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Original article

Serum paraoxonase 1 (PON1) activity and lipid metabolism parameters changes in different production cycle periods of Holstein-Friesian, Polish Red and Norwegian breeds

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Abstract

We investigated the measurement of paraoxonase 1 (PON1), as a potential marker of redox state changes in dairy cows, its involvement in lipid metabolism and compared it with superoxide dismutase (SOD) activity changes. We also evaluated lipid metabolism parameters associated with dairy production. PON1 paraoxonase and arylesterase acitvities, SOD activity, beta-hydroxybutyrate (BHB), uric acid (UA), high density lipoprotein (HDL), low density lipoprotein (LDL), cholesterol and triglyceride concentrations were measured in Holstein-Friesian, Polish Red and Norwegian breeds serum in two production cycles. Our data showed a significant postpartum depletion in PON1 activity and lipoprotein and lipid products concentrations, with elevated BHB values. However, there were no significant changes in SOD activity and uric acid concentrations in Holstein-Friesian and Polish Red breeds after calving. At lactation peak there was a significant SOD activity decrease correlated with standardized PON1 activity depletion in all examined breeds. The results suggest that PON1 might be a better parameter for minimal redox state changes in serum, shortly after labour in the examined breeds.

Key words: PON1, oxidative stress, dairy cows

Introduction

Paraoxonase 1 (PON1) is a calcium dependent esterase associated with apolipoprotein A-1 (apoA-1) in high density lipoprotein (HDL) (Blatter et al. 1993, Gugliucci et al. 2013). Its measurements could be a useful tool in monitoring antioxidative status in Holstein-Friesian cows in production cycle periods (Turk et al. 2005, Antoncić-Svetina et al. 2011). Previous studies shown a significant decrease of PON1 activity towards phenyl acetate 4-8 days after parturition in comparison to a dry period, with lowered total choles-

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terol and triglyceride concentrations. However, data obtained from those animals indicated a beta-hydroxybutyrate concentration increase in contrast to PON1 activity depletion. PON1 activity towards phenyl acetate significantly decreased but paraoxonase activity depletion had no significance (Kulka et al. 2014). Synthesized in the liver, PON1 has hydrolytic properties and an ability to hydrolize several organophosphates (Draganov and La Du 2004). Human and rabbit enzyme polymorphism has an influence on different serum paraoxonase activities in the population (Watson et al. 2001, Mahrooz et al. 2014). PON1 has protective properties against oxidative stress, thus playing an important role in many diseases and metabolic changes involving generation of reactive oxygen species (ROS). Paraoxonase activity changes were found in human atherosclerosis, diabetes and familial hypercholesterolemia (Mackness et al. 2002, Van Himbergen et al. 2005, Soran et al. 2009, El-Lebedy et al. 2014). This enzyme has an ability to protect low density proteins (LDL) against oxidation, which occurs during intravascular wall plaque development in atherosclerosis. An in vitro experiment with inactivated purified PON1, showed an increased production of oxidized LDL (ox-LDL) particles (Aviram et al. 1998), whereas marked attenuation of this process was seen in the presence of human HDL (Sangvanich et al. 2003). It is possible that PON1 possesses two separate active sides; one responsible for its esterolytic activity (ester lipid subtrates) and the second for hydroperoxide reduction. The first one is regulated by the oxidative cell status. In experiments with Cu^{2+} induced oxidation, diminished PON1 hydrolyzing activity was observed. Moreover, the esterolytic activity was affected by chelating factors, EDTA or citrate; hydroperoxide activity was, however unchanged (Karabina et al. 2005). PON1 is also treated as a negative acute phase protein, whose concentration is reduced during the inflammation process. Lipid peroxidation is correlated with the acute phase response (Steinberg 1997). During diabetes mellitus patients had a higher concentration of lipid hydroperoxides, whereas PON1 activity decreased (Ferretti et al. 2004). The periparturient period in dairy cattle is a time of very intensive metabolic changes, to which oxidative stress contributes (Bionaz et al. 2007). Furthermore, a negative energy balance which could appear around this nevralgic point of milk production in high yielding dairy cows could enhance the ROS concentration (Roche et al. 2000), thus leading to oxidative stress. The purpose of this study was to evaluate the measurement of serum PON1 as a potential marker of redox state changes in Holstein-Friesian cows and Polish Red native breed sera in different periods of the production cycle. We also examined PON1 changes in a Norwegian breed in which subclinical ketosis occurred.

