

The effect of duodenal infusion of histidine on milk yield, milk composition, and plasma amino acids in dairy cows*

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ABSTRACT

The objective of this study was to evaluate the effect of duodenal infusion of histidine on milk yield, milk composition, and plasma amino acids in lactating dairy cows. In the present experiment, three high-yield lactating Holstein cows fitted with duodenal closed T-shaped cannulas were used. The cows were allocated to two treatments: histidine deficient (control) and histidine supplemented (HIS). The experiment was divided into four periods of 7 d. Each period consisted of a 3-d preliminary period and a 4-d experimental period. A crossover design was used for the experiment. The cows were fed *ad libitum* a diet consisting of maize silage, lucerne hay, and a supplement mix. Dry matter intake did not differ ($P>0.05$) between treatments. Milk yield and the yields of protein, casein, and lactose were significantly higher in HIS in comparison with the control. The contents of protein, casein, fat, and lactose were not significantly different ($P>0.05$). The proportions of α -casein and β -casein did not show significant variations ($P>0.05$), but the κ -casein proportion was significantly higher ($P<0.01$) in HIS. The yield of each casein fraction in HIS was significantly higher compared with the control. No effect of duodenal infusion of histidine on the concentration of free amino acids in blood plasma was observed ($P>0.05$) except for histidine ($P=0.012$).

KEY WORDS: histidine, duodenal, milk, plasma, amino acids, fatty acids, dairy cows

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INTRODUCTION

Lysine and methionine have been identified as the first limiting and/or co-limiting amino acids (AA) for synthesis of milk and milk protein in dairy cows on maize-based diets (Rulquin and Delaby, 1997; Wu et al., 1997). Histidine (His) is the other AA that has been studied more extensively. Based on experiments with AA infusions, histidine has been identified as the first limiting AA in grass silage-based diets supplemented with cereal concentrates (Vanhatalo et al., 1999; Korhonen et al., 2000; Kim et al., 2001a) or it may be a limiting AA in dairy cows fed maize silage- and lucerne haylage-based diets that are metabolizable protein-deficient (Lee et al., 2012), although the average content of His in maize silage is similar to grass silage. According to Rulquin et al. (2001a), maize silage contains 2.05%-2.09% His digestible in the intestine (HisDI) and grass silage 2.02%-2.34% HisDI; this AA is not considered to be limiting for maize silage-based diets. Furthermore, in cows fed maize- and lucerne silage-based total mixed ration, milk yield and lactose yield increased and protein yield tended to increase when His was added to drinking water delivering 35 g d⁻¹ His post ruminally (Doelman et al., 2008). Post ruminal His infusion linearly increased milk yield, milk protein and lactose yields in dairy cows fed grass silage diets (Korhonen et al., 2000). These results suggest that the effect of histidine limitation in maize silage-concentrate diets is still unclear. Thus, the objective of the present study was to establish, based on changes in yield and composition of milk and plasma AA, the role of duodenally infused His as a possible third-limiting AA in milk production of cows fed a maize silage-concentrate-based diet.

MATERIAL AND METHODS

Animals and procedures

Three high-yield lactating purebred Holstein cows (mean liveweight 529 kg) in mid-lactation (110-113 days in milk) with similar milk production (27.2 kg; SEM=0.5) were used. The cows were housed in individual tie stalls bedded with sawdust. The animals were fitted with duodenal closed T-shaped cannulas (Bar Diamond, Inc., USA) and allocated to two treatments: histidine deficient (control) and histidine supplemented (HIS). The experiment was divided into four periods of 7 d. Each period consisted of a 3-d preliminary period and a 4-d experimental period. The design of the experiment was: in the first period, two cows were control (infusion of Glu-Na, Met, Lys and Leu) and one cow was experimental HIS (infusion of His, Met, Lys and Leu). In the subsequent period the cows were switched to the other treatment according to the crossover design by Ratkowsky et al. (1993).

