_2$ in ruminants (Bazer et al, 1997; Spencer et al., 1996).Since carprofen non-selectively suppress both $PGE_2$ and $PGF_{2\alpha}$, embryos dependent on $PGE_2$ could not be developed; thereby, no additive effect of CIDR and carprofen on P/AI was obtained in the current study.

Significantly higher pregnancy losses between 28-32 and 55-60 days in cows inseminated following $PGF_{2\alpha}$ or Ovsynch protocol compared to those inseminated following the detection of estrus or following CIDR and $PGF_{2\alpha}$ based synchronization program could reveal that higher fertility following natural or induced estrus compared to timed artificial insemination or selective estrus induction with $PGF_{2\alpha}$. With regard to the interaction effect of treatment by AI number on P/AI, higher pregnancy losses in cows inseminated thrice and four or more times in the CONT group could indicate the beneficial effects of progesterone and/or NSAID treatment (Figure 2). However, among repeat breeder cows, pregnancy losses were lower in carprofen and CIDR treatment but not its combinations compared to in the CONT group. This detrimental effect of combined treatment of NSAID and P4 on pregnancy maintenance was not expected in repeat breeder cows. Unlike the study reported by Amiridis et al. (2009), a combination of NSAID and P4 supplementation did not increase P/AI in repeat breeder cows; however, pregnancy loss was significantly lower in carprofen and progesterone treatment. This disagreement between the current study and the results of Amiridis et al. (2009) could be the experimental design. In the present study, all repeat breeder cows were supposed to be cycling since all of them had CL 14 days after the last AI, and induction of cyclicity would not be the problem. Moreover, a possible reason for this discrepancy could be differences for NSAID administration between present study and Amiridis et al. (2009). In this regard, Amiridis et al. (2009) administered meloxicam 16, 17 and 18 days after AI; whereas, carprofen was administered only once at 14 days following the last AI. Perhaps, higher pregnancy losses in the CARP+CIDR group could be due to the carryover effect of the disruption of embryonic growth in repeat breeder cows.In this matter, carprofen administration could suppressed $PGE_2$ which is needed for faster-growing embryo following P4 supplementation. Unlike current results, Amiridis et al. (2009) reported higher P/AI following a combined protocol including GnRH, P4 and meloxicam; however, they suggested that determination of the relative contribution of each of the treatment was very difficult.Moreover, Khoramian et al. (2011) reported higher P/AI inthe following used CIDR administration 5-6 days after AI for 10 days in repeat breeder cows. Similarly, repeat breeder cows were benefited from CIDR administration between days 14 and 21 after AI with lower pregnancy loss in current study.

## CONCLUSIONS

In conclusion, neither beneficial nor detrimental effects of carprofen or CIDR administration around the time of maternal recognition of pregnancy were observed based on P/AIin lactating dairy cattle. However, pregnancy losses were significantly lower following carprofen or CIDR administrations, but not its combinations, in repeat breeder cows. No increase in P/AIfollowing carprofen administration during the critical period of pregnancy recognition in this study warrants further research focusing on specifically suppression of $PGF_{2\alpha}$ and stimulate embryonic growth in lactating dairy cows.Furthermore, use of NSAID during maternal recognition of pregnancy in cows with subclinical and clinical disorders warrants further research to increase fertility. Moreover, higher rate of presence of CL following P4 administration; whereas, a lower rate of maintenance of CLfollowing NSAID with or without P4 administration in cows with optimal BCS could indicate that BCS should be considered for the cause of asynchrony of embryonic development among cows for the different therapeutic approaches in dairy herd fertility programs.

## ACKNOWLEDGMENTS

In this study, CIDR® and Rimadyl®XL were generously donated by Zoetis Animal Health, Turkey.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

**Table 1.** Treatment and selected variables by logistic regression stepwise elimination analyses for risk of presence of CL 21 days after AI.