Materials and Methods

Animals

Samples were taken from 17 clinical healthy Holstein-Friesian, 17 Polish Red dairy cows (native breed) in the 1st and 2nd lactation cycle and a Norwegian breed (12 subjects) in the 1st lactation. Average milk production of a Holstein-Friesian was 10500 kg of milk in the 1st and 9800 kg in the 2nd lactation. The Polish Red dairy cows had an average milk production of 3500 kg in the 1st and 3600 kg in the 2nd production cycle. The Norwegian breed had 6500 kg of milk in the 1st production cycle. The protocols in this study were approved by the Local Ethics Committee for Animal Experimentation of Warsaw University of Life Sciences. During the whole lactation period welfare, animal health and nourishment were monitored. The animals were fed using the TMR (total mix relations) system. The Holstein-Friesian cows were tested three times using Edmonson's Body Condition Score (BCS) (Edmonson et al. 1989), which is routinely used in high yielding dairy cows.

Blood sampling

The blood samples were taken from *v. jugularis externa* in volumes of 20 ml for EDTA-K2 (Collection Test tube; FL Medical s.r.l. Unipersonale, Italy) and 10 ml for clotting (Collection Test tube; FL Medical s.r.l. Unipersonale, Italy). Samples were taken 40-60 days before parturiton, 2-5 days postpartum and 35-50 days after labour in the lactation peak. Blood parameters were assessed after collection and serum was stored at -80°C until analysis.

Enzymatic activities

Paraoxonase activity was assayed using a slightly modified method described by Mackness et al. (1991) using a Shimadzu UV-1800 Spectrophotometer, Japan. 20 µl of serum was added to 800 µl of 100 mM Tris-HCl buffer pH 8.0 containing: 2 mM paraoxon (O,O-diethyl-O-p-nitrophenylphosphate, Sigma Chemical Co.) and 2 mM $CaCl_2$. The generation of p-nitrophenol was monitored at a wavelength of 412 nm at 25°C. The molar extinction coefficient used to calculate the rate of hydrolysis was 18.290 $M^{-1}cm^{-1}$. One unit of paraoxonase activity pro-

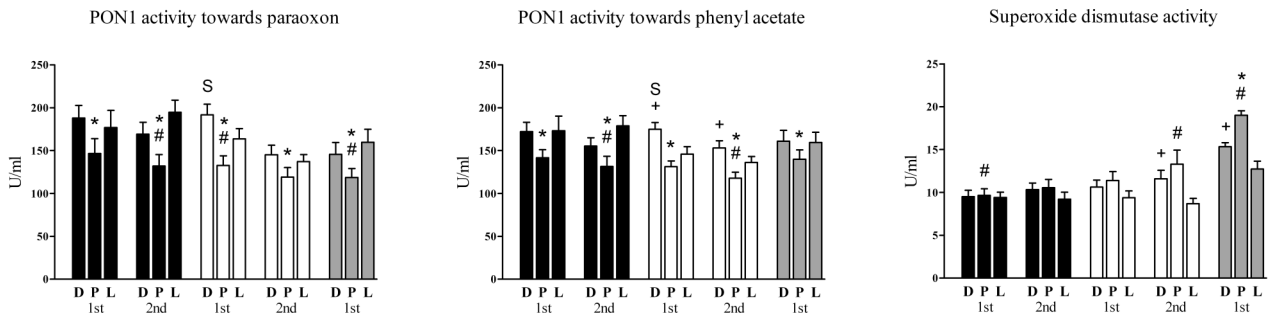

Fig. 1. Values are mean ± SD. Holstein-Friesian (black bars), Polish Red (white bars) and Norwegian (grey bars) breeds serum PON1 paraoxonase and arylesterase, superoxide dismutase activities in: dry period (D), postpartum (P), lactation peak (L) in two production cycles (1st and 2nd). Symbols indicate significant differences ($p<0.05$): * between postpartum and dry period, # postpartum and lactation peak, + between dry period and lactation peak, S a significant difference between 1st and 2nd production cycle in the same periods.

