Effects of standardized ileal digestible histidine to lysine ratio on growth performance of 7- to 11-kg nursery pigs[1]

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ABSTRACT: Histidine may be the sixth limiting amino acid (**AA**) in practical nursery diets supplemented with high amounts of feed-grade AA. Therefore, 2 experiments were conducted to determine the standardized ileal digestible (**SID**) His:Lys ratio requirement estimate for growth performance of 7- to 11-kg nursery pigs. A total of 360 and 350 pigs (DNA 241 × 600, Columbus, NE; initially 7.1 ± 0.31 and 6.6 ± 0.36 kg) were used in Exp. 1 and 2, respectively. There were 5 pigs per pen with 12 replicates per treatment in Exp. 1 and 10 replicates per treatment in Exp. 2. After weaning, pigs were fed a common pelleted diet for 10 d in Exp. 1 and 7 d in Exp. 2. Then, pens were assigned to treatments in a randomized complete block design with body weight (**BW**) as the blocking factor. Dietary treatments consisted of SID His:Lys ratios of 24%, 28%, 32%, 36%, 40%, and 44% in Exp. 1 and 24%, 28%, 30%, 32%, 34%, 36%, and 42% in Exp. 2. Experimental diets were fed in pellet form for 10 or 14 d in Exp. 1 and 2, followed by a common mash diet for 15 or 14 d, respectively. Data were analyzed using the GLIMMIX and NLMIXED procedures of SAS, fitting data with heterogeneous variance when needed. The competing statistical models utilized were quadratic polynomial, broken-line linear (**BLL**), and broken-line quadratic. In Exp. 1, increasing SID His:Lys ratio increased (quadratic, *P* = 0.001) ADG, ADFI, G:F, and day 10 BW. In Exp. 2, ADG, G:F, and day 14 BW increased (quadratic, *P* = 0.001), and ADFI increased linearly (*P* = 0.001) with increasing SID His:Lys ratio. The best-fitting model for all response variables analyzed was the BLL. In Exp. 1, requirement estimates were 29.7%, 29.1%, and 29.8% SID His:Lys ratio for ADG, ADFI, and G:F, respectively. In Exp. 2, the SID His:Lys ratio requirement estimates were 31.0% for ADG and 28.6% for G:F. These results suggest that the SID His requirement estimate for growth performance is no more than 31% of Lys and that the NRC (2012) SID His requirement of 34% of Lys may be overestimated for 7- to 11-kg pigs.

Key words: growth, histidine, lysine, modeling, swine

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INTRODUCTION

Practical nursery diets are formulated with high inclusion of crystalline amino acids (**AA**). In many situations, it is economical to add L-Lys, L-Thr, L-Trp, DL-Met, and L-Val. The NRC (2012) AA requirement estimates suggest that His may become the sixth limiting AA in many diets fed to 7- to 11-kg body weight (**BW**) pigs when

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supplemented with high amounts of these feed-grade AA. Therefore, the standardized ileal digestible (**SID**) His:Lys ratio requirement estimate could dictate the maximum inclusion of crystalline AA in nursery diets.

Amino acids requirements are often expressed as a SID ratio to Lys. The NRC (2012) estimates the SID His:Lys ratio requirement at 34% for nursery pigs from 7 to 11 kg. Recent research suggests that the NRC (2012) recommendations may overestimate the His requirement. Gloaguen et al. (2013) determined that a 32% SID His:Lys ratio was ideal for 11- to 20-kg pigs and Wessels et al. (2016) estimated the SID His:Lys ratio at 28% for 8- to 21-kg pigs. However, there is limited data validating these ratios or investigating the SID His:Lys ratio requirement for lighter pigs. Therefore, the objective of our study was to determine the SID His:Lys ratio requirement for growth performance of 7- to 11-kg pigs.

MATERIALS AND METHODS

The Kansas State University Institutional Animal Care and Use Committee approved the protocols used in these experiments. Two experiments were conducted at the Kansas State University Swine Teaching and Research Center in Manhattan, KS.

Animals and Diets

All diets were manufactured at the Kansas State University O.H. Kruse Feed Technology Innovation Center in Manhattan, KS. Corn, soybean meal, spray-dried whey, and whey protein concentrate were submitted to Ajinomoto Heartland, Inc. (Chicago, IL) for total AA content analysis (excluding Trp, method 994.12; AOAC International, 2012) and Trp (method 13904:2005; ISO, 2005) prior to diet formulation (Table 1). These values were multiplied by NRC (2012) standardized ileal digestibility coefficients and used in diet formulation.