| | % and proportion (*n*/*n*) | | Odds ratio (95% CI) | *P*-value |
|---|---|---|---|---|
| Treatment | | | | |
| CARP vs CON | 79.6 (168/211) vs 74.9 (149/199) | | 2.06 (1.18-3.61) | <0.09 |
| CIDR vs CON | 86.0 (196/228) vs 74.9 (149/199) | | 2.67 (1.57-4.55) | |
| CARP+CIDR vs CON | 80.0 (172/215) vs 74.9 (149/199) | | 1.48 (0.91-2.42) | |
| Type of reproductive management | | | | |
| CIDR-PGF$_{2\alpha}$ vs Estrous detection | 83.3 (170/204) vs 83.3 (434/521) | | 1.96 (1.17-3.31) | <0.01 |
| Ovsynch or PGF$_{2\alpha}$ induced estrus vs Estrous detection | 63.3 (81/128) vs 83.3 (434/521) | | 0.36 (0.23-0.57) | |
| Number of services | | | | |
| 1 vs 4 or more | 74.7 (280/375) vs 84.0 (152/181) | | 0.45 (0.26-0.78) | <0.01 |
| 2 vs 4 or more | 85.7 (156/182) vs 84.0 (152/181) | | 1.32 (0.72-2.42) | |
| 3 vs 4 or more | 84.4 (97/115) vs 84.0 (152/181) | | 1.14 (0.59-2.23) | |
| Treatment by BCS at AI | Poor BCS | Optimal BCS | | |
| CARP | 81.7 (125/153) | 74.1 (43/58) | 1.62 (1.10-2.40) | <0.05 |
| CIDR | 83.6 (153/183) | 95.6 (43/45) | | |
| CARP+CIDR | 80.1 (129/161) | 79.6 (43/54) | | |
| CON | 70.7 (111/157) | 90.5 (38/42) | | |

**Table 2.** Treatment and selected variables by logistic regression stepwise elimination analyses for risk of pregnancy at 28-32 days after AI.

| | % and proportion (*n*/*n*) | Odds ratio (95% CI) | *P*-value |
|---|---|---|---|
| Treatment | | | |
| CARP vs CON | 48.8 (103/211) vs 44.7 (89/199) | | NS |
| CIDR vs CON | 50.9 (116/228) vs 44.7 (89/199) | | |
| CARP+CIDR vs CON | 47.4 (102/215) vs 44.7 (89/199) | | |
| Milk yield at AI (Low vs High) | 57.0 (245/430) vs 39.0 (165/423) | 3.31 (1.73-6.36) | <0.01 |
| Number of services | | | |
| 1 vs 4 or more | 42.9 (161/375) vs 47.5 (86/181) | 0.81 (0.51-1.28) | <0.05 |
| 2 vs 4 or more | 55.5 (101/182) vs 47.5 (86/181) | 1.81 (1.17-2.80) | |
| 3 vs 4 or more | 53.9 (62/115) vs 47.5 (86/181) | 1.51 (0.93-2.44) | |

**Table 3.** Treatment and selected variables by logistic regression stepwise elimination analyses for risk of pregnancy losses between 28-32 days and 55-60 days after AI.

| | % and proportion (*n*/*n*) | | | | Odds ratio (95% CI) | *P*-value |
|---|---|---|---|---|---|---|
| Treatment | | | | | | |
| CARP vs CON | 3.9 (4/103) vs 6.7 (6/89) | | | | | NS |
| CIDR vs CON | 4.3 (5/116) vs 6.7 (6/89) | | | | | |
| CARP+CIDR vs CON | 5.9 (6/102) vs 6.7 (6/89) | | | | | |
| Type of reproductive management | | | | | | |
| CIDR-PGF$_{2\alpha}$ vs Estrous detection | 2.9 (3/102) vs 3.2 (8/248) | | | | 1.39 (0.30-6.40) | <0.01 |
| Ovsynch or PGF$_{2\alpha}$ induced estrus vs Estrous detection | 16.7 (10/60) vs 3.2 (8/248) | | | | 11.78 (3.03-45.82) | |
| Treatment by number of services | Number of Services | | | | | |
| | 1 | 2 | 3 | >3 | | |
| CARP | 2.1 (1/48) | 8.3 (2/24) | 0 (0/10) | 4.8 (1/21) | 1.12 (1.00-1.25) | <0.05 |
| CIDR | 2.5 (1/40) | 6.7 (2/30) | 0 (0/17) | 6.9 (2/29) | | |
| CARP+CIDR | 5.1 (2/39) | 7.4 (2/27) | 0 (0/18) | 11.1 (2/18) | | |
| CON | 0 (0/34) | 5 (1/20) | 11.8 (2/17) | 16.7 (3/18) | | |

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