Effects of pregnancy and lactation on thyroid hormones, insulin, and metabolic blood parameters of modicana dairy cows

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SUMMARY

Pregnancy and lactation induce endocrine and metabolic adaptations in dairy cows with the redirection of nutrients towards the fetal growing and milk production. Thus, the aim of the present study was to evaluate the effects of different physiological stages (before insemination: non-pregnancy), of gestation (<25, 26-100,>100 days), and lactation (<60, 61-120, 121-180, 181-240, and >240 days) on thyroid hormones, insulin, and metabolic blood parameters in Modicana cows under a dairy semi-intensive management. Blood samples were in a one-year period from 10 healthy multiparous Modicana cows to measure circulating thyroid stimulating hormone (TSH), total and free triiodothyronines (T_3, fT_3) and thyroxines (T_4, fT_4), insulin, glucose, triglyceride, and total cholesterol concentrations. The gestational phase showed higher T_4 at <25 and >100 d than non-pregnancy ($P < 0.01$), higher insulin at 26-100 d than the rest of pregnancy and non-pregnancy ($P < 0.0001$), and lower glucose concentrations at >100 d than non-pregnancy ($P < 0.007$). During lactation, the lowest insulin concentrations were found at <60 d and the highest at >240 d ($P < 0.02$), whereas the opposite trend was obtained for glucose ($P < 0.01$). The superimposed and significant increases of both T_4 (<25 and >100 d of pregnancy) and insulin (26-100 d of pregnancy) concentrations showed that these hormones are metabolically involved along this physiological period., and confirmed their role as growth-stimulatory hormones, having anabolic effects on fetal metabolism and increase cellular nutrient uptake and energy production for tissue accretion In addition, the highest concentrations of glucose at the start of lactation (>60) until 120 d, and the lowest values at the end, partially reflect the changes observed for insulin, confirming that glucose is the most important substrate for milk production and that insulin production and sensitivity is in part reduced for glucose uptake by peripheral cells, especially in the first part of lactation to mount the glucose uptake by the mammary gland. The assessment of breed-specific hormonal and metabolic changes allows to understand the adaptive response of local breeds that are not yet strictly selected for milk production but that could become.

KEY WORDS

Dairy cow; thyroid hormones; insulin; lactation; pregnancy.

INTRODUCTION

Thyroid hormones (THs) regulate a multitude of metabolic and cellular processes required for the physiological development of the placenta and fetus[1,2] and must be supplied by the maternal organism in the first months of pregnancy[3]. They regulate the energy metabolism and the balance among energy intake, expenditure and storage in specific target tissues[4]. Therefore, THs influence several metabolic pathways, including carbohydrate, protein, and lipid metabolism, thus increasing basal energy expenditure[5-7].THs also play a pivotal role in the development, maturation, and function of pancreatic cells[8].

On these bases, it is well known that THs increase fat mobilization thereby leading to increased concentrations of circulating fatty acids as well as to enhanced oxidation of them. THs stimulate insulin-dependent glucose uptake, and both gluconeogenesis and glycogenolysis. Hence, it possible to conclude that a peculiar feature of TH-dependent metabolic regulation is the acceleration of the rates of anabolic and catabolic activities[9].

Relevant knowledge about the pattern of THs metabolism and their role in ontogenetic development derived, for the most, from very old studies carried out in the ovine fetus and in the newborn models[3,10,11]. Moreover, few studies are available regarding bovine TH status during early pregnancy[12,13], but they were carried out on different breeds and originated very discordant data, making it difficult to find clear conclusions. For example, with regard to total thyroxine (T_4), some authors found similar concentrations in dairy cows at different reproductive stages[1], whereas other studies observed a slight decrease[14] or, instead, an increase along the pregnancy, with higher T_4 in pregnant than in open cows[15,16]. Among different endogenous factors, breed and physiological state are able to affect thyroid activity and circulating TH concentrations, acting at the level of hypothalamus, pituitary and/or thyroid gland, as well as on pe-

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ripheral monodeiodination[1,2], contributing to an extreme variability of the physiological range, which is of course very meaningful in each particular study.

