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Serum and Hair Trace Element and Mineral Levels in Dairy Cows in Relation to Daily Milk Yield

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Abstract
The objective of the present study was to assess hair and serum trace element and mineral levels in dairy cows in relation to daily milk yield. A total of 70 healthy 5–6-year-old Simmental cows were divided into two groups ($n=35$) with high and low daily milk yield using median as a cut-off value. Hair and serum trace element and mineral content was evaluated using inductively coupled plasma mass-spectrometry. A nearly twofold difference in daily milk yield (43.8 ± 9.7 vs 21.3 ± 7.1 L/day, $p<0.001$) was significantly associated with 11% lower hair Cu ($p=0.043$) and 35% higher Se levels ($p=0.058$) content when compared animals with lower daily milk yield. Serum trace element levels were found to be more tightly associated with milk productivity in dairy cows. Particularly, serum levels of Se and Zn were found to be 73 and 35% higher in cows with higher milk productivity in comparison to animals with lower milk production, respectively. Serum Co levels also tended to increase with higher milk productivity. Serum minerals including Ca, Mg, and P were also found to be higher in highly productive cows by 6%, 14%, and 71%, respectively. The overall regression model based on serum trace element and mineral levels accounted for 38% of daily milk production variability. Generally, improvement of essential trace element and mineral supply, as well as prevention of copper overload in dairy cows, may be considered the potential tool for modulation of milk productivity.

Keywords Dairy cows · Milk productivity · Copper · Selenium · Trace elements

Introduction

Trace elements and minerals are known to play a significant role in the organism functioning through their regulatory, catalytic, structural, and signaling functions. In ruminants, deficiency of essential trace elements and minerals results in impaired growth and development, lower immunity, and higher susceptibility to contagious diseases [1]. Zinc deficiency was shown to cause altered growth curves, skin, and hair diseases in cattle [2], whereas copper deficiency was shown to be tightly associated with infertility, anemia, bone disorders, and cardiovascular diseases [3]. At the same time, excessive intake of essential trace elements like copper may also negatively affect dairy cattle health [4]. Therefore, monitoring and prevention of both deficiency and toxicity of essential trace elements are required for livestock health and high production [5].

Lactation is associated with higher requirements of the organism in micronutrients and trace elements [6]. Deficiency of certain trace elements including zinc [7] and selenium [8] was shown to be associated with lower milk yield and lower milk quality. In turn, earlier data demonstrate that trace element and/or mineral supplementation in dairy cattle may significantly increase milk production. Particularly, the results of multiple trials demonstrated a significant increase in milk production in response to Zn supplementation in

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dairy cows [9]. Similarly, Se supplementation was associated with higher daily milk yield in Holstein cows [10]. Recent findings also demonstrate that deficiency of essential minerals, especially Ca [11], P [12], and Mg [13], is also associated with impaired lactation and reduced milk yield. However, the existing data on the association between trace element and mineral status of dairy cows and milk productivity are rather contradictory. Moreover, the association between trace element and mineral status and milk productivity of dairy cows is not sufficiently studied.

Therefore, the objective of the present study was to assess hair and serum trace element and mineral levels in dairy cows in relation to daily milk yield.

Materials and Methods

The protocol of the present study was approved by the Local Ethics Committee, 2–13/04/2021 (Orenburg State University, Orenburg, Russia). A total of 70 healthy 5–6-year-old Simmental cows of the Ural type, cultivated by the nurse-cow technique in the Southern Ural region, were examined. Only animals with the weight of 610–640 kg (627 ± 15 kg) were involved in the study. All sampling procedures were performed in the lactation period. The animals were fed a similar diet during all periods according to the dietary regimen specified earlier [14]. Daily intake of essential minerals and trace elements (Supplementary Table 1) was evaluated based on the earlier published data on diet composition and trace element content of the dietary items [15]. Individual dietary intake of minerals and trace elements was not assessed as the cows were not handled individually.

Milk samples from the examined animals were obtained at milking stations with evaluation of daily milk yield. Based on the median values of milk yield the animals were divided into groups with high and low daily milk yield.