In Exp. 1, 360 pigs (DNA 241 × 600, Columbus, NE; initial average BW of 7.1 ± 0.31 kg) were used in a 25-d growth trial, where test diets were fed for 10 d and a common diet was then fed for 15 d. In Exp. 2, 350 pigs (DNA 241 × 600, Columbus, NE; initial average BW of 6.6 ± 0.36 kg) were used in a 28-d growth trial, where test diets were fed for 14 d and a common diet was fed for the next 14 d. Pigs in both trials were weaned at approximately 21 d of age and placed in pens of 5 pigs each based on initial BW and sex. A common phase 1 pelleted diet was fed for 10 d in Exp. 1 and 7 d in Exp. 2. At day 7 or 10 after weaning, which was considered day 0 of the trial, pens of pigs were allotted to treatment in a randomized complete block design with BW as the blocking factor. There were 12 replicates per

Table 1. Total amino acid analysis of ingredients (as-fed basis)

Item	Corn	Soybean meal	Whey protein concentrate	Spray-dried whey
Amino acids, %				
Ala	0.62	1.95	3.49	0.47
Arg	0.40	3.12	2.95	0.28
Asp	0.58	5.01	7.21	0.99
Cys	0.22	0.69	1.64	0.25
Glu	1.51	7.80	10.93	1.58
Gly	0.34	1.86	1.91	0.23
His	0.22	1.13	1.66	0.20
Ile	0.30	2.09	3.54	0.56
Leu	0.99	3.46	7.49	1.03
Lys	0.26	2.73	5.97	0.78
Met	0.20	0.63	1.41	0.15
Met and Cys	0.42	1.32	3.05	0.40
Phe	0.39	2.31	2.92	0.36
Pro	0.74	2.23	3.94	0.52
Ser	0.40	2.23	4.55	0.53
Thr	0.30	1.75	4.74	0.62
Tyr	0.17	1.37	1.91	0.15
Val	0.39	2.11	3.81	0.53
Trp	0.07	0.64	1.34	0.18

A representative sample of each ingredient was obtained, homogenized, and submitted for amino acid analysis (Ajinomoto Heartland, Inc., Chicago, IL) prior to diet formulation.

Table 2. Diet composition, Exp. 1 and 2 (as-fed basis)

Item	Exp. 1 and 2 24% SID[1] His:Lys	Exp. 1 44% SID His:Lys	Exp. 2 42% SID His:Lys
Ingredients, %			
Corn	60.20	59.94	59.97
Whey protein concentrate	7.75	7.75	7.75
Spray-dried whey	7.25	7.25	7.25
Soybean meal, 45% CP	5.63	5.63	5.63
Sucrose	10.00	10.00	10.00
Monocalcium phosphate, 21.5% P	1.43	1.43	1.43
Calcium carbonate	0.98	0.98	0.98
Sodium chloride	0.30	0.30	0.30
Sodium bicarbonate	0.75	0.75	0.75
Potassium chloride	0.11	0.11	0.11
L-Lys HCl	0.65	0.65	0.65
DL-Met	0.24	0.24	0.24
L-Thr	0.24	0.24	0.24
L-Trp	0.07	0.07	0.07
L-Val	0.26	0.26	0.26
L-Ile	0.14	0.14	0.14
L-Phe	0.34	0.34	0.34
L-His	–	0.25	0.23
Glutamic acid	1.50	1.50	1.50
Glycine	1.50	1.50	1.50
Zinc oxide	0.25	0.25	0.25
Vitamin premix[2]	0.25	0.25	0.25
Trace mineral premix[3]	0.15	0.15	0.15
Phytase[4]	0.03	0.03	0.03
Total	100	100	100
Calculated analysis			
SID AA, %			
Lys	1.25	1.25	1.25
Ile:Lys	55	55	55
Leu:Lys	105	105	105
Met:Lys	39	39	39
Met and Cys:Lys	60	60	60
Thr:Lys	65	65	65
Trp:Lys	19.8	19.8	19.8
Val:Lys	70	70	70
His:Lys	24	44	42
NE, kcal/kg	2,511	2,504	2,504
CP, %	18.2	18.3	18.3
Ca, %	0.72	0.72	0.72
STTD P, %	0.52	0.52	0.52

In Exp. 1, diets were fed from 7.1 to 11.4 kg BW. Diets were blended to form the intermediate treatments: 28%, 32%, 36%, and 40% SID His:Lys ratio. In Exp. 2, diets were fed from 6.6 to 11.2 kg BW. Diets were blended to form the intermediate treatments: 28%, 30%, 32%, 34%, and 36% SID His:Lys ratio.

[1]SID = standardized ileal digestible.

[2]Provided per kg of premix: 3,527,399 IU vitamin A; 881,850 IU vitamin D; 17,637 IU vitamin E; 1,764-mg vitamin K; 15.4-mg vitamin B12; 33,069-mg niacin; 11,023-mg pantothenic acid; 3,307-mg riboflavin.