As dairy cattle become more productive, it is important to study other traits to determine how they have responded to selection for yield. Among other traits of interest and importance are hormone concentrations in blood. The physiological pathways by which the hypothalamic-pituitary-ovarian axis is informed about the energetic status of the animal are complex, and involve several metabolites and hormones, such as THs and insulin[17]. A role of these hormones in regulating steroidogenesis has been reported[18], but data regarding their effect on reproductive function are limited and controversial[19]. Significant changes of T_4 and insulin were recently described, with higher values at the end of pregnancy than at >60-120 d or in non-pregnant cows. Along the lactation phase, T_4 initially decreased, reaching the lowest values at >60-120 d, and then increased until the end of lactation[16].

The increase in insulin concentration from peak to mid lactation was previously recorded, and correlation between insulin and milk production has been strong or slightly negative[17,20]. When peak and midlactation data were pooled for analysis, stage of lactation significantly affected also T_4 concentration, correlated negatively with milk yield[17]. These results may vary because hormone concentrations in ruminants are affected by many environmental factors.

During pregnancy, the maternal body also undergoes major adaptations in the systems regulating glucose homeostasis to cope with the increased demand for glucose, providing a constant supply across the placenta for the successful growth and development of offspring[21]. As part of these changes, insulin concentrations are elevated during pregnancy and lower in lactation; moreover, maternal tissues such as muscle and fat become relatively insulin-resistant, thereby impeding glucose uptake and favoring increased delivery of glucose to the fetus[21]. At the end of pregnancy and in early lactation, all dairy cows experience a transient state of a decreased response to insulin in the peripheral tissues[22]. This homeorhetic adaptation represents a mechanism to preserve a sufficient glucose supply for the fast-growing fetus and the mammary gland to ensure milk production[22].

The aim of the present study was to evaluate the plasticity of endocrine and metabolic responses of non-pregnant, pregnant, and lactating cows of Modicana dairy cows, a local breed reared in Sicily with a semi-extensive system.

MATERIALS AND METHODS

Animals and Breeding

The experimental protocol was approved by the Ethical Committee of the Department of Veterinary Science, University of Messina, Italy (code 041/2020). The research complied with guidelines of Good Clinical Practices (EMEA, 2000) and the Italian and European regulations on animal welfare (Directive 2010/63/EU).

The present study included 10 healthy multiparous Modicana dairy cows, randomly selected from a large group of 100 animals, bred under the traditional semi-extensive farming system in the same commercial farm located in Ragusa, Italy (36°53’47» N, 14°42’24.8» E, 500 mt above sea level). Animals were raised in accordance with an approved UE disciplinary method called “QS Sicilia”, which contributes to recovering agro-industrial by-products by including up to 10% of olive cake in dairy cow feed. For this reason, animals were fed with the same diet composed of *ad libitum* meadow hay and an average of 10 kg/head/day of concentrate integrated with 8% of dried and pitted olive cake (DM 95.6; CP 10.4; EE 15.9; NDF 49.4; ADF 39.4; ADL 23.1; ash 3.7; starch 1.5% as feed); the concentrate (5 kg/head/meal) was administered at 7:00 a.m. and 2:00 p.m. every day. Water was *ad libitum.* Pasture was available in spring and autumn (for a minimum of 6 h during daylight, from 8:00 a.m. to 2:00 p.m.), but not in summer. The indoor housing was a free-stall barn equipped with automatic system fans and sprinklers that were activated during the hot season.

Inclusion criteria for enrolled cows were: (i) a physiological cyclicity during the previous breeding seasons, (ii) the absence of reproductive diseases, and (iii) the absence of any systemic or local inflammatory process and/or related antibiotic or anti-inflammatory pharmacologic treatment within a month before the start of sampling and throughout the whole experimental period.