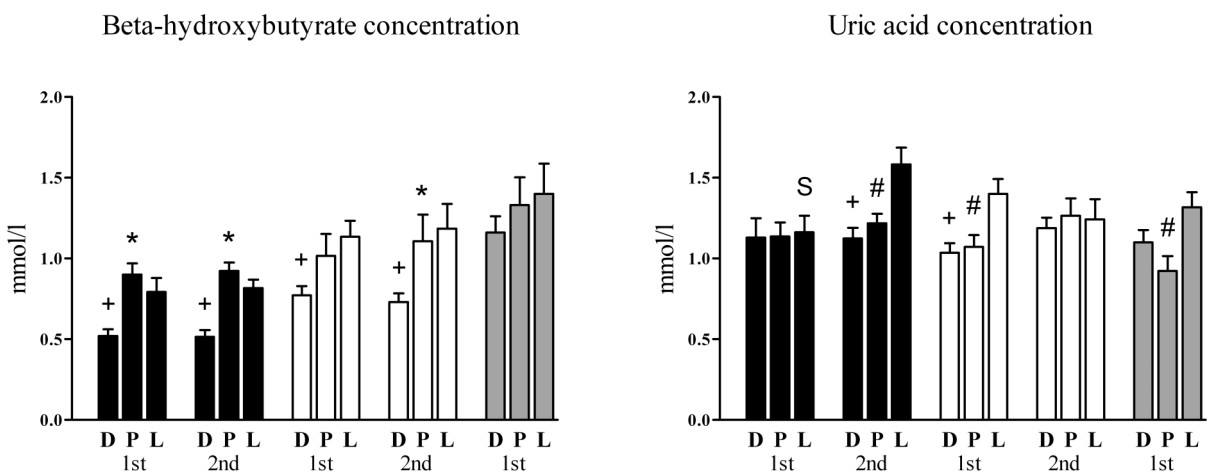

Fig. 2. Values are mean ± SD. Holstein-Friesian (black bars), Polish Red (white bars) and Norwegian (grey bars) breeds serum beta-hydroxybutyrate, uric acid concentrations in: dry period (D), postpartum (P), lactation peak (L) in two production cycles (1st and 2nd). Symbols indicate significant differences ($p<0.05$): * between postpartum and dry period, # postpartum and lactation peak, + between dry period and lactation peak, S a significant difference between 1st and 2nd production cycle in the same periods.

duced 1 nmol of p-nitrophenol per min. The blank sample (incubation mixture without serum) was run simultaneously to correct for spontaneous substrate breakdown. Activity towards phenyl acetate was measured in the reaction mixture (3 ml) containing 1 mM substrate and 2 mM $CaCl_2$ in 100 mM Tris-HCl buffer pH 8.0. After adding 10 µl of serum to the mixture the increase in absorbance at 270 nm was monitored for 1 min at 37°C. The results were expressed in U/ml; 1 U hydrolyzes 1 µmol of phenyl acetate/min. The molar extinction coefficient used to calculate the rate of hydrolysis was 1310 $M^{-1}cm^{-1}$. Superoxide dismutase (SOD) activity in the serum was assayed using a Superoxide Dismutase Assay Kit (Cayman Chemical Company, USA) and an Epoch Microplate Spectrophotometer (BioTek Instruments, Inc., USA).

Hematological and other biochemical analysis

Red and white blood cells and platelets were evaluated using an Abacus Junior Vet hematology analyzer (Diatron MI PLC, Hungary). Uric acid, beta-hydroxybutyrate, total cholesterol, LDL, HDL and triglyceride serum concentrations were assayed using a Pointe Scientific Kit (Pointe Scientific, Inc., USA) with a Miura One fully-automated clinical chemistry analyser (I.S.E. S.r.l., Italy).

Statistical analysis

Statistical analysis was performed using GraphPad Prism software 5.00 (GraphPad Software, Inc., USA).