[3]Provided per kg of premix: 73-g Zn from Zn sulfate; 73-g Fe from iron sulfate; 22-g Mn from manganese oxide; 11-g Cu from copper sulfate; 0.2-g I from calcium iodate; 0.2-g Se from sodium selenite.

[4]Ronozyme HiPhos 2700 (DSM Nutritional Products, Basel, Switzerland) provided 676 FTU per kg of feed.

treatment in Exp. 1 and 10 replicates per treatment in Exp. 2.

In Exp. 1 and 2, the same basal diet containing corn, spray-dried whey, and whey protein concentrate was formulated to 24% SID His:Lys ratio (Table 2). Then, a high SID His:Lys ratio diet (44% or 42% in Exp. 1 and 2, respectively) was formulated. Crystalline L-His replaced corn to form the high SID His:Lys ratio diet. Within each experiment, the low and high diets were blended at the feed mill to achieve the intermediate SID His:Lys ratio diets. In brief, large batches of the low and high SID His:Lys ratio diets were manufactured and bagged in 23-kg bags. Then, bags were randomly selected and blended in different proportions to achieve the desired treatment diet. In Exp. 1, 6 dietary treatments were created to contain SID His concentrations at 24%, 28%, 32%, 36%, 40%, and 44% of Lys. To add more data points around the suggested requirement from Exp. 1, 7 dietary treatments containing SID His at 24%, 28%, 30%, 32%, 34%, 36%, and 42% of Lys were used in Exp. 2. Based on Clark et al. (2017b), who determined the SID Lys requirement of 7- to 11-kg pigs at 1.45%, the experimental diets were formulated to contain 1.25% SID Lys to ensure that Lys was the second limiting AA. All other AA met or exceeded the NRC (2012) requirement estimates. Experimental diets were pelleted and the average processing parameters were 50.6 °C conditioning temperature, 68.9 °C hot pellet temperature, 330/1625-mm die size (length/diameter ratio = 5.0), 707-kg/h production rate, 29.8 °C ambient temperature, and 82% relative humidity. The common diet was provided in mash form.

Each pen (1.5 × 1.5 m) was equipped with a 4-hole, dry self-feeder and a cup waterer to provide ad libitum access to feed and water. Pigs were weighed and feed disappearance was measured on days 0, 7, 10, 18, and 25 in Exp. 1 and on days 0, 7, 14, 21, and 28 in Exp. 2 to determine ADG, ADFI, and G:F.

Chemical Analysis

Representative diet samples were obtained from all feeders of each treatment and stored at −20 °C until analysis. Samples were analyzed (Ward Laboratories, Inc., Kearney, NE) for DM (method 935.29; AOAC International, 1990), CP (method 990.03; AOAC International, 1990), Ca (method 985.01; AOAC International, 1990), P (method 985.01; AOAC International, 1990), Na (Kovar, 2003), and Cl (method 969.10, AOAC International, 1990). Feed samples were also analyzed for total AA content (excluding Trp, method 994.12; AOAC International, 2012) and Trp (method 13904:2005; ISO, 2005) at Ajinomoto Heartland, Inc. (Chicago, IL).

Statistical Analysis

Data were analyzed as a randomized complete block design with block as a random effect and pen as the experimental unit. Polynomial contrasts were constructed to evaluate the linear and quadratic effects of increasing SID His:Lys ratio on ADG, ADFI, G:F, and BW. Contrast coefficients were adjusted for unequally spaced treatments in Exp. 2. Data were analyzed using the GLIMMIX procedure of SAS (SAS Institute Inc., Cary, NC). Results were considered significant at $P \le 0.05$ and marginally significant at $0.05 < P \le 0.10$. Competing dose response models consisted of quadratic polynomial (**QP**), broken-line linear (**BLL**), and broken-line quadratic (**BLQ**). Broken-line regression models were fitted using the NLMIXED procedure of SAS according to the procedures of Gonçalves et al. (2016). Models were expanded to account for heterogeneous variance when needed. Competing models were compared using the Bayesian information criteria, with decreases by 2 or more units considered an improved fit. Results reported correspond to the best fitting model.

RESULTS

Chemical Analysis

The analyzed DM, CP, Ca, P, Na, Cl, and total AA were consistent with formulated values (Tables 3 and 4). As expected, AA analysis showed a stepwise increase in total His concentrations.

