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Melatonin implants in late pregnancy increase yield and enhance milk quality in dairy goats

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ABSTRACT

This study investigated the effects of melatonin implants in pregnancy on milk production and composition, and the quality of colostrum in dairy goats. Thirty days before kidding, 92 goats (group MEL) received one melatonin implant, and the remaining 177 goats (group CON) did not. Three monthly milk evaluations included milk yield (kg/d), composition (%Fat, %Protein, % Lactose), daily yield (Fat, g/d Protein, g/d Lactose). A sample of colostrum was obtained from 165 goats, from which its composition, IgG concentration were measured. MEL had a significantly ($P<0.01$) higher milk yield in the second month (3.16 ± 0.10 kg/d) than CON (2.78 ± 0.07 kg/d). In the three milk samplings, fat concentrations were significantly higher ($P<0.05$) in the MEL than in the CON does. In the second milk sampling, does that had received a melatonin implant produced higher ($P<0.05$) daily milk yield components than did non-implanted (Fat: 144 ± 6.0 vs 115 ± 3.4; Protein: 104 ± 3.4 vs 91 ± 2.5; Lactose: 148 ± 5.8 vs 131 ± 4.3 g/d). In conclusion, melatonin implants administered 30 d before kidding increased milk production, the amounts of milk daily components in the second month of lactation, and the concentration of fat milk.

Keywords: goat, melatonin, dairy, milk composition, fat, colostrum

Introduction

Since the 1960s, the world's goat population has increased, mainly because of changes in human food preferences and incomes, and climate change, which limits the areas suitable for livestock farming. There has been a continuous increase in dairy goat numbers globally, with dramatic increases in the 1990s, particularly in Asia and Africa, although with a minor net decrease observed in Europe (–0.9%) and Americas (–0.7%) (Miller and Lu 2019). In spite of this figures, dairy goat production is more popular in Europe, particularly in the Mediterranean basin, where it is vital economically, environmentally, and socially for the Mediterranean countries of Spain, France, Italy, and Greece (Dubeuf et al. 2004). Goat milk production in the world, from over one billion head of goats, amounts to about 18.6 million tons, of which 15.14% in Europe (2.8 million tons). There are over 15 million dairy goats in the EU. In particular, the total production of goat milk in the EU in the amount of 2.2 million tons, the largest share belongs to Greece (26.16%), followed by France (27.45%), followed by Spain (22.85%) (Sredojević et al. 2020).

Cheese yield is a crucial economic target for dairy goat farmers, specially in the EU, which has emerged as the leading cheese-producing region, contributing 10.39 mmt in 2023 (Langat, 2024). Cheese yield depends on milk fat and protein concentrations (Pazzola et al. 2019), therefore, improving these parameters can enhance profitability in dairy farmers. Although goat colostrum is not commercialized, it is crucial for immune system development of the kids (Hernández-Castellano et al. 2014) as it provides essential nutrients, such as protein, lactose, fat, vitamins, minerals and several biologically active compounds (Kráčmar et al. 2005). Currently, new management practices have been adopted that reduce the use of chemical inputs and medications (antibiotics) in food animal production (Miller and Lu 2019; More 2020), which can impact in both goat milk and colostrum quality. In this context, exogenous melatonin can be an alternative for improving productive and health indicators in dairy goats.

Melatonin is a natural neuro-endocrine hormone, and since its discovery, most research has focused on its effects on reproduction in photoperiod-dependent breeding animals. Recently, the potential of melatonin to enhance lactation and colostrogenesis in small ruminants has been investigated (Avilés et al. 2019; Abecia et al. 2020; Yang et al. 2020; Abecia et al. 2021; Canto et al. 2022). In a study of Creole goats, two melatonin implants administered in the dry period increased milk yield during the first 14 weeks of lactation, but melatonin treatment did not have a significant effect on milk components (Avilés et al. 2019). Conversely, in Cashmere goats that received melatonin implants twice during early lactation, daily milk yield, milk protein and milk lactose decreased, while milk fat content increased (Yang et al. 2020). Additionally, melatonin has been shown to protect against oxidative damage (Andrés et al. 2009; Bouroutzika et al. 2021), improve mammary health (Jiménez et al. 2009; Canto et al. 2022) and enhance immune colostrum quality in meat and dairy ewes (Abecia et al. 2020; Canto et al. 2022). Although, the role of melatonin in the mammary gland as a target tissue has not been identified (Zhang et al. 2019), and the effects of melatonin on milk production in several ruminant species have been contradictory (Asher et al. 1994; Abecia et al. 2005) and with limited evidence of its role in goats.