Hair samples (0.4 g) were collected from three sites in withers using ethanol-precleaned stainless steel scissors. Only brown-colored hair samples were collected in order to avoid the potential differences in trace element and mineral content in hair of different color. Only proximal parts of hair strands were used for subsequent analysis. Blood was collected from caudal vein using 6-ml Vaccuette® tubes (Greiner Bio-One International AG, Austria). The obtained blood samples were centrifuged at 1000 g (10 min) using ELMI CM-6 M (Latvia).

The obtained hair samples were washed with acetone and rinsed thrice with distilled deionised water (18 MΩ cm). After drying on air, the samples were introduced to HNO3-containing (Sigma-Aldrich Co., St. Louis, MO, USA) Teflon tubes and subsequently loaded into Berghof SW4 system (Berghof Products & Instruments, Eningen, Germany) for microwave degradation (20 min at 170–180 °C).

Serum samples were diluted (1:15; v/v) with an acidified (pH = 2.0) diluent containing 1% 1-Butanol (Merck KGaA, Germany), 0.1% Triton X-100 (Sigma-Aldrich, Co., USA), and 0.07% HNO3 (Sigma-Aldrich, Co., USA) in distilled deionized water (Merck Millipore, USA).

Hair essential trace element (Co, Cu, Fe, Mn, Se, Zn) and mineral (Ca, K, Mg, Na, P) levels were evaluated using inductively coupled plasma mass-spectrometry at NexION 300D (PerkinElmer Inc., Shelton, CT, USA) equipped with ESI SC-2 DX4 autosampler (Elemental Scientific Inc., Omaha, NE, USA). The system was calibrated using stock solutions from Universal Data Acquisition Standards Kit (PerkinElmer Inc., Shelton, CT, USA). Standard (10 µg/l) solutions of Yttrium-89 and rhodium-103 were prepared from Yttrium (Y) and Rhodium (Rh) Pure Single-Element Standard (PerkinElmer Inc.) and used for internal on-line standardization. The certified reference materials of hair (GBW09101, Shanghai Institute of Nuclear Research, Academia Sinica, China) and plasma (ClinChek® Plasma Control, lyophil., for Trace Elements, Recipe, Munich, Germany) was used for laboratory quality control with the recovery rates of 90–110%.

The obtained data were processed using Statistica 10.0 software (StatSoft, Tulsa, OK, USA). Assessment of data distribution normality was performed using Shapiro–Wilk test. Due to skewed distribution the medians and interquartile range (IQR) boundaries were used as descriptive statistics, as mean values do not provide adequate information upon non-Gaussian distribution. Medians were also used as cutoffs for grouping of animals according to milk productivity. After ln-transformation of the data, group comparisons were performed using one-way analysis of variance (ANCOVA) with subsequent Bonferroni adjustment. In order to reveal the association between milk yield and mineral/trace element levels in hair or serum multiple linear regression analysis was performed. The level of significance was set as $p < 0.05$ for all statistical tests.

Results

The median milk yield in the examined cows was 34.1 L day that was used as a cutoff. Dairy cows with higher milk productivity (above median) were characterized by a more than twofold higher daily milk yield as compared to those with lower productivity (43.8 ± 9.7 vs 21.3 ± 7.1 L/day, $p < 0.001$).

The difference in daily milk production was significantly associated with both hair and serum trace element levels (Table 1). Highly productive dairy cows had 11% lower hair Cu content when compared animals with lower daily milk yield. In turn, hair Se levels tended to be 35% higher in animals with higher milk productivity, although the difference

Table 1 Hair and serum trace element content in dairy cows with low and high daily milk yield