Experiment 1

From days 0 to 10, when experimental diets were fed, ADG, ADFI, and G:F increased, then plateaued (quadratic, $P = 0.001$) with increasing SID His:Lys ratio (Table 5). For all response variables, the best fitting model was the BLL. For ADG, the estimated breakpoint was 29.7% (95% CI: [27.8, 31.6%]) SID His:Lys ratio and the regression equation (Figure 1) was as follows:

$$\text{ADFI, g} = 463.23 - 23.96 \times (29.69 - \text{SID His:Lys}) \quad \text{if SID His:Lys} < 29.7\%,$$

$$\text{ADG, g} = 463.23 \text{ if SID His:Lys} \ge 29.7\%.$$

For ADFI, the estimated breakpoint was 29.1% (95% CI: [27.6, 30.6%]) SID His:Lys ratio and the regression equation for the BLL model (Figure 2) was as follows:

$$\text{ADFI, g} = 562.24 - 19.45 \times (29.1 - \text{SID His:Lys}) \quad \text{if SID His:Lys} < 29.1\%,$$

$$\text{ADFI, g} = 562.24 \text{ if SID His : Lys} \geq 29.1\%.$$

For G:F, the maximum mean value was estimated at 29.8% (95% CI: [27.6, 31.2%]) SID His:Lys ratio and the estimated regression equation for the BLL model (Figure 3) was as follows:

$$\text{G : F, g / kg} = 815.95 - 18.34 \times (29.8 - \text{SID His : Lys}) \text{ if SID His : Lys} < 29.8\%,$$

$$\text{G : F, g / kg} = 815.95 \text{ if SID His : Lys} \geq 29.8\%.$$

During the post-test period (days 10 to 25), pigs previously fed low SID His:Lys ratios appeared to have a compensatory response in growth performance. Average daily gain and G:F increased (linear, $P < 0.05$) in pigs previously fed diets with the lower SID His:Lys ratios compared with pigs previously fed adequate SID His:Lys ratio. There was a quadratic response ($P < 0.01$) for BW on days 10 and 25. Overall (days 0 to 25), ADG and ADFI were greater (quadratic, $P < 0.05$) and there was a marginally significant improvement in G:F (quadratic, $P = 0.096$) with increasing SID His:Lys ratio.

Experiment 2

From days 0 to 14, when experimental diets were fed, ADG and G:F increased, then plateaued (quadratic, $P = 0.001$) and ADFI linearly increased ($P = 0.001$) with increasing SID His:Lys ratio (Table 6). The response for ADFI was not modeled due to its linear nature. Similar to Exp. 1, the best fitting model was the BLL for ADG and G:F.

Table 3. Chemical analysis of diets (as-fed basis; Exp. 1)

	SID[1] His:Lys ratio, %					
Item	24	28	32	36	40	44
Proximate analysis, %						
DM	90.5	90.9	91.0	91.6	91.4	91.5
CP	17.3	17.0	17.4	17.3	17.9	18.6
Ca	0.82	0.77	0.85	0.83	0.84	0.85
P	0.60	0.58	0.62	0.57	0.58	0.57
Na	0.35	0.37	0.37	0.39	0.35	0.42
Cl	0.48	0.51	0.48	0.48	0.51	0.60
Amino acids, %						
Lys	1.28	1.32	1.38	1.33	1.33	1.32
Ile	0.68	0.70	0.72	0.70	0.70	0.72
Leu	1.36	1.39	1.42	1.40	1.39	1.43
Met	0.45	0.46	0.46	0.45	0.47	0.45
Met and Cys	0.75	0.75	0.77	0.76	0.77	0.77
Thr	0.87	0.90	0.90	0.89	0.91	0.89
Trp	0.24	0.24	0.26	0.25	0.26	0.26
Val	0.88	0.91	0.92	0.90	0.91	0.92
His	0.33	0.37	0.43	0.45	0.50	0.55

A representative sample of each diet was collected from all feeders for each treatment, homogenized, and submitted for proximate analysis (Ward Laboratories, Inc., Kearney, NE). Amino acid analysis was conducted on composite samples by Ajinomoto Heartland, Inc., Chicago, IL.

[1]SID = standardized ileal digestible.

Table 4. Chemical analysis of diets (as-fed basis; Exp. 2)

	SID[1] His:Lys ratio, %						
Item	24	28	30	32	34	36	42
Proximate analysis, %							
DM	91.8	91.4	91.2	92.1	91.4	91.2	91.7
CP	16.6	17.2	17.6	17.4	17.5	16.9	18.1
Ca	0.90	0.78	0.84	0.84	0.83	0.84	0.90
P	0.58	0.59	0.60	0.59	0.57	0.59	0.61
Na	0.43	0.40	0.39	0.41	0.46	0.41	0.42
Cl	0.53	0.54	0.53	0.53	0.57	0.54	0.54
Amino acids, %							
Lys	1.19	1.25	1.26	1.20	1.22	1.24	1.27
Ile	0.67	0.70	0.71	0.68	0.69	0.69	0.73
Leu	1.29	1.31	1.31	1.28	1.29	1.29	1.30
Met	0.41	0.43	0.42	0.41	0.42	0.42	0.44
Met and Cys	0.66	0.70	0.69	0.66	0.68	0.69	0.69
Thr	0.80	0.82	0.81	0.81	0.82	0.82	0.83
Trp	0.22	0.24	0.23	0.23	0.21	0.23	0.24
Val	0.84	0.86	0.87	0.84	0.85	0.86	0.87
His	0.33	0.36	0.38	0.39	0.39	0.44	0.50

A representative sample of each diet was collected from all feeders for each treatment, homogenized, and submitted to Ward Laboratories, Inc., Kearney, NE for proximate analysis. Amino acid analysis was conducted on composite samples by Ajinomoto Heartland, Inc., Chicago, IL.