The cows were fed individually twice daily at 7.00 a.m. and 5.00 p.m. *ad libitum* the diet based on maize silage, lucerne hay, and a supplement mix (Table 1). The diet was formulated to provide 100% of NEL (net energy of lactation) and 95% of PDI (protein digestible in the intestine) requirements (Sommer, 1994). Based on Rulquin et al. (2001a), the formulated diets were calculated to be deficient in Met (approx. 24.5%), Lys (approx. 4.3%), His (approx. 18.9%) and Leu (approx. 3.5%). The deficient AA were supplemented by means of duodenally infused AA mixture that was calculated to meet 110% of the requirement (Rulquin et al., 2001b) for better manifestation of the response. The composition of the infusate in HIS was (g d^{-1}): Met 15.9, Lys 25.7, His 13.6 and Leu 24.3 (Ajinomoto Co. Inc., Japan). In the control, histidine was replaced with monosodium l-glutamate (37.4 g d^{-1}) to ensure the isonitrogenicity of both infusates. AA were dissolved in 4-5 l of fresh tap water separately for each cow daily and infused continuously *via* a four-channel infusion pump (Dávkovací čerpadla Ing. Kouřil, Czech Republic) into the duodenum.

Table 1. Composition of diet

Component	Content
Maize silage, g kg^{-1}	480
Lucerne hay, g kg^{-1}	82
Supplemental mixture ¹ , g kg^{-1}	438
PDIE ² , g kg^{-1}	87.4
NEL ³ , MJ kg^{-1}	6.80

¹ supplemental mixture contained, g kg^{-1} : barley 428, oat 184, linseed 50, soyabean meal 50, dietary peas 250, sodium chloride (NaCl) 6.0, dicalcium phosphate (CaHPO_4) 12.0, limestone (CaCO_3) 15.0, sodium bicarbonate (NaHCO_3) 1.0, MgP 3.0, microelements and vitamin mixture 1.0; ² digestible protein in the intestine when energy supply is limiting; ³ net energy of lactation

Analytical procedures

Individual feed intake and refusals were monitored daily during the experiment and an aliquot of them was analysed. Dry matter (DM) was determined by drying at 55°C for 24 h followed by milling through a 1 mm screen and drying for another 4 h at 103°C .

The cows were milked twice daily at 7.15 a.m. and 5.15 p.m. Milk yield was recorded and milk samples were taken at each milking during the experimental period. The milk samples for determination of basal constituents were conserved with 2-bromo-2-nitropropane-1,3-diol (Bronopol), cooled to 6°C and subsequently analysed by an infrared analyzer (Bentley Instruments 2000, Bentley Instruments Inc., USA). The urea content was determined using a UREA K VANT apparatus (AGROSLUŽBY Olomouc, s.r.o., Czech Republic) and the casein content was measured on a Kjeltec auto 1030 Analyser (Tecator AB, Höganäs, Sweden) after precipitation with 10% acetic acid. Casein fractions were determined using a Mini-Protein III Cell Electrophoresis apparatus according to the method described by Hadrová et al. (2007).

On the last day of each experimental period, blood samples were taken into heparinized tubes from the jugular vein (at 7.45 a.m.) for determination of the plasma AA profile. The heparinized blood plasma was deproteinized with sulphosalicylic acid and centrifuged for 10 min at 3 000 g. The supernatant was stored at -80°C until analysis. The profile of free plasma AA was determined in an Automatic Aminoanalyser AAA 400 (Ingos, Praha, Czech Republic) using the programme ChromuLan v. 0.7.

For analysis of milk fatty acids, to 100 mg of extracted milk fat, 0.5 mol·l⁻¹ methanolic KOH was added and the mixture heated under a reverse cooler at 130/150°C for 30 min. FAs were released in the form of fatty acid methyl esters (FAMES) that were separated using a Gas Chromatograph 6820 GC System (Agilent, USA) with a capillary column VB-WAX (60 m x 0.32 mm x 0.25 µm; VICI and VacoBond, USA). The temperature ranged from 50°C to 240°C with an increase of 5°C/min. Injector and detector temperatures were 280°C and 300°C, respectively. Nitrogen was the carrier gas. FAMES were detected with a flame ionization detector (FID) and identified using Supelco TM 37 Component FAME Mix (Supelco, USA) external fatty acid standards.