The objective of this study was to measure the effects of melatonin treatment at pregnancy on milk production and composition, and colostrum quality in dairy goats reared under commercial farm conditions. The rational for choosing the last month of gestation is that the transfer of prepartum components from the maternal circulation into colostrum occurs during this period, and is a critical period for mammary gland development. Additionally, a single subcutaneous implant is an effective method for slow-release melatonin, which has demonstrated positive effects on colostrogenesis and lactation, as demonstrated in previous studies conducted by our group with sheep (Abecia et al. 2020, 2021; Canto et al. 2022). Thus, we support the hypothesis that exogenous melatonin administered in late pregnancy can affect the function of the mammary gland, and consequently, lactogenesis and colostrogenesis.

Material and methods

Experimental treatments

Four commercial dairy goat farms that raise the Murciano Granadina breed in Spain participated in this study. Approximately 30 (±S.D) d (28.5 ± 0.88 d) before the expected onset of the kidding date, goats were randomly chosen from among 269 multiparous animals with no diseases, and a comparable body condition score (BCS). At that time, 92 goats (group MEL) (parity number: 3.78 ± 0.20; BCS: 3.43 ± 0.24) were administered subcutaneously at the base of the ear one melatonin implant (18 mg melatonin; Melovine, CEVA Salud Animal, Barcelona, Spain). Those implants provide a continuous release of melatonin for approximately 10 wk and high plasma concentrations are maintained throughout the day (Delgadillo, 2011). The remaining 177 goats (parity number: 3.61 ± 0.17; BCS: 3.41 ± 0.21) did not receive an implant and constituted the control group (CON).

Animal management

In each farm, the two groups were managed as a single flock, and were subjected to the same nutritional and husbandry practices throughout the experiment, under an intensive system, with permanent stabling. Kidding occurred indoors over seven weeks in Aug and Sep. After parturition, kids were separated from their does and reared on an artificial lactation program until commercialization. In lactation, goats were milked twice per day and were offered a total mixed ration (TMR) of concentrates and forage to meet their liveweight maintenance and milk production requirements. Water was provided *ad libitum.*

Milk records

In the experiment, three monthly milk samplings were performed on each farm. The first milk sampling was performed two weeks after kidding, and subsequent milk collections occurred every 30 d. Table 1 presents the mean (±SEM) Days In Milk (DIM) at each sampling day, and the interval between melatonin implantation and milk sampling. In each sampling, measurements of individual milk yield were recorded by volumetric meters integrated in the milking system such that the milk production of each animal is recorded on a daily basis, alternating between mornings and afternoons (ICAR 2016). The Official Milk Control technique, which has been certified by the International Committee for Animal Recording (ICAR 2016), was used to measure daily milk production, and was calculated as follows:

Daily milk yield = (Registered milk × 24)/(Time between milk records)

Monthly milk productions were calculated based on the ICAR Method, which takes a monthly alternate milk sample (ICAR 2016).

Sample collection

At the time that milk yield was measured, a milk sample was collected and preserved at 4°C for subsequent laboratory analysis. For the SCC, an aliquot of each milk sample was conserved in bronopol (0.1%). Colostrum samples were obtained from 165 goats immediately after birth (CON: n= 88, MEL: n= 77), which were frozen and kept at -20° C until assayed for immunological and nutritional composition.