Enrolled animals were homogeneous for age (3.2 ± 1.8 years), body condition score (2.9 ± 0.3 at the time of the first sampling), lactation stage (40 ± 22 d at the time of the first sampling), and average milk production (15 ± 2 kg/head/day). The non-pregnant phase was defined as the time interval between parturition and the following conception. All included cows were inseminated and became pregnant at about 71-165 d of lactation.

Samples

The whole sampling was carried out over the course of one year, from February 2021 to February 2022. At the time of the first sampling, all the cows were at 40 ± 22 d of lactation. Blood sampling was carried out at the same time point (from 7 a.m. to 8 a.m., before total mixed ration distribution) through venipuncture from the jugular into 10 mL tubes containing clot activator and separating gel (Terumo Corporation, Tokyo, Japan,). Blood samples were centrifuged for 10 min at 2000 *g*; the supernatant serum was collected and stored at -20 °C until analyses.

Serum thyroid stimulating hormone (TSH), total and free triiodothyronines (T_3, fT_3) and thyroxines (T_4, fT_4), insulin, and glucose concentrations were assessed using a human homologous solid-phase, two-site chemiluminescent immunometric assay (Immulite® 2000, Siemens Medical Solutions, Diagnostics, Erlangen, Germany), according to the manufacturer’s instructions. All assays were validated for linearity using cows’ serum prior to use. The intra- and inter-assay coefficients of variation (CVs) were the following: for TSH, 5.5% and 9.5% at TSH concentrations of 0.2 and 2.35 ng/mL; for T_3, 12% and 5.5% at T_3 concentrations of 73 ng/dL and 171 ng/dL; for fT_3, 9.1% and 5.4% at fT_3 concentrations of 3.2 pg/dL and 13 pg/dL; for T_4, 11.1% and 5.6% at T_4 concentrations of 1.8 g/dL and 16 g/dL; and for fT_4, 3.0% and 10.2% at fT_4 concentrations of 4.82 ng/dL and 0.51 ng/dL, 1.56% and 4.07% at insulin concentrations of 16.54 and 45.804 IU/mL. The sensitivity of the assay was 0.01 ng/mL for TSH, 19 ng/dL for T_3, 1.0 pg/mL for fT_3, 0.3 μg/dL for T_4, 0.11 ng/dL for fT_4, and 0.5 μIU/mL for insulin concentrations.

Serum glucose, triglycerides, and total cholesterol were assessed by automated spectrophotometry (BT 3500, Biotecnic Instruments S.p.a., Roma, Italy) using the colorimetric enzymatic method by GOD/POD/PAP, CHOD/POD/PAP, and

GPO/POD/PAP kits for glucose, total cholesterol, and triglycerides dosage, respectively.

2.4. Statistical Analyses

The software used for the statistical analyses of the data was JMP®, Version 16 (SAS Institute Inc., Cary, NC, USA). Appropriate descriptive statistics were generated for all analysed variables. Prior to analyses, data were subject to normality and homoscedasticity by Kolmogorov-Smirnov or Levene's test and logarithmic transformations were applied where necessary. ANOVA and post hoc Tukey-Kramer tests were used to identify significant ($p < 0.05$) differences among the different 60-day phases of lactation and pregnancy. The correlation between all the variables was expressed by Pearson's correlation coefficient (r).

RESULTS

Pregnant and Non-Pregnant Dairy Cows

Table 1 reports circulating thyroid-stimulating hormone (TSH), total and free triiodothyronines (T_3, fT_3) and thyroxines (T_4, fT_4), insulin, glucose, triglyceride, and total cholesterol concentrations of non-pregnant cows and along the first half of pregnancy. The blood analytes that resulted significantly affected by the pregnancy phase were also represented in Figure 1.