Statistical analysis

The effect of carry-over of the experimental treatment was tested using the statistical model of Cochran and Cox (1957), as applied by Martz et al. (1990):

$$Y_{ijk} = \mu + T_i + C_j + P_k + R_m + \varepsilon_{ijk}$$

where: μ - general mean, T_i - the effect of the treatment ($i=2$), C_j - the effect of the cow ($j=3$), P_k - the effect of a period ($k=4$), R_m - the effect of carry-over ($m=2$), ε_{ijk} - error term.

A carry-over effect was not proved, therefore the data obtained in the experiment were analysed using the GLM procedure of the Statgraphics 7.0 package (Manugistics Inc. and Statistical Graphics Corporation. Rockville, MA, USA) according to the model:

$$Y_{ijk} = \mu + T_i + C_j + P_k + \varepsilon_{ijk}$$

where: μ - general mean, T_i , C_j and P_k - the effects of treatment ($i=2$), cow ($j=3$) and period ($k=4$), ε_{ijk} - error term.

For all statistical evaluations, period means were used. Values of $P < 0.05$ were considered to be significant.

RESULTS

Intake of nutrients, milk yield and composition

Intakes of dry matter (DM) and other nutrients are given in Table 2. No significant differences between the treatments were found ($P>0.05$). Milk yield, content and yield of milk components are presented in Tables 3 and 4. The average milk yield in HIS was higher ($P<0.01$) than in the control; the calculated energy-corrected milk yield was affected ($P<0.05$) between the

Table 2. The effect of duodenally infused histidine on nutrient intake in dairy cows

Intake	Control ¹	HIS ²	SEM	P
Dry matter, kg d ⁻¹	19.5	19.4	0.11	0.685
Organic matter, kg d ⁻¹	18.0	18.0	0.10	0.719
Crude protein, kg d ⁻¹	2.46	2.45	0.02	0.669
NDF ³ , kg d ⁻¹	5.93	5.91	0.04	0.769
ADF ⁴ , kg d ⁻¹	2.85	2.84	0.02	0.806
NEL ⁵ , MJ day ⁻¹	135	135	0.82	0.685

¹ control, supplemented with duodenally infused methionine (15.9 g day⁻¹), lysine (25.7 g day⁻¹), leucine (24.3 g day⁻¹) and Glu-Na (37.4 g day⁻¹); ² experimental, supplemented with duodenally infused methionine (15.9 g day⁻¹), lysine (25.7 g day⁻¹), leucine (24.3 g day⁻¹) and histidine (13.6 g day⁻¹); ³ neutral detergent fibre, ⁴ acid detergent fibre, ⁵ net energy for milk production

Table 3. The effect of duodenally infused histidine on milk yield and composition

Indices	Control ¹	HIS ²	SEM	P
Milk yield, kg d ⁻¹	26.8	27.9	0.25	0.004
ECM ³ , kg d ⁻¹	29.6	30.5	0.28	0.037
Fat, g ml ⁻¹	46.4	45.1	1.02	0.368
Lactose, g ml ⁻¹	49.6	49.4	0.13	0.244
Protein, g ml ⁻¹	36.02	36.49	0.29	0.266
Casein, g kg ⁻¹	28.80	28.93	0.24	0.721
<i>Casein fractions, %</i>				
α-casein	56.23	55.68	0.39	0.341
β-casein	38.74	38.65	0.37	0.879
κ-casein	5.03	5.67	0.15	0.006
Urea, mg 100 ml ⁻¹	21.73	21.29	0.41	0.470

^{1,2} see Table 2; ³ energy corrected milk yield calculated according to Sjaunja et al. (1991): ECM = milk yield (kg) x ((383 x milk fat % + 242 x protein % + 165 x lactose % + 20.7)/3140)