Milk and colostrum quality analysis

Fat, protein, and lactose contents were measured based on the methods used by the IDF (2010a). Milk samples were subjected to direct reference analysis for fat content (Gerber method), crude protein content (Kjeldahl method), and lactose content in accordance with International Dairy Federation Standard 105 (IDF 2008), International Dairy Federation Standard 020-5 (IDF 2001), and International Dairy Federation Standard 214 (IDF 2010b), respectively. The milk samples were analyzed for SCC by an electronic fluorescence-based cell-counting Fossomatic 5000 (Foss Electric, Hillerød, Denmark) following the guidelines of the International Dairy Federation's (IDF 2013).

A digital Brix refractometer (Deltatrak, Pleasanton, CA, USA), which had a detection range of 0%-53% was used for Brix refractometry at room temperature. Before testing, colostrum samples were completely homogenized following the manufacturer's instructions. Total colostral IgG concentration was measured by a direct enzyme immunoassay, sandwich ELISA Calokit–Cabra Test (ZEULAB, Zaragoza, Spain).

Samples were diluted to fit the operating range of IgG quantification (mg/ml) in the ELISA test, and the results were read by a 450-nm absorbance Multiskan microplate reader (Labsystems, Helsinki, Finland). The concentration of goat IgG in the colostrum sample was calculated by interpolating the absorbance reading on the calibration curve. The samples were diluted to 1:2 before the nutritional analysis. Fat, protein, and lactose concentrations in the colostrum samples were estimated by an indirect method that involved an ultrasonic analyzer (Lactoscan SP+), which had been calibrated for goats following the guidelines provided by the manufacturer (Milkotronic Ltd., Tsentar, Nova Zagora, Bulgaria).

Statistical analysis

Daily yield (g/d) of each milk component was calculated for individual goats as follows: (milk yield × component content (%) of milk) / 100. To compare statistically significant differences in milk yield, colostrum and milk composition, and daily milk yield components, a multifactorial model based on the Least Squares Method of the GLM procedure in SPSS v.26 (IBM, Chicago, Il, USA) was used. The analysis included farm and melatonin treatment as fixed effects, and their interaction. A general representation of the model is as follows:

$$Y_{ij} = \mu + F_i + M_j + F_i \times M_j + E_{ij},$$

where Y_{ij} is the analyzed parameters (milk yield, colostrum and milk composition, and daily milk yield components); μ is the overall mean; F_i is the effect of the farm (*i*= Farm 1, Farm 2, Farm 3, Farm 4); M_j is the effect of the melatonin treatment (*j*= MEL and CON group); $F_i \times M_j$ is the effect of the interaction between farm and melatonin treatment; and E_{ij} is the random residual effect. Within fixed effects, significant differences in milk and daily yield components, and colostrum and milk composition were identified by an ANOVA. Statistical significance was defined as a P-value $\leqslant$ 0.05.

Results

Milk yield, composition and quality

In each of the three milk samplings, farm had a significant ($P < 0.05$) effect on milk yield. In the first sampling, the treatment x farm interaction had a significant ($P < 0.0001$) effect on milk yield. Goats that had received a melatonin implant 30 d before kidding had a significantly ($P < 0.01$) higher milk yield (3.16 ± 0.10 kg/d) than did the CON goats (2.78 ± 0.07 kg/d) in the second month of lactation (Fig. 1); however, in the first and the third month of sampling, melatonin treatment did not have a significant effect (Fig. 1).

Farm had a significant ($P < 0.05$) effect on the content of fat, protein, and lactose in milk in each of the three milk samplings. The effects of the farm x melatonin treatment interaction on the concentrations of fat and protein in the milk were significant ($p < 0.0001$) in the first sampling, only. In the experiment, fat concentration was significantly higher in the MEL than it was in the CON does (Month 1: $P < 0.05$; Month 2: $P < 0.001$; Month 3: $P < 0.05$). Melatonin treatment did not have a significant effect on the concentrations of protein and lactose in the milk (Fig. 2).