T_4 concentrations were significantly higher at 0-25 and >100 d than in non-pregnant animals (P = 0.0193, Figure 1A). Pregnant cows showed a constant trend of TSH and T_3 concentrations from 0-25 d of pregnancy to >100 d, with the highest values in nonpregnant cows (P = 0.1588 and 0.6104, respectively). Higher, but not significant, fT_3, fT_4 and total cholesterol concentrations were observed at 26-100 d than the rest of pregnancy and non-pregnancy period (P = 0.9919, 0.8384, and 0.8135, respectively). Circulating triglycerides concentrations showed a constant trend in both pregnant and nonpregnant cows (P = 0.9538). Pregnant cows also showed significantly higher insulin concentrations at 26-100 d than the rest of pregnancy and non-pregnancy (P = 0.0001, Figure 1B), and lower glucose concentrations at >100 d than non-pregnancy (P = 0.0075, Figure 1C).

Non-pregnant dairy cows showed significant and positive correlations between T_3; T_4 (r = 0.5328; P = 0.040), fT_3; T_3 (r = 0.54; P = 0.002), fT_4: T_4, and T_4: glucose (r = -0.5216; P = 0.0461). Pregnant dairy cows, instead, showed a significant and positive correlation between fT_4 and fT_3 (r = 0.7798; P = 0.0006).

Lactating Phases

The circulating TSH, T_3, fT_3, T_4, fT_4, insulin, glucose, triglycerides, and total cholesterol concentrations of lactating cows are reported in Table 2. The graphical representation of the variables significantly affected by the lactation phase can be found in Figure 2.

A variable but not significant trend was observed for THs along the whole lactation. Modicana cows showed a constant trend of TSH from 0-240 d, with the lowest values at >240 d of lac-

Table 1. Mean values ± standard deviation of serum parameters assessed in Modicana cows at different pregnancy phases.

Gestation phase	Non-pregnant	0 - 25 d	26 - 100 d	> 100 d	P-value
Glucose (mg/dl)	57.87±6.50	50.83±4.58	52.50±6.95	46.80±5.63	**0.008**
Insulin (mUI/ml)	0.60±0.19	0.78±0.08	1.12±0.05	0.60±0.14	**0.0001**
Triglycerides (mg/dl)	18.40±2.16	18.17±2.40	18.00±3.41	18.80±2.05	0.95
Total cholesterol (mg/dl)	143.53±47.64	145.67±36.91	148.00±28.52	126.20±31.57	0.81
TSH (ng/ml)	0.16±0.06	0.11±0.04	0.10±0.04	0.11±0.06	0.16
T_3 (ng/dL)	73.32±13.73	62.42±20.11	69.88±21.89	63.98±27.79	0.61
fT_3 (pg/ml)	2.11±0.55	2.10±0.59	2.16±0.44	2.05±0.86	0.99
T_4 (mg/dl)	3.81±0.88	5.30±1.29	4.51±1.23	5.33±1.39	**0.02**
fT_4 (ng/ml)	1.04±0.31	1.15±0.60	1.22±0.35	1.10±0.38	0.84