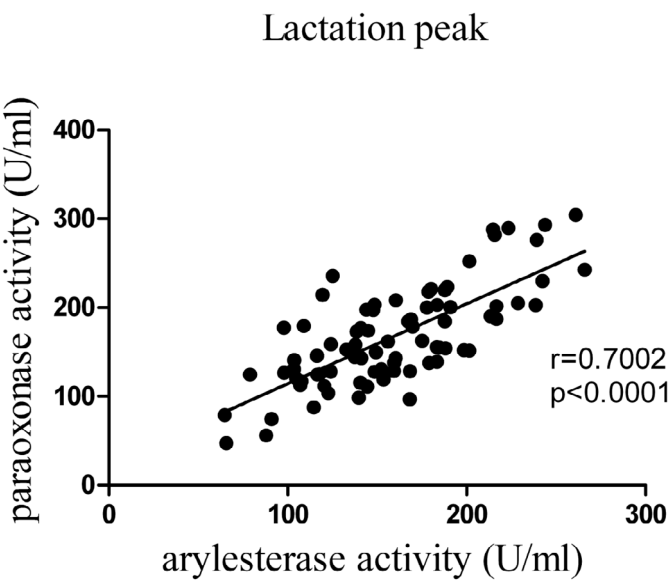

Fig. 3. Correlation between paraoxonase (U/ml) and arylesterase activity (U/ml) in serum of Holstein-Friesian, Polish Red and Norwegian cows in lactation peak.

All values were expressed as a mean with standard deviation (SD), and $p<0.05$ was considered as statistically significant. Statistics were performed using the Wilcoxon signed-rank test, Mann-Whitney U test and D'Agostino-Pearson omnibus normality test. The linear relationship between all pairs of our results were investigated using Spearman's rank – correlation analysis.

Results

Hematological parameters

All morphological blood parameters were within the reference values in all periods with no significant differences.

Body Condition Scoring

The Holstein-Friesian cows' BCS in the dry period and at the onset of lactation was 3.25±0.05. At the lactation peak the score was 3.0±0.1.

PON1 activity

The Holstein-Friesian breed had a significantly lower PON1 serum activity towards paraoxon and phenyl acetate 2-5 days postpartum in comparison to the dry period (approximately 22% lower) in both cycles and to the lactation peak (26% – 32%) in the 2nd production cycle. A similar situation occurred with the Polish Red breed and Norwegian cows, where PON1 activities towards both substrates were significantly depleted shortly after labour in comparison to the dry period, with the lowest arylesterase activity value in the Polish Red cows serum in the 2nd cycle. Polish Red serum arylesterase activity in the lactation peak significantly decreased in comparison to the dry period in both production cycles (Fig. 1).

The activity values in Holstein-Friesian were: towards paraoxon 178.69±57.77 U/ml, and towards phenyl acetate 163.78±42.16 U/ml in the dry period, 139.25±62.69 U/ml, 136.55±43.33 U/ml after labour and 186±69.50 U/ml, 176.01±58.88 U/ml in lactation peak. The activity values in Polish Reds were: towards paraoxon 168.54±52.31 U/ml, and towards phenyl acetate 146.47±41.21 U/ml in the dry period, 126.03±44.90 U/ml, 124.66±27.60 U/ml after labour and 150.44±42.92 U/ml, 141.15±31.56 U/ml in lactation peak. The PON1 activity values in Norwegian cow serum were: towards paraoxon 145.8±47.74 U/ml and towards phenyl acetate 161.0±44.23 U/ml in the dry period, 118.7±35.70 U/ml, 139.9±38.25 U/ml after labour and 159.9±52.03 U/ml, 159.6±40.92 U/ml in lactation peak. The overall activity values towards paraoxon were 169.4±55.26 U/ml, and towards phenyl acetate 163.5±39.56 U/ml in the dry period, 132.6±52.91 U/ml, 132±37.57 U/ml postpartum and 167±59.41 U/ml, 158.7±49.15 U/ml in lactation peak. Paraoxonase/arylesterase overall ratio in dairy cows (P/A ratio) was 1.1 in the dry period, 1.03 postpartum and 1.07 in lactation peak. Bovine paraoxonase and arylesterase activities were significantly correlated

Table 1. Serum PON1/HDL ratio of Holstein-Friesian, Polish Red, Norwegian breeds in 2 production cycles. Values are mean ± SD.

Breed	PON1/HDL ratio			
	Production cycle	Dry period	Postpartum	Lactation peak
Holstein-Friesian	I	55.33 ± 19.79[a,c]	72.11 ± 28.59[b]	40.77 ± 14.75
	II	62.77 ± 22.62	71.91 ± 31.06[b]	49.23 ± 20.40
Polish Red	I	64.33 ± 19.75[c]	63.68 ± 37.63[b]	43.75 ± 13.69
	II	49.08 ± 21.76[a]	64.54 ± 26.24[b]	41.19 ± 12.30
Norwegian	I	54.74 ± 28.84	61.96 ± 21.98[b]	43.43 ± 17.06

Letters indicate significant differences ($p<0.05$): a – between dry period and postpartum, b – between postpartum and lactation peak, c – between dry period and lactation peak.