Table 4. The effect of duodenally infused histidine on a daily yield of milk components

Indices	Control ¹	HIS ²	SEM	P
Fat, g d ⁻¹	1234	1250	23.11	0.645
Lactose, g d ⁻¹	1330	1377	13.17	0.018
Protein, g d ⁻¹	960	1015	9.43	0.001
Casein, g d ⁻¹	768	805	7.76	0.002
<i>Casein fractions, g</i>				
α-casein	431.7	447.9	4.98	0.031
β-casein	297.5	311.2	4.52	0.044
κ-casein	38.4	45.4	1.19	0.001

^{1,2} see Table 2

treatments. The contents of protein and casein were not significantly different ($P>0.05$) between the treatments. The protein and casein yields were significantly higher ($P<0.001$ and $P<0.01$) in HIS in comparison with the control. Neither the content nor the yield of fat were affected ($P>0.05$) between the treatments. The lactose content did not respond ($P>0.05$) to the treatment, but its yield was significantly higher ($P=0.018$) in HIS in comparison with the control. The relative proportions of α -casein and β -casein were unaffected ($P>0.05$), but the κ -casein proportion was significantly higher ($P<0.01$) in HIS in comparison with the control. The yield of each casein fraction was significantly higher ($P<0.05$ and $P<0.001$, respectively) in HIS. No significant effect of histidine infusion was observed on the urea concentration ($P>0.05$).

Plasma amino acids

The changes in plasma concentrations of free amino acids (AA) are given in Table 5. The concentrations of free AA in blood plasma did not react to the

Table 5. The effect of duodenally infused histidine on plasma concentrations of free amino acids, μmol^{-1} of plasma

Amino acids	Control ¹	HIS ²	SEM	P
<i>Essential amino acids (EAA)</i>				
arginine	95.3	89.3	7.23	0.596
histidine	25.2	78.9	9.54	0.012
isoleucine	65.7	75.6	6.95	0.372
leucine	130.0	116.0	15.0	0.540
lysine	93.3	99.4	9.57	0.677
methionine	83.0	83.7	6.37	0.943
phenylalanine	27.0	28.7	3.19	0.712
threonine	103.0	122.0	8.92	0.214
valine	157.0	163.0	12.8	0.759
<i>Non-essential amino acids (NEAA)</i>				
alanine	238.0	213.0	37.8	0.673
asparagine	52.5	55.9	4.36	0.612
aspartic acid	15.3	13.0	1.25	0.265
citrulline	73.6	90.5	6.95	0.156
cysteine	63.7	93.8	10.7	0.112
glutamine	344.0	408.0	47.9	0.399
glutamic acid	82.1	70.0	6.38	0.249
glycine	480.0	535.0	50.9	0.493
ornithine	68.8	71.9	6.42	0.751
proline	81.0	75.4	3.56	0.335
serine	125.0	115.0	9.76	0.517
tyrosine	30.2	31.1	3.34	0.858
<i>Sum of amino acids</i>				
EAA	780	857	70.2	0.488
NEAA	1654	1773	135	0.573
total AA	2434	2630	198	0.528

^{1,2} see Table 2

treatment ($P>0.05$) except for the histidine concentration that differed significantly ($P=0.012$) between the treatments.

Fatty acid profile of milk

The effect of duodenal infusion of histidine on the milk FA profile is shown in Table 6. The proportions of short- and medium-chain FA were not significantly different ($P>0.05$) between the treatments, but the proportions of short-chain FA tended to be higher in HIS compared with the control. Furthermore, the content of C14:1, C15:0, C16:0, C17:1, and C17:0 tended to be higher in the

Table 6. The effect of duodenally infused histidine on milk fatty acid profile, %