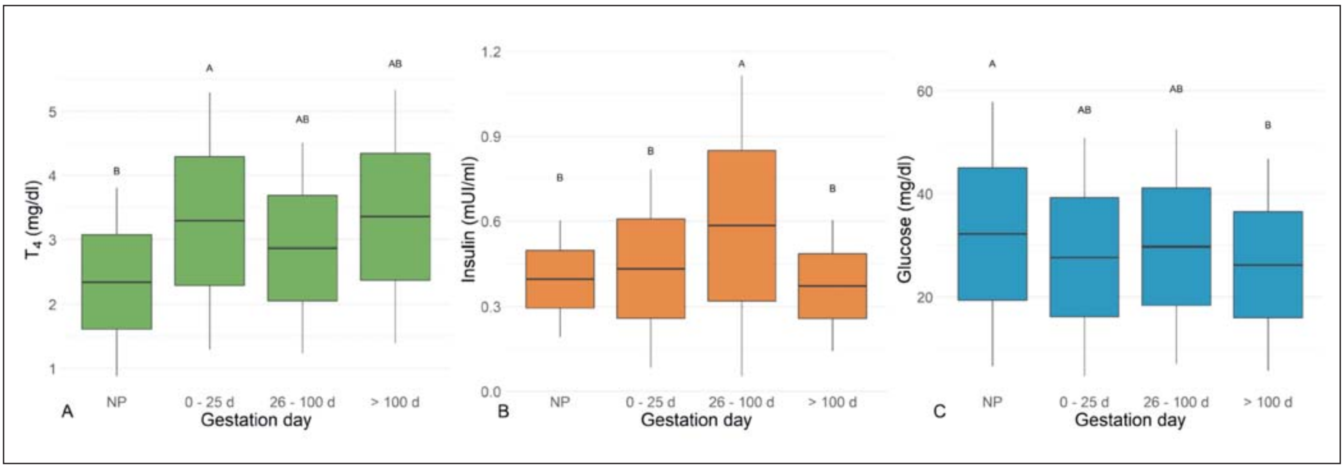

Figure 1 - Boxplots of the blood parameters significantly affected by the gestation phase: T4 (A), insulin (B), and glucose (C).

Table 2. Mean values ± standard deviation of serum parameters assessed in Modicana cows at different lactation phases.

Lactation phase	0 - 60 d	61 - 120 d	121 - 180 d	180 - 240 d	> 240 d	P-value
Glucose (mg/dl)	59.14±6.47	57.33±6.02	51.11±5.13	49.44±8.50	50.25±3.20	**0.02**
Insulin (mUI/ml)	0.58±0.17	0.88±0.17	0.73±0.17	0.73±0.28	1.12±0.00	**0.03**
Triglycerides (mg/dl)	18.29+2.50	17.44±2.13	18.11±3.10	18.56±3.94	19.75±2.36	0.77
Total cholesterol (mg/dl)	130.14±56.51	153.00±36.18	141.78±45.05	150.78±37.35	154.50±68.38	0.85
TSH (ng/ml)	0.17±0.06	0.12±0.04	0.13±0.07	0.11±0.06	0.09±0.05	0.17
T_3 (ng/dL)	72.24±9.37	81.34±14.26	68±19.26	62.26±30.77	63.93±17.78	0.35
fT_3 (pg/ml)	2.08±0.42	2.18±0.35	2.31±0.61	1.69±0.58	2.17±0.91	0.20
T_4 (mg/dl)	3.76±1.09	4.75±1.48	4.47±0.62	4.99±1.50	5.14±0.80	0.27
fT_4 (ng/ml)	1.05±0.44	1.27±0.34	1.10±0.29	1.06±0.61	1.57±0.43	0.21