[1]SID = standardized ileal digestible.

Table 5. Least square means for growth performance of nursery pigs fed increasing standardized ileal digestible (SID) His:Lys ratio from 7- to 11-kg body weight (BW), Exp. 1

	SID His:Lys ratio, %							Probability, *P*<	
Item	24	28	32	36	40	44	SEM	Linear	Quadratic
BW, kg									
day 0	7.1	7.1	7.1	7.1	7.1	7.1	0.31	0.910	0.679
day 10	10.3	11.3	11.8	11.8	11.5	11.7	0.42	0.001	0.001
day 25	18.2	18.9	19.3	19.1	19.1	19.0	0.60	0.010	0.003
Experimental period (days 0 to 10)									
ADG, g	327	423	469	474	448	462	15.16	0.001	0.001
ADFI, g	463	541	570	572	567	566	19.59	0.001	0.001
G:F, g/kg	709	782	826	829	791	818	11.34	0.001	0.001
Post-test period (days 10 to 25)									
ADG, g	524	505	506	488	505	488	15.11	0.025	0.440
ADFI, g	802	801	807	792	810	791	25.14	0.745	0.789
G:F, g/kg	653	631	627	617	624	618	7.62	0.002	0.071
Overall (days 0 to 25)									
ADG, g	445	472	491	482	482	477	13.02	0.007	0.002
ADFI, g	667	697	712	704	712	701	20.89	0.043	0.038
G:F, g/kg	668	678	690	685	678	683	6.80	0.224	0.096

A total of 360 pigs (DNA 241 × 600, Columbus, NE; initially 7.1 kg) were used in a 25-d growth trial 5 pigs per pen and 12 replicates per treatment.

Experimental diets were fed from days 0 to 10 and a common diet was fed from days 10 to 25.

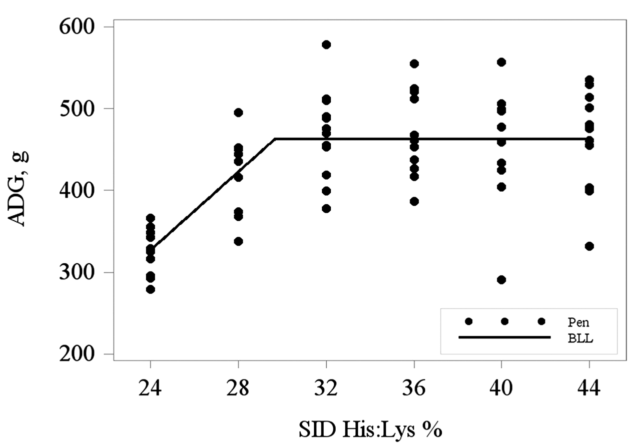

Figure 1. Fitted broken-line linear (BLL) regression model on ADG as a function of increasing SID His:Lys ratio for 7- to 11-kg pigs in Exp. 1. The maximum mean ADG was estimated at 29.7% (95% CI: [27.8, 31.6%]) SID His:Lys ratio. The estimated regression equation was ADG, g = 463.23 – 23.955 × (29.69 – SID His:Lys) if SID His:Lys < 29.7% and ADG, g = 463.23 if SID His:Lys ≥ 29.7%.

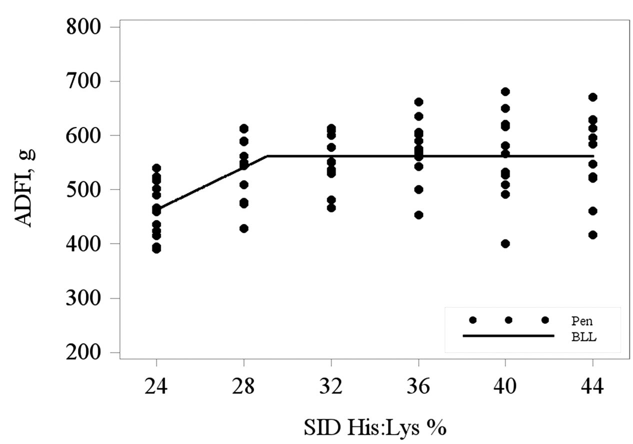

Figure 2. Fitted broken-line linear (BLL) regression model on ADFI as a function of increasing SID His:Lys ratio for 7- to 11-kg pigs in Exp. 1. The maximum mean ADFI was estimated at 29.1% (95% CI: [27.6, 30.6%]) SID His:Lys ratio. The estimated regression equation was ADFI, g = 562.24 – 19.448 × (29.1 – SID His:Lys) if SID His:Lys < 29.1% and ADFI, g = 562.24 if SID His:Lys ≥ 29.1%.