In the second sampling, farm had a significant ($P < 0.0001$) effect on each of the daily milk components, and melatonin treatment had a significant ($P < 0.05$) effect on daily fat yield. In the third sampling, farm had a significant effect on daily fat ($P < 0.001$) and protein ($P < 0.05$) yields, and the farm x melatonin treatment interaction with had a significant (P < 0.05) effect on daily lactose yield. Does that receive a melatonin implant had a significantly higher daily fat (P < 0.001), daily protein (P < 0.001), and daily lactose (P < 0.05) milk yield than did non-implanted goats (Fat: 144 ± 6.0 vs 115 ± 3.4; Protein: 104 ± 3.4 vs 91 ± 2.5; Lactose: 148 ± 5.8 vs 131 ± 4.3 g/d, resp.) in the second milk sampling, but not in the first and the third milk samplings.

Farm (P < 0.05) and melatonin treatment (P < 0.01) had significant effects on SCC in the first sampling. In the second and third month, melatonin treatment did not have a significant effect on SCC, although the SCC in goats that had received a melatonin implant tended (P = 0.17) to be lower than in those that did not (Table 2).

Colostrum quality

Farm had a significant effect on the components of goat colostrum (°Brix, IgG, Fat: P < 0.0001; Protein, Lactose: P <0.001), and MEL goats tended (P = 0.17) to have higher colostrum protein concentrations than did CON goats. Brix degree, IgG, fat, and lactose concentrations did not differ significantly between the two groups (Table 3).

Discussion

In our experiment, goats that had received one melatonin implant 30 d before kidding significantly increased milk production in the second month of lactation, approximately 75 d post-melatonin implantation. These findings are consistent with studies by Mabjeesh et al. (2013), who exposed dairy goats to a short photoperiod (60 d prepartum), and Avilés et al. (2019), who administered two melatonin implants to Creole goats during the drying-off phase (21 d prepartum), increasing milk production throughout lactation. Similarly, in our study of Assaf sheep conducted under commercial conditions, one or two melatonin implants administered 40 d before lambing increased milk production in the first three months of lactation (Canto et al. 2022). This suggests that melatonin treatment, or exposure to a short-day photoperiod during the dry period, increases milk yield in the subsequent lactation of small ruminants. Mabjeesh et al. (2013) proposed that the sensitivity to prolactin, particularly during the transition to lactation, may be the mechanism behind this effect. Supporting this hypothesis, Wall et al. (2005) found that cows exposed to a short-day photoperiod (linked to a high endogenous melatonin secretion) during the dry period, underwent more extensive mammary remodeling and cell renewal. However, our results were in contrast with the inhibitory effects of a short daily photoperiod or melatonin treatment during lactation on milk yield reported for sheep (Molik et al. 2013), goat (Yang et al. 2020; Zhang et al. 2019) and cattle (Auldist et al. 2007). This reduction in milk production could be caused by melatonin administration, which decreases prolactin secretion by protecting and stimulating dopaminergic neurons (Lacasse et al. 2019; Li et al. 2020; Liu et al. 2023). Additionally, these different melatonin responses in milk production on animals could be attributed to a wide range of factors, including significant species differences (Asher et al. 1994; Avilés et al. 2019), dosage variations (Cosso et al. 2021), or melatonin release characteristics (Yang et al. 2020).

In our study, providing melatonin to Murciano Granadina goats in late pregnancy increased the concentration of fat in their milk. This increase in milk fat content appears to be more consistent, as it has been observed in cows that received three repeated doses of melatonin during mid-lactation (Auldist et al. 2007), or in goats that received two doses at mid and late lactation (Yang et al. 2020), or in dairy ewes that received two melatonin implants 40 d before lambing (Canto et al. 2022); moreover, meat-type ewes that received a melatonin implant 24 h after lambing also presented an increment of fat proportion in milk (Abecia et al. 2021). There is an evidence that melatonin affects the gut microbiota in mice through mechanisms of AMP induction (Kim et al. 2020), and the rumen microflora of cows and lambs (Ouyang et al. 2021; Ma et al. 2022). These alterations in the bacterial biota can affect the fat content of milk, thereby significantly affecting ruminal lipid metabolism in both goats and cows (Toral et al. 2016). In addition, research involving bovine intramuscular preadipocytes demonstrated that melatonin regulates adipose differentiation via the melatonin receptor MT2 (Yang et al. 2017). This regulatory effect on fat cells aligns with findings from a recent analysis of the dairy metabolome, which revealed that melatonin treatment reduced most metabolites linked to lipid oxidation, implying increased fat accumulation in cows. This fat accumulation might alter the concentration of fat in the milk (Fu et al., 2023).