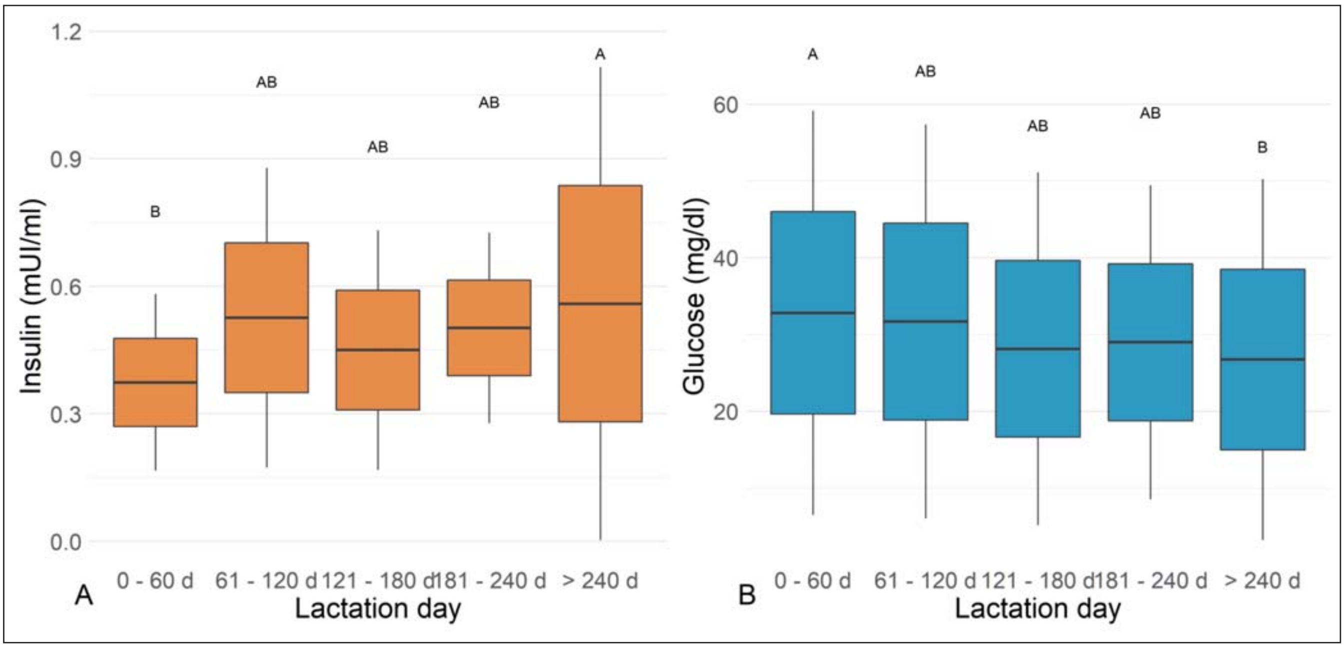

Figure 2 - Boxplots of the blood parameters significantly affected by the lactation phase: insulin (A) and glucose (B).

tation (P = 0.1739); a tendency of T_3 concentrations to increase from 0 to 120 d, with a constant lowest trend in the following phases (P = 0.3467); an opposite trend was observed for T_4 concentrations, with the lowest values at 0-60 d and the highest at >240 d (P = 0.2684); circulating fT_3 and fT_4 concentrations were variable along the whole lactation as well (P = 0.1971 and 0.2603, respectively). Similarly, triglycerides and total cholesterol were not significantly affected by the lactation phase (P = 0.7725 and 0.8549, respectively), even if the highest values were found at >240 d for both of them.

Significant lowest insulin concentrations were found at <60 d and the highest at >240 d (P = 0.0282, Figure 2A), whereas the opposite trend was obtained for glucose (P = 0.0150, Figure 2B).

Lactating dairy cows showed significant correlations between T_4: T_3 (r = 0.3647; p = 0.0244), T_3: fT_3 (r = 0.3872; P = 0.0163), T_4: fT_4 (r = 0.5121; P = 0.001), and T_3: glucose (r =0.4306; P = 0.0070).

DISCUSSION

The results obtained from the Modicana cows enrolled in the present study for serum THs, glucose, insulin, and lipid concentrations were in line with those recorded for bovine species by different authors[23-25].

In particular, T_4 concentration peaked in the first 25 days of pregnancy and then tended to decrease; however, the lowest values were observed in non-pregnant cows. This might happen as a consequence of the consistently increased metabolic rate of the mother, mirroring the increasing demands for THs aimed at neonatal development during a phase in which the embryo/fetus lacks its own functional thyroid tissue and is, therefore, dependent on maternal TH supply[3]. It is, in fact, well known that fetuses of ruminants synthesize endogenous THs only from the 2nd half of pregnancy[26,27].