Element	Milk yield		Milk yield
	Below median (< 34.1 L/day)	Above median (> 34.1 L/day)	
Hair			
Co	0.017 (0.01–0.033)	0.024 (0.018–0.038)	0.479
Cu	9.41 (8.305–10.105)	8.385 (7.7–8.91)	0.043 *
Fe	49.06 (26.925–160)	56.215 (40.05–129)	0.404
Mn	2.595 (1.85–3.92)	2.555 (2.06–3.73)	0.453
Se	0.573 (0.45–0.715)	0.771 (0.569–0.878)	0.058
Zn	118 (109–129)	113 (103–134)	0.703
Serum			
Co	0.42 (0.3–0.54)	0.55 (0.41–0.68)	0.061
Cu	0.579 (0.462–0.767)	0.663 (0.565–0.797)	0.158
Fe	1.96 (1.22–2.71)	1.9 (1.48–2.67)	0.303
Mn	2.3 (1.9–2.9)	2.65 (2.2–3.1)	0.246
Se	0.037 (0.029–0.062)	0.064 (0.057–0.075)	< 0.001 *
Zn	0.664 (0.563–0.903)	0.899 (0.777–0.969)	0.001 *

Data are expressed as median and IQR; *significant group difference according to one-way ANOVA with Bonferroni adjustment

was only border-significant. Serum trace element levels were found to be more tightly associated with milk productivity in dairy cows. Particularly, serum levels of Se, and Zn were found to be 73 and 35% higher in cows with higher milk productivity in comparison to animals with lower milk production, respectively. In turn, serum Co levels also tended to increase with higher milk productivity, although the group difference was only nearly significant.

In contrast to trace elements, no significant group difference in hair mineral levels was observed in cows with low and high daily milk yield (Table 2). Despite the observation of nearly twofold higher hair Ca and Mg levels in cows with high milk yield, this difference was not considered significant due to high variability. At the same time, serum minerals including Ca, Mg, and P were also found to be higher in highly productive cows by 6%, 14%, and 71%, respectively.

Multiple regression analysis also demonstrated a significant association between both hair and serum trace element and mineral levels and milk productivity (Table 3). It has been demonstrated that hair Cu and Se levels were inversely and directly associated with daily milk yield, respectively. It is notable that hair Mn content also tended to be positively interrelated with milk productivity. Despite these associations, the overall model incorporating hair trace element and mineral levels did not have significant predictive value.

Table 2 Hair and serum mineral concentrations in dairy cows in relation to daily milk yield

Element	Milk yield		*p*
	Below median (< 34.1 L/day)	Above median (> 34.1 L/day)	
Hair			
Ca	1059 (795.5–2593)	2218 (1265–2916)	0.913
K	5347 (4159–6048.5)	5752 (4241–6840)	0.961
Mg	274.5 (219–569)	525.5 (269–638)	0.980
Na	1839 (1586–2491)	1642 (1434–2334)	0.295
P	262 (189–288.5)	266 (231–305)	0.151
Serum			
Ca	79.58 (70.78–85.47)	84.325 (78.73–88.27)	0.018 *
K	184 (162–247)	205.5 (191–240)	0.505
Mg	23.62 (19.44–27.08)	26.94 (25.42–29.21)	0.001 *
Na	3232 (3136–3485)	3124 (3006–3387)	0.172
P	140 (82.18–206)	240 (209–262)	< 0.001 *

Data are expressed as median and IQR; *significant group difference according to one-way ANOVA with Bonferroni adjustment

Table 3 Regression analysis of the association of trace element and mineral levels in hair and serum with daily milk yield

Element	Hair		Serum	
	β	p	β	p
Ca	−0.231	0.778	−0.123	0.623
Co	0.287	0.222	−0.122	0.411
Cu	−0.680	0.034 *	−0.726	0.039 *
Fe	−0.376	0.100	−0.239	0.170
K	0.215	0.531	0.104	0.613
Mg	−1.537	0.191	0.084	0.662
Mn	1.171	0.070	0.789	0.028 *
Na	−0.033	0.904	−0.028	0.881
P	0.058	0.854	0.213	0.427
Se	0.689	0.037 *	0.463	0.040 *
Zn	0.002	0.992	−0.057	0.743
Multiple R	0.580		0.737	
Multiple R^2	0.336		0.544	
Adjusted R^2	0.028		0.382	
p for a model	0.557		<0.001 *	

Data expressed as regression coefficient (beta) and the respective p value; *the association is significant at $p<0.05$

Similar to hair, serum Cu concentration was found to be significantly inversely associated with milk productivity in dairy cows in a model adjusted for all trace elements and minerals studied, although no significant group difference in serum Cu concentrations was observed. Serum Mn and Se levels were considered positive predictors of daily milk yield. At the same time, the overall model based on serum trace element and mineral levels accounted for 38% of daily milk production variability.