In our study, melatonin implants did not have a significant effect on protein and lactose concentrations in goat milk. Similarly, in other studies, melatonin implants administered 49 d prepartum in goats did not affect protein and lactose concentrations (Avilés et al. 2019), and implants given 40 d prepartum in sheep did not affect the lactose concentrations in milk (Canto et al. 2022). In small ruminants, under various farming and feeding systems, protein content is more stable than fat content in milk (Barillet 2007; Morand-Fehr et al. 2007) and milk lactose concentrations do not vary appreciably (Zervas and Tsiplakou 2013).

In our study of goats, melatonin implants did not reduce the SCC of milk, in contrast to findings from studies on cows and sheep (Yang et al. 2017; Canto et al. 2022), which might reflect species-specific differences (Avilés et al. 2019). These specie specific differences are mainly due to the higher SCC in uninfected goat halves, the higher apocrine component of goat milk secretion compared to sheep (Paape et al. 2001; Contreras et al. 2007). Moreover, there is a distinction in SCC profiles reflected in the predominant cell types present. Polymorphonuclear neutrophilic leukocytes (PMNs) were the predominant cell type in milk from healthy uninfected goats, comprising 40 to 80% of the SCC. In contrast, milk from healthy uninfected sheep primarily contains macrophages, accounting for 45–88% of the SCC, while PMNs constitute 10–35%, lymphocytes 10–17%, and epithelial cells 2–3% (see review Kaskous et al. 2023).

Although the primary husbandry and feeding practices across the flocks were consistent, there was a significant effect of the farm ($P<0.05$) on milk yield and composition. Therefore, the high variability across different farms may hinder the interpretation of the results. In addition, Morand-Fehr et al. (2007) highlighted the complexity of different farming systems, indicating that not all variables can be controlled. In our study, uncontrolled factors that might have contributed to farm effect variability include environmental factors, such as temperature and humidity (Zhu et al. 2020); genetic factors, including individual genetic effects (Goetsch et al. 2011), intra-breed variability (Idowu and Adewumi, 2017), and the presence of genomic single nucleotide polymorphisms (SNP) (Mucha et al. 2018); and sociodemographic characteristics (Lianou and Fthenakis 2021).

In our study, the immunity and chemical quality of colostrum did not differ significantly between treated and control goats. Concerning the immunity quality, IgG levels were elevated and exceeded the 28.2 mg/ml recorded in the same goat breed (Romero et al. 2013), which suggested that the animals in the two groups in our study were in good nutritional and immunological condition (Agenbag et al. 2021). The observed level of colostrum fat aligns with findings from other studies on goats. However, in our study, protein and lactose concentrations were lower and higher, respectively, than previously reported in the literature (Argüello et al. 2006; Keskin et al., 2007; Yang et al., 2009; Moreno-Indias et al., 2012; Romero et al., 2013). These variations may be related to the goat breed and the intensive concentrated feeding method used in the study. Sánchez-Macías et al. (2014) indicated that the lower protein concentrations might be linked with highly productive goat breeds, while, higher lactose concentrations seem consistently associated with increased starch and energy in the diet (Banchero et al., 2015; Hare et al., 2021). Moreover, a similar trend (low protein and high lactose) was described by Agradi et al. (2023) in Oborica goats, where the authors highlighted that these results were anticipated due the osmotic effects of lactose. Consequently, a higher percentage of lactose leads to an increased water influx, which in turn results in a higher dilution of the protein.