The maximum mean ADG was estimated at 31.0% (95% CI: [29.7, 32.3%]) SID His:Lys ratio and the estimated regression equation (Figure 4) was as follows:

$$\text{ADG, g} = 355.01 - 17.22 \times (31.0 - \text{SID His:Lys}) \text{ if SID His:Lys} < 31.0\%,$$

$$\text{ADG, g} = 355.01 \text{ if SID His:Lys} \geq 31.0\%.$$

For G:F, the estimated breakpoint was 28.6% (95% CI: [27.1, 30.0%]) SID His:Lys ratio and the regression equation for the BLL model (Figure 5) was as follows:

$$\text{G:F, g/kg} = 726.40 - 38.48 \times (28.6 - \text{SID His:Lys}) \text{ if SID His:Lys} < 28.6\%,$$

$$\text{G:F, g/kg} = 726.40 \text{ for SID His:Lys} \geq 28.6\%.$$

During the post-test period (days 14 to 28), ADFI decreased (linear, *P* = 0.003) and G:F increased (quadratic, *P* = 0.001) in pigs previously fed diets with the lower SID His:Lys ratios compared with pigs previously fed adequate SID His:Lys ratio. There was a quadratic response ($P < 0.01$) for BW on days 14 and 28. Overall (days 0 to 28), ADG, ADFI, and G:F were greater (quadratic, $P < 0.05$) with increasing SID His:Lys ratio.

DISCUSSION

Most modern commercial nursery diets are formulated with high additions of crystalline AA. The replacement of intact protein sources by feed-grade AA increases as the feed-grade AA become available and economically justifiable. This strategy results not only in reduced diet cost but also lower CP diets and reduced N excretion to the environment (Kerr and Easter, 1995). Moreover, low CP diets may decrease fermentable protein in the hindgut and consequently decrease the incidence of postweaning diarrhea (Heo et al., 2008). Considering the NRC (2012) SID His requirement estimate of 34% of Lys, His would be the sixth limiting AA after Val in many nursery diets. Therefore, in a practical diet formulated with L-Lys, L-Thr, L-Trp, DL-Met, and L-Val, the SID His:Lys ratio would dictate the maximum inclusion of crystalline AA.

In a requirement study, it is recommended that 25% of the treatments are placed below and above the anticipated requirement and 50% of the treatments around the anticipated requirement (Shearer, 2000). Based on the results of Exp. 1, Exp. 2 treatments were formulated with the intention to be more closely spaced around the expected breakpoint and ultimately provide a more precise requirement estimate. Moreover, it is critical that the basal diet is deficient in the test AA (Boisen, 2003). This may be especially true for His, because it has been shown that carnosine and hemoglobin degradation can provide His and partially alleviate the negative effects of a His-deficient diet (Clemens et al., 1984). In this study, growth performance was

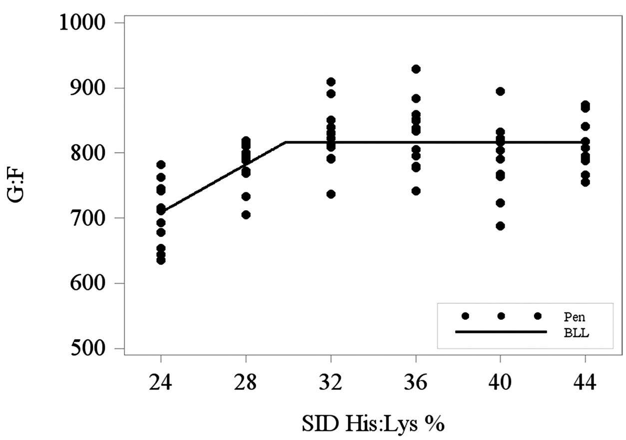

Figure 3. Fitted broken-line linear (BLL) regression model on G:F as a function of increasing SID His:Lys ratio for 7- to 11-kg pigs in Exp. 1. The maximum mean G:F was estimated at 29.8% (95% CI: [27.6, 31.2%]) SID His:Lys ratio. The estimated regression equation was G:F, g/kg = 815.95 – 18.344 × (29.8 – SID His:Lys) if SID His:Lys < 29.8% an G:F, g/kg = 815.95 if SID His:Lys ≥ 29.8%.