Discussion

The obtained data demonstrate that daily milk yield is associated with higher levels of essential trace elements and minerals in the organism. At the same time, hair and serum Cu levels were negatively interrelated with milk productivity in dairy cows.

Generally, the particular values of hair trace element content correspond to the earlier estimated reference limits for Hereford cows from the Southern Ural region [14]. At the same time, hair Cu levels in the studied sample of cows was found to be border-line higher when compared to the reference values of 3.0–7.5 µg/g, being indicative of higher risk of copper overexposure. The latter may be related to copper mining and smelting in the region, resulting in increased Cu levels in the environment [16]. A recent study demonstrated low Cu excretory capacity in cattle resulting in hepatic Cu accumulation [17] that may also aggravate Cu overload. Moreover, globally hepatic Cu levels were found to increase gradually during the last two decades (2007–2018) [18]. Being a redox metal copper is capable of induction of oxidative stress and inflammation [19]. Specifically, copper exposure and accumulation in liver was shown to be associated with hepatic oxidative stress markers including 4-hydroxynonenal and 3-nitrotyrosine levels in dairy cows [20].

Earlier data demonstrated adverse effects of copper exposure in dairy cows. Particularly, daily milk production was also inversely associated with milk Cu levels in Holstein dairy cattle [21]. Reduced milk production was also reported in cows exposed to excessive Cu levels from supplements [22]. Dairy cows from Cu-polluted area were characterized by the lowest milk yield when compared to unexposed animals [23]. Although feeding with increasing Cu doses did not have a significant impact on milk yield, 40 mg/kg Cu significantly increased serum cholesterol levels in Holstein cows as well as affected fatty acid content of milk [24]. It has been also proposed that increased blood and milk Cu levels may be associated with higher occurrence of mastitis and thus lower milk yield [25]. In turn, reduction of excessive Cu supplementation was shown to have beneficial health effect in female Jersey calves [26]. Therefore, reducing the risk of copper toxicity in cattle requires significant attention and efforts [27]. It is also notable that dietary molybdenum may significantly affect Cu toxicity in cattle through interference with Cu absorption [28], and evaluation of Mo intake and accumulation could be beneficial in assessment of biological effects of Cu in cows including alteration of milk production.

Of essential trace elements, selenium, zinc, manganese, and cobalt were found to be associated with higher milk productivity.

Selenium deficiency is considered a rather frequent disorder in ruminants, being associated with altered reproduction, lactation, and other adverse health effects [8]. In turn, a 16-week supplementation with selenized yeast resulted in a significant increase in milk yield in Holstein cows [10]. In another study Se supplementation was shown to increase milk PUFA levels, although no significant effect on milk yield was observed [29]. Se supplementation through Se-fortified forage significantly reduced milk somatic cell count in lactating dairy cows [30]. The positive effect of Se supplementation may be associated with increased antioxidant selenoprotein levels and certain immunological parameters [31], as well as reduced risk of mastitis under adequate Se status [32].

Higher zinc levels were associated with both increased daily milk yield, being in agreement with the observed role of zinc nutrition in cattle health and adverse effects of zinc deficiency [7]. Correspondingly, plasma Zn levels were found to be directly correlated with milk production in Zn-supplemented Holstein–Friesian lactating cows [33].

A summary of twelve trials demonstrated that Zn supplementation resulted in a significant increase in total, energy-corrected, and fat-corrected milk as compared to control animals [9]. In turn, supplementation with organic zinc chelates resulted in a significant increase in plasma Zn levels as well as significantly increased milk yield, antibody response, and rumen fermentation [34]. It is also notable that Zn supplementation significantly improves mammary epithelial barrier as assessed by occludin and E-cadherin expression [35]. An increase in milk yield along with reduction of milk amyloid A levels was also observed in Zn-supplemented dairy cows [36]. Beneficial effect of Zn may be at least partially mediated by the earlier demonstrated Zn-induced increase in estrogen, progesterone, T3 and T4 levels, as well as improved metabolic profile in Zn-deficient cattle [37].