Conclusion

In conclusion, the administering of subcutaneous melatonin implants 30 d before kidding had a significant effect on milk yield and composition in goats reared under commercial farm conditions. Specifically, exogenous melatonin increased milk yield and milk daily components in the second month of lactation and fat milk concentration at the beginning and at mid-lactation. Factor such as fat and protein milk yield might be the best for price incentives, particularly, if the milk is used to produce cheese, and administering exogenous melatonin in goats at the end of pregnancy might be a means of increasing income in dairy goat production systems.

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Ethical Considerations Statement

The Ethics Committee for Animal Experiments at the University of Zaragoza approved all of the procedures performed in the study. The care and use of animals were in accordance with the Spanish Policy for Animal Protection RD1201/05, which meets the European Union Directive 2010/63 on the protection of animals used for experimental and other scientific purposes.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Table 1

Mean (±SEM) Days In Milk (DIM) in the first three monthly milk samplings, and the interval between melatonin implantation and day of milk sampling in Murciano Granadina dairy goats that either did (MEL) or did not (CON) receive a melatonin implant 30 d before kidding.

	Numbers of goats/farm (F)	Days In Milk (DIM)			Interval implant-sampling (d)		
	F1 F2 F3 F4	Month 1	Month 2	Month 3	Month 1	Month 2	Month 3
CON (n=177)	97 27 24 29	13.67±0.59	42.64±0.67	75.08±0.72	--	--	--
MEL (n=92)	20 24 20 28	16.99±0.90	47.51±0.91	79.33±0.89	45.34±0.79	76.17±0.80	107.17±0.62

Table 2

Mean (± SEM) daily fat, protein, and lactose yield (g/d), and somatic cell count (SCC) in Murciano Granadina dairy goats that either did (MEL) or did not (CON) receive a melatonin implant 30 d before kidding in early- and mid-lactation under commercial farms conditions ([a,b]: different superscripts indicate significant differences between groups, within each month, $P < 0.05$) ([x,y]: indicate differences among groups, $p = 0.10$) .

	CON	MEL
Milk daily yield Month 1		
Fat (g/d)	104 ± 3.7	113±5.3
Protein (g/d)	85±2.7	89±3.9
Lactose (g/d)	117±3.9	122±5.5
Milk daily yield Month 2		
Fat (g/d)	115±3.4[a]	144±6.0[b]
Protein (g/d)	91±2.5[a]	104±3.4[b]
Lactose (g/d)	131±4.3 [a]	148±5.8 [b]
Milk daily yield Month 3		
Fat (g/d)	112±3.0	118±5,2
Protein (g/d)	94±2.2	94±3.6
Lactose (g/d)	134±3.6	139±6.5
Milk quality		
SCC month 1 (10^3/ml)	1.487±195[x]	1.094±163[y]
SCC month 2 (10^3/ml)	1.906±420	1.360±417
SCC month 3 (10^3/ml)	1.240±154	1.151±144