Our results support that the THs have an active and pivotal metabolic effect, as previously recorded in pregnant goats[28], camels[29], mares[30,31], donkeys[32], and frequently in cosmopolitan dairy cows[16], suggesting their essential role as being part of a generalized development rather than a result of any specific developmental function. In addition, it is possible to presume that the regulation of THs originating from the mother potentially plays a role in placental development and function, influencing the fetal development, both at the beginning of pregnancy (<25 d) and again at >100 d, ensuring both substrate utilization and energy balance, as previously observed in goats[33]. The prevailing high metabolic priority is expected to be related to guarantee maximal placental growth, differentiation, and vascularization during the early phase of pregnancy, but also during the advancing of pregnancy (>100 d) when the development of production-oriented tissues, such as muscle, occurs. Moreover, other additional explanations may be related to the development of placentomes in cows, which are present at 40-60 d, and the placenta expansion, which occurs during the first half of gestation[34]. Recently, the report of Steinhauser et al.[2] carried out on sheep described a variety of TH transporters that may be present in the placenta, moving and transporting different forms of THs. On these bases, it is hypothesized that the abundance of T_4 may play a key role in protecting the fetus from deficiencies of THs over the first period of gestation.

The breed may play an unknown but physiologically important role during the different pregnancy periods, presumably due to innate endocrine and metabolic differences, contributing to guarantee the homeostatic responsiveness[35]. This suggests that some cows may innately have higher circulating concentrations of THs and/or be able to better maintain thyroid hormone levels during early pregnancy, making them more suited to support the normal growth of the fetus while it is not able to synthesize endogenous THs[26,27].

Circumstantial evidence suggests that fT_4 is the major secretory product of the thyrocyte and circulating fT_3 mainly comes from 5'deiodinase activity in peripheral tissues[36]. It is therefore feasible that the non-significant changes of both fT_3 and fT_4, but also the constant trend of T_3, observed in pregnant cows along different periods could be due either to the homeostatic alternation of peripheral deiodinases' activities approaching the pregnancy or to their constant but dynamic secretory synthesis, as corroborated by the existence of a significant and positive correlation between fT_3 and fT_4. With respect to the absence of significant differences in total and free iodothyronines along the different lactation phases, the significant positive correlations between T_3:fT_3 and T_4:fT_4 values observed in lactating cows are consistent with other physiological periods, such as growing, pregnancy, and non-pregnancy, reporting that changes of total iodothyronine concentrations often follow those of the free forms[28,37]. These active metabolic priorities were corroborated by the existence of a significant negative correlation between T_4 and glucose in non-pregnant cows, and positive between T_3 and glucose in lactating dairy cows, acknowledging the active metabolic role of THs. Thus, the diminished or increased energy intake in both non-pregnant or pregnant and lactating dairy cows could be due to different THs' sensitivity, involved in the regulation of metabolic effects.

With regard to the analyzed energetic substrates, Koch et al.[38] observed in Holstein dairy cows a shift in substrate utilization, from fat to glucose, that might contribute to reducing circulating glucose concentrations along the late pregnancy and early lactation, specifically at three weeks before and after parturition; this metabolic change, with a consequent decrease of endogenous heat production, preserves the hepatic gluconeogenesis for fetal growth as well as maturation for the resting pregnancy. Even though temporally different, a similar metabolic condition was also observed in Modicana dairy cows around mid-gestation (>100 days), thus confirming a homeorhetic adaptation to the advanced of gestation, characterized by a reduced glucose utilization; this trend may temporarily change the metabolic requirements to cope with an intensive lactogenesis/galactopoiesis phase, represented in early lactation by a significant glucose increase just at <60 d. Likewise, the evidence of the higher insulin concentrations recorded at 26-100 d of pregnancy than all the other examined pregnancy and non-pregnancy phases, is in line with its marked excite-anabolic roles, when the metabolic T_4 role resulted poorly represented. It is then reasonable to assume that, taken together, the significantly increased involvement of both T_4 (<25 and >100 d of pregnancy) and insulin (26-100 d of pregnancy) suggest their metabolic contribution throughout the whole physiological period. So, on this basis, it is possible to presume that insulin would act as an «anabolic effect» at the time when T_4 is low.