Table 2. Dairy cow serum HDL and LDL concentrations in 2 production cycles. Values are mean ± SD, mmol/l.

Breed	HDL				LDL		
	Production cycle	Dry period	Postpartum	Lactation peak	Dry period	Postpartum	Lactation peak
Holstein--Friesian	I	3.57 ± 0.87[A]	2.00 ± 0.36	4.44 ± 1.09	2.58 ± 0.93[c,A]	0.92 ± 0.19[b,A]	2.78 ± 0.86[A]
	II	2.81 ± 0.73	1.89 ± 0.46	4.28 ± 1.08	1.42 ± 0.86[c]	0.66 ± 0.30[b]	1.83 ± 1.23
Polish Red	I	3.23 ± 1.1	2.36 ± 0.73	3.87 ± 0.81	2.02 ± 0.89[c]	1.10 ± 0.69[b]	1.77 ± 1.11
	II	3.02 ± 0.77	2.01 ± 0.49	3.47 ± 0.88	1.75 ± 0.82[c]	0.94 ± 0.51[b]	1.66 ± 0.93
Norwegian	I	2.87 ± 0.58	2.04 ± 0.63	3.85 ± 0.75	1.54 ± 0.81	0.95 ± 0.56[b]	2.07 ± 0.69

HDL concentration differences are all significant ($p<0.05$). Significant differences ($p<0.05$) in LDL concentrations are indicated by letters: b – between postpartum and lactation peak, c – between dry period and postpartum, A – between 1st and 2nd cycle.

in each period. Overall ($n=80$) significant correlation ($p<0.0001$) in the dry period was $r=0.6670$, at the onset of lactation $r=0.6397$ and in lactation peak $r=0.7002$ (Fig. 3).

Serum PON1/HDL ratio

There were significant differences in standardized PON1 activity (Bin Ali et al. 2003) between postpartum (the highest values) and lactation peak in all examined breeds. Significant differences were also measured between the dry period and at the onset of lactation in Holstein-Friesian and Polish Red cows. There is a correlation ($p<0.05$) between PON1/HDL ratio values and SOD activity in the 1st lactation peak in Holstein-Friesian, Polish Red and Norwegian breeds (Table 1).

Superoxide dismutase activity

A significant SOD activity decrease was observed in all examined breeds between the first week postpartum and the lactation peak. There was also a decrease in Polish Red and Norwegian sera collected in the lactation peak in comparison to the dry period. SOD values increased in postpartum in comparison to the dry period in Norwegian cows (Fig. 1). The data showed no correlation ($p>0.05$) in serum between SOD activity and PON1 paraoxonase and arylesterase activities in postpartum.

Beta-hydroxybutyrate concentrations

BHB concentrations significantly increased in postpartum and in the lactation peak, with the highest BHB levels in the Polish Red breed in the lactation peak – 1.185 mmol/l (Fig. 2). In Norwegian cows serum BHB values were 1.16 mmol/l in the dry period, 1.331 mmol/l after labour and 1.403 mmol/l in the lactation peak.

Uric acid concentrations

The data showed an increase in uric acid (UA) concentration, with the highest ($p<0.05$) values in the lactation peak in Holstein-Friesian 2nd (also higher than in the 1st) and Polish Red 1st production cycle (Fig. 2). In Norwegian cow serum there was a signifi-

Table 3. Bovine serum cholesterol and triglyceride concentrations in 2 production cycles. Values are mean ± SD, mmol/l.

Breed	cholesterol				triglyceride		
	Production cycle	Dry period	Postpartum	Lactation peak	Dry period	Postpartum	Lactation peak
Holstein--Friesian	I	5.06 ± 1.47^{a,A}	2.42 ± 0.5^{b}	6.12 ± 1.53	0.23 ± 0.13^{a}	0.07 ± 0.03	0.10 ± 0.04
	II	3.63 ± 1.29^{a}	2.19 ± 0.59^{b}	5.30 ± 1.73	0.18 ± 0.06^{a}	0.09 ± 0.05	0.10 ± 0.09
Polish Red	I	4.42 ± 1.56^{a}	2.92 ± 1.09^{b}	5.07 ± 1.17^{A}	0.20 ± 0.08^{a}	0.07 ± 0.05	0.08 ± 0.06
	II	3.76 ± 0.82^{c}	2.41 ± 0.65^{b}	4.11 ± 1.13	0.19 ± 0.11^{a}	0.10 ± 0.09	0,07 ± 0.05
Norwegian	I	3.48 ± 0.61^{a}	2.38 ± 0.75^{b}	4.66 ± 1.05	0.21 ± 0.06^{a}	0.10 ± 0.05	0.08 ± 0.05