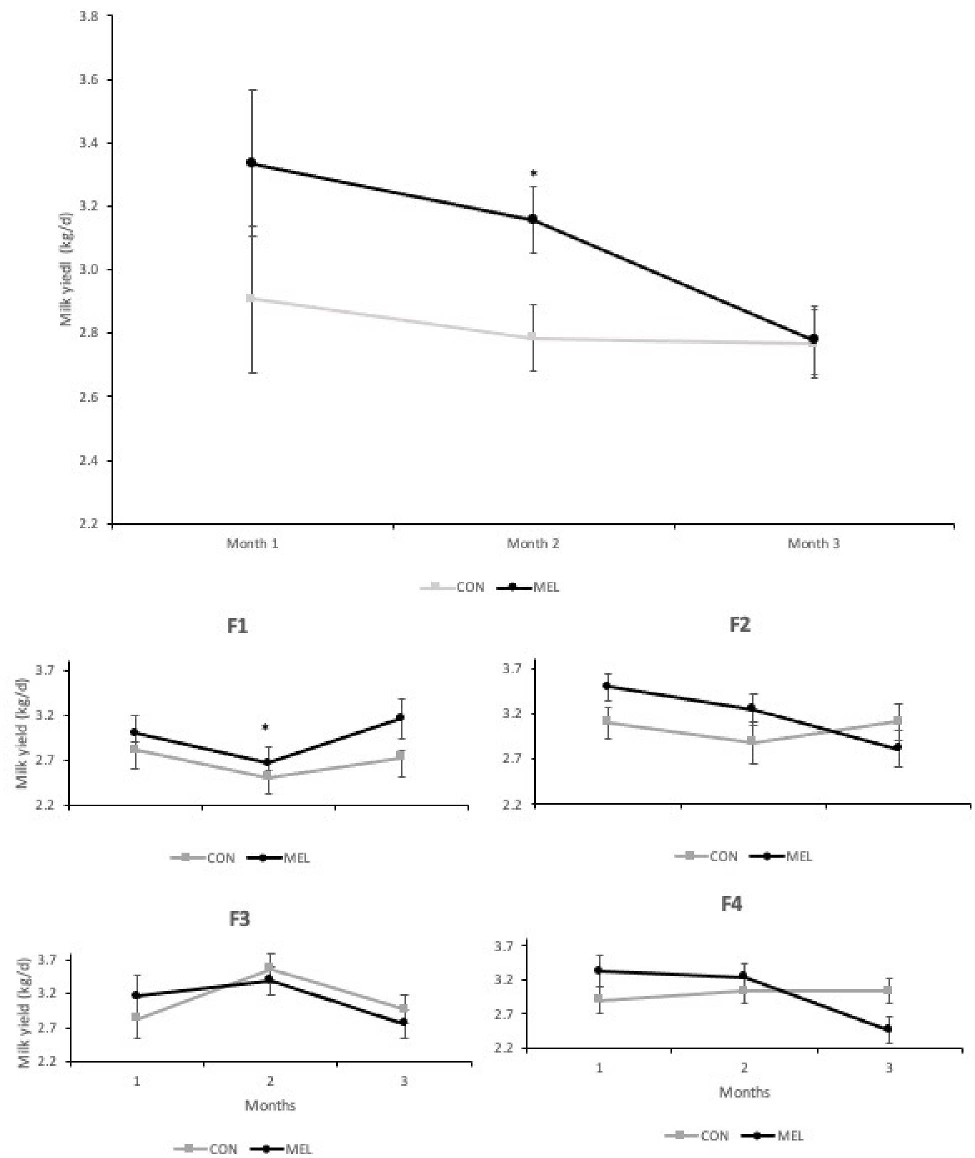
Table 3

Brix (°), IgG (mg/ml), fat (%), protein (%), and lactose (%) in colostrum from goats that either did (MEL) or did not (CON) receive a melatonin implant (18 mg) 30 d before kidding that had been collected immediately after parturition in Murciano Granadina dairy goats on commercial farms (Mean ± SEM) (x,y: indicate differences between groups, p = 0.10).

	CON	MEL
°Brix (%)	23.73±0.57	24.11±0.68
IgG (mg/ml)	51.06±3.04	52.27±3.84
Fat (%)	8.82±0.42^{x}	9.69±0.49^{y}
Protein (%)	6.42±0.13	6.59±0.17
Lactose (%)	9.72±0.21	9.98±0.25

Fig. 1. Mean (±SEM) daily milk yield (kg/d) in the first three months of lactation in Murciano Granadina dairy goats that either did (MEL) or did not (CON) receive a melatonin implant 30 d before kidding by treatment (upper panel), and the interaction treatment x farm 1 (F1), farm 2 (F2), farm 3 (F3) and farm 4 (F4) (lower panel). *: significant difference between groups, within the month, at $P \leqslant 0.05$.

Fig. 2. Mean (± SEM) daily fat, protein, and lactose milk content (%) in Murciano Granadina dairy goats that either did (MEL) or did not (CON) receive a melatonin implant (18 mg) 30 d before kidding by treatment (upper panel), and the interaction treatment x farm 1 (F1), farm 2 (F2), farm 3 (F3) and farm 4 (F4) (lower panel), reared under commercial farms conditions. * and** indicate significant differences between groups, within month ($P \leqslant 0.05$ and 0.01, resp.).