On the other hand, in non-pregnant cows, the existence of significant and positive correlations between T_3:fT_3, T_4:fT_4, fT_3:fT_4, and T_4:T_3 showed the involvement of total and free THs in baseline energy expenditure conditions, obtained activating the carbohydrate, protein, and lipid metabolism. Specifically, at the end of pregnancy and approaching the lactation, dairy cows generally showed a reduced sensitivity to insulin effect in the peripheral tissues, preserving a sufficient glucose store for the fast-growing both of fetus and mammary gland tissues[21,39]. Partially in line with literature data, it is possible to presume that these tissues use most of the available glucose over the remainder of pregnancy, as confirmed by its lowest concentrations recorded at >100 d. Nevertheless, approaching the lactation, the mammary gland of Modicana cows probably appears protected and/or less sensitive to insulin effects, as supported by the significantly highest glucose concentration just at <60 d of lactation, with concomitant lowest insulin concentrations at the same time. This glucose increase confirms that during early lactation, gluconeogenesis and glycogenolysis are typically increased to provide glucose for milk lactose production[40,41]. Moreover, the low insulin concentration observed in this first phase of lactation probably favors the partitioning of nutrients between mammary and non-mammary tissues in a period of great energy utilization and reserve mobilization for the start of milk production, thus reducing the possible problems caused by nutrient deficiencies in body tissues. It must also be noted that, during lactation, the water metabolism to the mammary gland through the vascular system is physiologically increased, thus causing possible hemodilution of the insulin, as previously observed in lactating cosmopolitan dairy cows and ewes for many hormonal, hematological, and biochemical parameters[16,42].

Taken together, these homeorhetic adaptations in early lactation confirm that glucose is the most important substrate for milk production[22] and the most essential fuel and precursor for both immune cells and mammary epithelial cells[43], and that insulin is a trigger of glucose uptake by peripheral cells. Hence, it is possible to conclude that the prioritization of mammary supply during early lactation is a physiologic principle in all mammals. Moreover, as previously recorded by Bossaert et al.[44], it is well known that the insulin-independent glucose utilization by lactating mammary gland leads to greater glucose clearance, supporting the related nutrient fluxes to the mammary gland[45,46], making difficult to provide clear conclusions about peripheral insulin sensitivity.

CONCLUSIONS

In this study, we added knowledge on dairy cows' endocrine and metabolic patterns, showing dynamic and physiological crosstalk between functional periods and related adaptive responses in this peculiar podolian-derived breed, not comparable in environmental, productivity and genetic conditions with other highly productive dairy cows. The genetic selection of cosmopolitan dairy breeds carried on in the last 30 years has primarily focused on prioritizing milk production over other physiological functions, thus exacerbating the adaptative metabolic changes occurring during milk synthesis and secretion[39]. This fact contributed to extreme variability of physiology of pregnancy and lactation, which accounts for the frequently not comparable data obtained from different breeds of the same species.

Modicana's milk production can be considered good in terms of quality, when compared with other dairy cow breeds, but low in terms of yield. However, when the breeding environment is taken into consideration, Modicana cows result rather productive despite the high utilization of poor pastures and by-products. To study local breeds adapted to particular conditions even from a physiological point of view can help optimize their management as well as better understand the mechanisms that promote optimal pregnancy and lactation.

Our results aim to encourage further research on these main topics, for developing genetic improvement and improving environmental conditions where Modicana is reared, which could be a useful biodiversity in relation to climate change and its ability to adaptability.

Acknowledgements

The authors wish to thank Azienda Agricola Cilone and the responsible Rosario Tumino for guesting the in-field trials.

Funding

This study was funded by P.O. FESR SICILIA 2014/2020. Obiettivo Tematico 1-Ricerca, Sviluppo Tecnologico e Innovazione Obiettivo specifico 1.1-Incremento dell'attività di innovazione delle imprese Azione 1.1.5-Sostegno all'avanzamento tecnologico delle imprese attraverso il finanziamento di linee pilota e azioni di validazione precoce dei prodotti e di dimostrazione su larga scala. Project BIOTRAK. Grant number 08SR1091000150 - CUP G69J18001000007 (Principal investigator: Prof. Luigi Liotta).

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