Letters indicate significant differences ($p<0.05$): a – between dry period and postpartum and between dry period and lactation peak, b – between postpartum and lactation peak, c – between dry period and postpartum. A – between 1st and 2nd production cycle.

cant difference in uric acid concentration between postpartum and lactation peak.

HDL and LDL concentrations

All differences between periods in HDL levels are significant ($p<0.05$). HDL serum levels are higher in the 1st cycle in comparison to the 2nd production cycle. There was a significant depletion in LDL concentration after parturition and a significant increase between this period and lactation peak in both production cycles of Holstein-Friesian and Polish Red breed sera. The Holstein-Friesian serum LDL levels were significantly higher in all periods in the 1st cycle in comparison to the 2nd cycle (Table 2).

Cholesterol and triglyceride concentrations

There were significant differences between all the periods in cholesterol concentrations exept an insignificant difference ($p>0.05$) between the dry period and lactation peak in Polish Red breed 2nd cycle. Furthermore, Holstein-Friesian cholesterol serum levels were significantly reduced in the dry period between the 1st and 2nd production cycles. Triglyceride concentrations in both breeds were significantly reduced ($p<0.05$) after calving and in the lactation peak in comparison to the dry period. Results are shown in Table 3.

Discussion

The diminished PON1 activity in postpartum could be caused by a low oxidative status (Gaál et al. 2006). The elevated PON1/HDL ratio is a result of decreased HDL levels. The lowest HDL concentration as well as depleted cholesterol levels at that time are due to lipomobilisation syndrome occuring around the transition period (Mazur et al. 1988, Grummer 1993). Our data seems to confirm previous observations made by Turk et al. (2013, 2004) concerning postpartum PON1 activity decrease in Holstein-Friesian cows. Furthermore we noted a similar pattern occuring in Polish Red and Norwegian breeds.

Interestingly, Turk et al. (2013) demonstrated lowered PON1 activity and total antioxidative status (TAS) concentrations a week before labour, but only a PON1 significant decrease after calving, indicating that PON1 could be a better parameter for oxidative stress and negative energy balance than TAS (there were also no significant differences in postpartum TAS levels in our examined breeds – data unpublished).

In this study a representative of enzymatic antioxidant system SOD activity was evaluated. Serum SOD activity measurements showed no significant difference between the dry and postpartum periods (in contrast to SOD activity in hemolysate – data unpublished) in Holstein-Friesian and Polish Red cows, suggesting that PON1 might be an earlier indicator of serum minimal changes in oxidative status at the very beginning of the lactation stage. A postpartum serum SOD increase found in the Norwegian breed seems to support this hypothesis. SOD activity elevation might be a compensatory response to the presence of subclinical ketosis.

Subclinical ketosis is suspected when the serum BHB concentrations exceed 1.2 mmol/l according to some authors (Leblanc 2010, Suthar et al. 2013), or 1.4 mmol/l according to others (Raboisson et al. 2014). After calving in Holstein-Friesian and Polish Red cows, BHB levels significantly increased but their values seems to confirm no negative energy balance. In the Norwegian breed BHB values of 1.331 mmol/l after calving and 1.403 mmol/l in the lactation peak are associated with negative energy balance.

PON1 postpartum significant changes in para-

oxonase and arylesterase activities are present in all examined breeds, suggesting a decreased oxidative status presence in animals used in intensive and extensive dairy production. However, a postpartum PON1 activity decrease occurred in Holstein-Friesian cows with BCS 3.25 during the dry period and at the onset of lactation, and 3.0 values during lactation peak (Gugliucci et al. 2013). Bernabucci et al. (2005) observed an optimal proantioxidant state in animals with such BCS.