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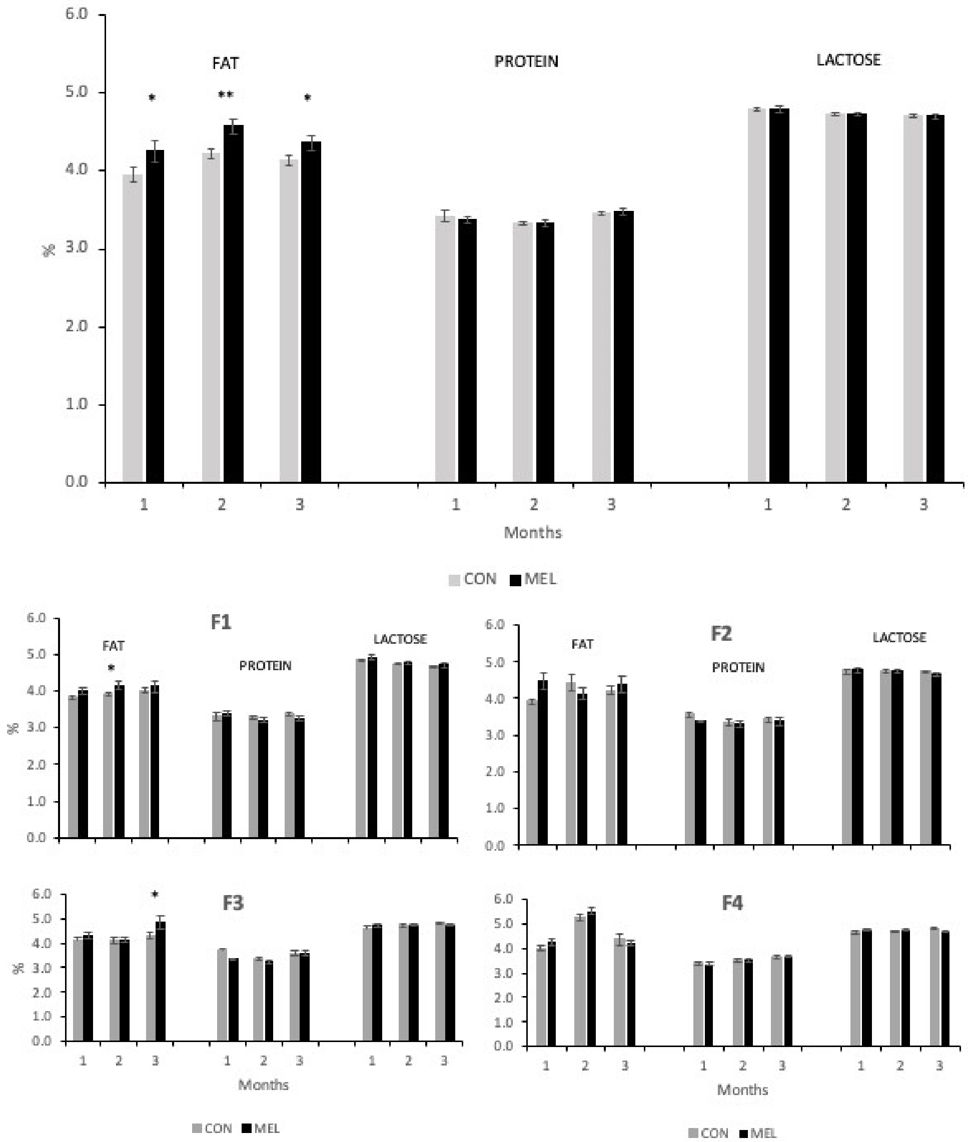

Mean (± SEM) daily fat, protein, and lactose milk content (%) in Murciano Granadina dairy goats that either did (MEL) or did not (CON) receive a melatonin implant (18 mg) 30 d before kidding by treatment (upper panel), and the interaction treatment x farm 1 (F1), farm 2 (F2), farm 3 (F3) and farm 4 (F4) (lower panel), reared under commercial farms conditions. * and** indicate significant differences between groups, within month (P ⩽ 0.05 and 0.01, resp.).

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