Table 6. Least square means for growth performance of nursery pigs fed increasing standardized ileal digestible (SID) His:Lys ratio from 7- to 11-kg body weight (BW), Exp. 2

	SID His:Lys ratio, %								Probability, $P<$	
Item	24	28	30	32	34	36	42	SEM	Linear	Quadratic
BW, kg										
Day 0	6.6	6.6	6.6	6.6	6.6	6.6	6.6	0.36	0.826	0.857
Day 14	9.8	10.9	11.0	11.5	11.8	11.5	11.6	0.58	0.001	0.001
Day 28	17.2	18.3	18.5	18.7	19.1	18.7	18.9	0.81	0.001	0.003
Experimental period (days 0 to 14)										
ADG, g	232	309	321	350	372	351	357	16.80	0.001	0.001
ADFI, g	428	442	466	470	492	483	493	21.39	0.001	0.168
G:F, g/kg	550	704	689	740	754	729	723	20.17	0.001	0.001
Post-test period (days 14 to 28)										
ADG, g	524	526	533	519	522	517	528	20.61	0.960	0.831
ADFI, g	754	797	826	813	840	826	841	30.58	0.003	0.106
G:F, g/kg	694	660	645	640	623	626	627	8.62	0.001	0.001
Overall (days 0 to 28)										
ADG, g	378	417	427	435	447	434	442	17.17	0.001	0.003
ADFI, g	591	620	646	641	666	654	667	23.70	0.001	0.050
G:F, g/kg	639	674	660	677	672	664	662	9.31	0.209	0.016

A total of 350 pigs (DNA 241 × 600, Columbus, NE; initially 6.6 kg) were used in a 28-d growth trial with 5 pigs per pen and 10 replicates per treatment.

Experimental diets were fed from days 0 to 14 and a common diet was fed from days 14 to 28.

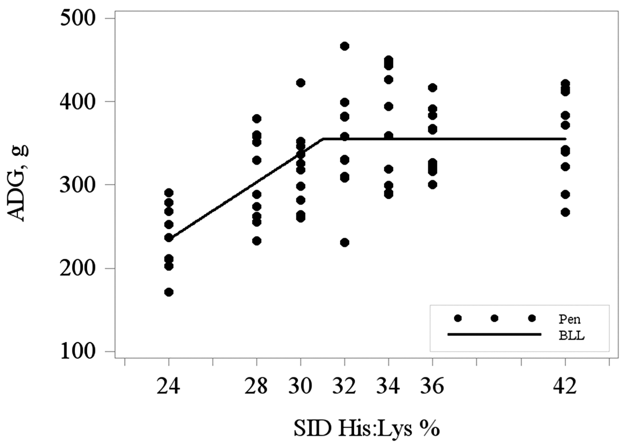

Figure 4. Fitted broken-line linear (BLL) regression model on ADG as a function of increasing SID His:Lys ratio for 7- to 11-kg pigs in Exp. 2. The maximum mean ADG was estimated at 31.0% (95% CI: [29.7, 32.3%]) SID His:Lys ratio. The estimated regression equation was ADG, g = 355.0 – 17.22 × (31.0 – SID His:Lys) if SID His:Lys < 31.0% and ADG, g = 355.0 if SID His:Lys ≥ 31.0%.

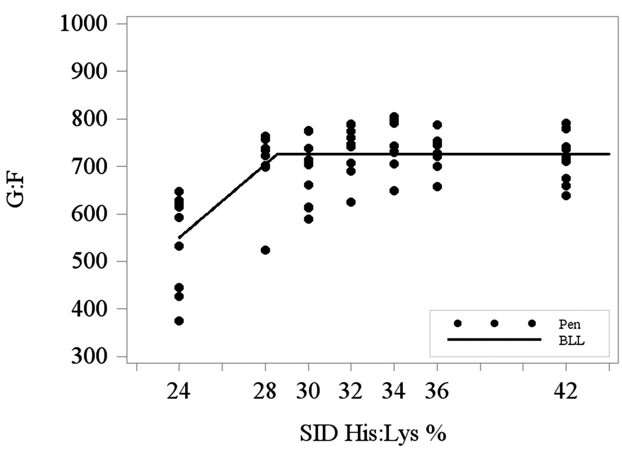

Figure 5. Fitted broken-line linear (BLL) regression model on G:F as a function of increasing SID His:Lys ratio for 7- to 11-kg pigs in Exp. 2. The maximum mean G:F was estimated at 28.6% (95% CI:[27.1, 30.0%]) SID His:Lys ratio. The estimated regression equation was G:F, g/kg = 726.4 – 38.48 × (28.6 – SID His:Lys) if SID His:Lys < 28.6% and G:F, g/kg = 726.4 if SID His:Lys ≥ 28.6%.

dramatically reduced when pigs were fed the 24% SID His:Lys ratio diet, demonstrating that it was deficient in the test AA. Finally, Lys should be the second limiting AA in requirement studies to avoid underestimation of the AA:Lys ratio requirement (Boisen, 2003). The SID Lys level of 1.25% was selected based on a study (Clark et al., 2017b) conducted in the same facilities with similar BW pigs.