As lactation increases, several changes such as oxidative processes enhancement and compensatory response decrease take place (Bernabucci et al. 2005). Our data showed the lowest PON1/HDL ratios in lactation peak. Lower PON1/HDL was measured on the 63rd lactation day in comparison to the final week of dry period by Bionaz et al. (2007). Lowered SOD activity correlated with PON1/HDL ratio in all examined breeds seems to confirm low antioxidative capacity. Standardized PON1 activity (PON1/HDL ratio) could be inhibited by increasing oxidative stress (Antoncić-Svetina et al. 2011). As milk production increased to its peak, a significant elevation of UA concentrations was seen in comparison to postpartum. Higher serum UA levels are associated with increased levels of reactive oxygen metabolites (d-ROM) in humans (Ishizaka et al. 2014).

During the dry period an increase in non esterified fatty acids (NEFAs) is seen even in animals that received feed with predicted energy requirement. After calving, large amounts of NEFAs are released into the blood and mobilisation in the liver takes place (Bauchart 1993). In ruminants hepatic estrification exceeds a slow rate of triglyceride export as very low density lipoproteins. Lipid accumulation in the liver might lead to liver failure and fatty liver development (Van der Top et al. 2005). Cows have a slow, hepatic very low density lipoprotein (VLDL) secretion rate in comparison to nonrumiants, thus influencing triglyceride serum level, and therefore VLDL is proposed as the main (the most important) triglyceride carrier (Bauchart 1993). Our data confirmed a previous preliminary study (Kulka et al. 2014). In both production cycles in all breeds serum triglyceride concentrations significantly reduced in the postpartum period, with lower values in the next onset of lactation (45.1% – 52.3%). A decreased VLDL serum concentration could be an effect of mammary metabolism demands for an additional endogenous source of fatty acids (Bell 1995). A lower hepatic VLDL synthesis might reduce the amount of HDL particles produced by the liver and LDL serum levels (Mazur et al. 1988). Nascent HDL particles are formed by lipidation of apoA-1. The lower secretion of VLDL might stand for reduced LDL formation, by intravascular degradation process via intermediate-density lipoprotein (IDL) (Van der Top et al. 2005).

Total cholesterol concentrations were lower shortly after parturition in examined breeds due to being a negative acute phase reactant (-AP) (Bossaert et al. 2009). The decrease in the onset of lactation could be caused by many factors; one of them is sterol regulatory element-binding factor 1 (SREBF-1), responsible for HMG-CoA reductase mRNA synthesis rate and in this way synthesis of the mevalonate rate-limiting step in cholesterol formation (Shimano et al. 1999). SREBF-1 downregulation was noticed one weak after parturition, which might lead to lowering of cholesterol production (Gross et al. 2011). Reduced triglyceride with higher cholesterol concentrations in serum were found in Holstein-Friesian cows on about the 50th day of lactation (Kulka et al. 2014). Also, higher concentrations of cholesterol and HDL-C were found in lactating cows than in heifers (Antončić--Svetina et al. 2011).

Human and rabbit phenotypes show a characteristic trimodal pattern based on paraoxonase and arylesterase activities ratio (P/A ratio). Human genotypes were characterized by P/A ratio respectively: QQ with P/A ratio below 5.0, QR within 5-11 and RR with P/A over 11 (Nakanishi et al. 2003). Isoform PON1 R192 had higher paraoxonase activity than PON1 Q192. Analogical isotypes were found in New Zealand White rabbits based on P/A ratio respectively: $A \leq 2.2$, AB = 2.3-3.6, $B \geq 3.7$ (Watson et al. 2001). Our studies show no trimodal pattern in Holstein-Friesian, Polish Red and Norwegian breeds. There was a significant correlation between paraoxonase and arylesterase activity values in each period, with the highest value in the lactation peak. This might indicate that there is no polymorphism that can be distinguished by difference in P/A ratio in the studied serum samples, as well as no polymorphism or trimodal pattern was seen in Holstein-Friesian and Japanese Black cows (Miyamoto et al. 2005).

Both PON1 and SOD parameters are useful in obtaining good health assessment during milk production. Their activity changes were seen in the Norwegian breed due to subclinical ketosis. However, our data suggest that PON1 might be a better indicator of minimal redox state changes shortly after parturition in Holstein-Friesian cows and Polish Red native breed. PON1 might be a valuable marker used in antioxidative capacity diagnostics and for monitoring herd welfare.

Acknowledgments

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