In contrast to zinc and selenium, the existing data on the association between Mn and Co status and dairy cattle health as well as milk productivity are single.

Manganese deficiency in ruminants is known to be associated with infertility due to altered endocrine system [38]. Correspondingly, improvement of Mn status in dairy cattle is also associated with reduced incidence of reproductive disorders [39]. When supplemented along with Zn, Mn increased rumen fermentation, conversion ratio, as well as milk yield and milk quality in dairy Friesian cows [40].

The symptoms of Co deficiency in ruminants were largely attributed to low B12 status causing anemia [41]. Co deficiency is also known to be associated with oxidative stress and hyperhomocysteinemia [42]. Correspondingly, increased Co intake in dairy cows was associated with increased B12 levels in milk and liver without a significant effect on milk productivity [43]. In turn, improvement of B12 status was shown to prevent weight loss during lactation, as well as increase protein:fat ratio through improvement of energy metabolism [44]. Cobalt along with Cu, Zn, and Mn is also known to be a component of functional dietary supplements resulting in increased milk yield, milk protein, and fat levels [45].

Minerals, especially Ca, Mg, and P, were also found to be significantly associated with milk productivity. These findings corroborate earlier data on the essential role of mineral nutrition in dairy cows. Specifically, a positive correlation between serum Ca levels and milk yield was observed [46], whereas limited Ca intake during lactation was shown to reduce milk production [11]. Significant reduction in dietary P levels from 3.4 to 2.3 g P/kg in dairy cows resulted in a significant decrease in milk yield, milk protein levels, as well as plasma Ca concentrations [12]. However, an earlier study demonstrated a significant reduction in blood Ca and P levels in high-productive dairy cows, whereas blood Mg levels increased with milk yield [47]. Oral Mg supplementation in Mg-deficient cows resulted in a significant increase in milk production [48]. In turn, increased milk production is associated with higher Mg requirements [49]. Being in agreement with the results of the present study, increased K intake during lactation was shown to be associated with improved milk yield and fatty acid content [50].

Despite significant associations between hair and serum trace element levels with milk yield, the relationship for different samples was inconsistent. The latter may be mediated by different marker ability of blood serum and hair, with the latter being indicative of long-term status due to lack of homeostatic regulation of hair trace element levels and irreversible incorporation of the elements into hair matrix [51].

The study methodology has certain limitations. First, monitoring of individual intake of trace elements and minerals would be beneficial to estimate whether the observed associations are mediated by dietary factors. Second, additional information could be obtained from analysis of functional markers of trace element status including selenoprotein, hemoglobin, and ceruloplasmin levels for selenium, iron, and copper, respectively.

Conclusions

Generally, the results of the present study demonstrated that higher serum and/or hair levels of essential minerals (Mg, Ca, P) and trace elements (Co, Mn, Se, Zn) are associated with increased milk yield due to the role of the elements in ruminant health and lactation. In turn, higher serum and hair Cu content is associated with lower milk production in dairy cows through prooxidant and overall toxic effect of increased Cu levels. Therefore, improvement of essential trace element and mineral supply, as well as prevention of copper overload in dairy cows, may be considered the potential tool for modulation of milk productivity and quality.

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Author Contribution Elena A. Sizova (conceptualization, investigation, funding acquisition, methodology, data curation, formal analysis, writing–original draft), Sergey A. Miroshnikov (conceptualization, supervision, funding acquisition, validation, resources, writing–review and editing), Svetlana V. Notova (conceptualization, investigation, methodology, data curation, writing–review and editing), Olga V. Marshinskaya (formal analysis, investigation, writing–original draft) Tatiana V. Kazakova (formal analysis, investigation, writing–original draft), Alexey A. Tinkov (investigation, data curation, formal analysis, writing–original draft), Anatoly V. Skalny (conceptualization, supervision, validation, writing–review and editing).

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Availability of Data and Material Data will be made available on reasonable request.

Code Availability Not applicable.

Declarations

Ethics Approval The protocol of the present study was approved by the Local Ethics Committee, 2–13/04/2021 (Orenburg State University, Orenburg, Russia).

Conflict of Interest The authors declare no competing interests.

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