A similar requirement estimate to our study was observed by Gloaguen et al. (2013), who determined the SID His:Lys requirement for 11- to 20-kg pigs at 31.6% for ADG and 28.8% for G:F using the BLQ model. Li et al. (2002) observed that the optimum His:Lys ratio for 10- to 20-kg pigs is 30%. In an N balance study, Heger et al. (2003) determined the ideal His:Lys ratio for 20-kg pigs at 33%. Wessels et al. (2016) determined the SID His:Lys requirement for 8- to 21-kg pigs at 26.5% using the BLL model and 27.9% using the BLQ model, which is moderately lower than our findings. The slightly greater breakpoint for ADG in Exp. 2 compared with Exp. 1 was driven by a marginal increase in growth rate of the pigs fed the SID His:Lys ratio of 32% and the addition of the diet with 30% SID His:Lys ratio. Furthermore, the requirement for maximum ADG was greater than that for maximum G:F, which is consistent with requirement studies for His (Gloaguen et al., 2013) and other AA, such as Ile (Gloaguen et al., 2013) and Trp (Gonçalves et al., 2015). Conversely, Wessels et al. (2016) found similar His requirements for ADG and G:F, and some AA, such as Lys (Nemechek et al., 2012) and Val (Clark et al., 2017b), seem to have a greater requirement for G:F than for ADG.

Taken together, these observations suggest that the NRC (2012) recommendation of 34% SID His:Lys ratio overestimates the His requirement of nursery pigs. Therefore, based on our results, practical nursery diets can be formulated with higher inclusions of crystalline AA before His becomes limiting. It is important to acknowledge that the NRC (2012) AA requirement estimates for nursery pigs, with the exception of Lys, are based on a factorial approach established by estimating the requirements for maintenance and growth rather than empirical studies. Moreover, in a summary of His requirement trials provided by the NRC (2012), only the early study of Izquierdo et al. (1988) is mentioned, clearly demonstrating the lack of research in this area.

The exact mode of action for the reduction in feed intake when pigs are fed diets deficient in histidine remains unknown. Histidine is a precursor of histamine, a neurotransmitter that plays an important role in appetite regulation (Kurose and Terashima, 1999). Dietary intake of neurotransmitter precursors is critical for normal growth. For instance, the amount of dietary Trp, a precursor of serotonin, has a profound effect on feed intake (Ettle and Roth, 2004; Gonçalves et al., 2015). Excessive neural histamine has been reported to suppress feed intake through H_1 receptors in the brain satiety centers, namely, ventromedial hypothalamic nucleus and paraventricular nucleus (Sakata et al., 1997). High levels of dietary L-His (Kasaoka et al., 2004) or injection of L-His (Sheiner et al., 1985; Yoshimatsu et al., 2002) have been shown to cause acute anorectic effects in rats. In the current study, we did not observe reduction in intake even when the highest levels of His were fed. It seems that a substantial amount of dietary L-His is required to provoke anorectic effects (Okusha et al., 2017). In our study, pigs fed diets with low SID His:Lys presented a dramatic decrease in intake, which is similar to that observed by Li (2002), Gloaguen et al. (2013), and Wessels et al. (2016) and seems to be the primary responsible for decreased growth performance. Radcliffe and Morrison (1981) observed a decrease in feed intake in rats fed His-free diets and Tobin and Boorman (1978) reported that the infusion of L-His in cockerels receiving a His deficient diet resulted in increased feed intake. Interestingly, knock-out mice, unable to synthesize histamine, presented no differences in caloric intake and BW compared with normal mice (Provensi et al., 2016). At this point, it is unclear whether histamine is involved in the anorectic response of pigs fed low His diets.

We observed compensatory growth, defined as an accelerated gain that occurs after a period of nutritional restriction (Heyer and Lebret, 2007), during the post-test period. Pigs previously fed the low SID His:Lys ratio diets had improved ADG (Exp. 1) and G:F (Exp. 1 and 2). The reasons for differences in post-treatment growth performance between experiments as well as the ADFI response in Exp. 2 are unclear. Nevertheless, the improvement in growth performance in the post-test period was not enough to change the overall results. Interestingly, pigs fed diets deficient in Ile (Clark et al., 2017a) and Val (Clark et al., 2017b) did not show evidence of compensatory growth during the post-test period.

In summary, our results suggest that the SID His required to optimize growth performance is no more than 31% of Lys for 7- to 11-kg pigs. The SID His requirement estimates observed in these studies are lower than the current NRC (2012) estimates of 34% of Lys. Therefore, low CP- and AA-fortified nursery diets can be balanced to meet the pig's SID His:Lys ratio requirement for growth performance, allowing for greater use of the currently available feed-grade AA.

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