Fatty acid	Control ¹	HIS ²	SEM	P
C4:0	1.20	1.23	0.077	0.773
C6:0	0.78	0.84	0.052	0.467
C8:0	0.56	0.66	0.038	0.090
C10:0	2.47	2.54	0.127	0.705
C12:0	4.19	4.27	0.156	0.731
C14:0	12.90	13.07	0.183	0.538
C14:1	1.36	1.34	0.038	0.696
C15:0	2.57	2.35	0.121	0.208
C16:0	39.24	38.43	0.378	0.148
C16:1	2.63	2.32	0.086	0.017
C17:1	0.90	0.85	0.037	0.457
C17:0	0.40	0.36	0.016	0.083
C18:0	7.48	7.99	0.172	0.049
C18:1n9	18.34	18.57	0.368	0.684
C18:2n6t	0.23	0.24	0.018	0.679
C18:2n6c	2.07	2.24	0.052	0.039
C18:3n6	0.06	0.06	0.002	0.041
C18:3n3	0.61	0.70	0.020	0.007
SFA ³	72.50	72.42	0.486	0.907
MUFA ⁴	23.36	23.22	0.411	0.818
PUFA ⁵	4.14	4.36	0.147	0.301
UFA ⁶	27.50	27.58	0.486	0.907
SFA/MUFA	3.22	3.18	0.078	0.748
SFA/PUFA	18.53	16.91	0.643	0.091
SFA/UFA	2.73	2.67	0.066	0.519
MUFA/PUFA	5.78	5.39	0.161	0.103
SCFA ⁷	9.68	10.00	0.419	0.607
MCFA ⁸	60.04	58.75	0.329	0.011
LCFA ⁹	30.29	31.25	0.525	0.216

^{1,2} see Table 2; ³ saturated fatty acids including C6:0, C8:0, C11:0, C13:0, C20:0, C21:0, C22:0;

⁴ monounsaturated fatty acids including C15:1, C20:1n9; ⁵ polyunsaturated fatty acids including C20:2, C20:3n6, C20:3n3, C20:5n3; ⁶ unsaturated fatty acids; ⁷ short-chain fatty acids including C6:0, C8:0, C11:0, C13:0; ⁸ medium-chain fatty acids; ⁹ long-chain fatty acids including C20:0, C20:1n9, C20:2, C20:3n3, C20:5n3, C22:0, C22:2

control compared with HIS. The content of C16:1 was significantly higher ($P<0.05$) in control than in HIS. Long-chain FA were unaffected ($P>0.05$), except for the contents of C18:0, C18:2n6c, and C18:3n3, which were higher ($P<0.05$) in HIS. The proportions of saturated FAs and unsaturated FAs (both MUFA and PUFA) were not significantly different ($P>0.05$); MCFAs were significantly higher ($P<0.05$) in the control compared with HIS.

DISCUSSION

Dry matter intake did not differ significantly between the treatments; this finding is in agreement with Vanhatalo et al. (1999) or Korhonen et al. (2000). In this experiment, the duodenal infusion of histidine significantly increased milk yield in HIS compared with the control. A significant increase in milk yield caused by the infusion of histidine was also observed in other studies (e.g., Vanhatalo et al., 1999; Korhonen et al., 2000; Huhtanen et al., 2002). In contrast, neither feed intake nor milk yield were changed when cows received a diet of grass silage and barley-soyabean meal with or without an intravenous supplement of histidine (Kim et al., 2001a). Milk yield was unaffected by duodenal infusion of graded amounts of histidine at 0, 36, 55, and 74 g·d⁻¹ (Rulquin and Pisulewski, 2000). This experiment confirmed our hypothesis assuming a deficit of histidine in a basal diet consisting of maize silage with concentrate. The presented results are in accordance with Moon et al. (2004), who studied the effect of the intravenous histidine infusion on milk production on maize/lucerne silage-based TMR diet in dairy cows, and also with experiments on grass silage-based diets (Vanhatalo et al., 1999; Korhonen et al., 2000; Kim et al., 2001a,b).

In the present experiment, the protein content in milk was unaffected, but the yield of milk protein was significantly higher in HIS compared with the control. Similarly to our results, the protein yield was increased linearly by duodenal infusion of graded amounts of His (Rulquin and Pisulewski, 2000). The abomasal infusion of 6.5 g His significantly increased the yield of milk protein, but did not affect the milk protein content. The milk protein content was higher, however, when His was combined with Met (Vanhatalo et al., 1999). In one experiment by Kim et al. (2001a), the content of milk protein was increased and the milk protein yield was not affected in cows receiving the basal diet (grass silage and barley-soyabean meal) supplemented intravenously with Met, Lys, and Trp (3 AA) and with His, Met, Lys, and Trp (4 AA) in comparison with His alone or the basal diet. Post ruminal infusion in the amounts of grade 0, 2, 4 and 6 g·d⁻¹ His linearly increased the yield of milk protein, but the milk protein content was not affected by the treatment (Korhonen et al., 2000). In another study, the milk

protein content and yield were affected by intravenous infusion of histidine in lactating dairy cows (Moon et al., 2004). Both the concentration and the yield of milk protein were increased by inclusion of soyabean meal in the basal diet based on grass silage with or without intravenous supplementation of histidine in comparison with the diet containing only barley (Kim et al., 2001a). On the other hand, intravenous infusion of 9 g d⁻¹ of histidine reduced the yield of milk protein compared with a lower dose, which implies that histidine given in higher doses was beyond the level that is limiting for milk production and milk protein synthesis in dairy cows (Kim et al., 2001b).

In this experiment, the content of milk fat was unaffected by the treatment, but the yield of fat tended to be higher in HIS compared with the control. The fat content decreased when histidine was infused alone and tended to be higher when His was combined with other AA (Vanhatalo et al., 1999; Kim et al., 2001a). In the current study, infusion of histidine resulted in a significantly higher yield of lactose in HIS compared with the control, but the lactose content was not affected. Similarly to our results, in another study post ruminal infusion of histidine significantly increased the milk lactose yield, while the content of lactose was unchanged (Korhonen et al., 2000). Intravenous infusions of histidine had no influence on the lactose content of milk (Kim et al., 2001b). In contrast, infusion of histidine also significantly decreased the content of lactose, but its yield was unaffected by the treatment (Vanhatalo et al., 1999).

The content of urea was unaffected between the treatments. Similar results were reported by Vanhatalo et al. (1999) and Korhonen et al. (2000).

The effect of duodenal infusion of histidine was also observed on casein and its fractions. Casein is an important milk protein for cheese making. The casein content did not significantly differ between the treatments; the relative proportions of α -casein and β -casein were unaffected, but the κ -casein proportion was significantly higher, as were the yields of each casein fraction in HIS compared with the control. According Hadrová et al. (2007), the content and yield of casein were significantly higher and the yield of each casein fraction was significantly higher after the administration of soya protein with lysine, methionine and histidine in the form of rumen protected (RP) tablets compared with the control group.

The concentration of plasma AA was not affected between the treatments, except for histidine that was significantly higher in HIS. Similarly to our results, Kim et al. (2001b) reported a linear increase in plasma histidine as a result of intravenous infusion of histidine at graded doses, without a response for the other amino acids. Lee et al. (2012) reported that the blood plasma histidine concentration in cows increased when a diet deficient in metabolizable protein was supplemented with RP lysine, RP methionine, and RP histidine in comparison with the other diets deficient in metabolizable protein, but blood plasma concentrations

of histidine and lysine were lower than when a diet adequate in metabolizable protein was fed.

CONCLUSIONS

Histidine (His) has been identified as the first limiting amino acid in grass silage-cereal based diets. The calculated His deficiency in the diet used in the present experiment was approximately 18.9%. Milk yield and the yields of protein and casein were significantly higher in lactating dairy cows after duodenal infusion of histidine. The κ -casein proportion was significantly higher and the yield of every casein fraction was significantly higher in histidine supplemented cows compared with the control. Our results indicate that His may be a limiting amino acid in high-producing dairy cows fed a diet based on maize silage with amino acids (Met, Lys and Leu) balanced to meet requirements.

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