Ann. Anim. Sci., Vol. 18, No. 2 (2018) 441–452 *DOI: 10.1515/aoas-2017-0040*

DE GRUYTER
OPEN

IMPROVED MILK GLUTAMINE LEVEL AND GROWTH PERFORMANCE OF SUCKLING PIGLETS BY GLUTAMINE SUPPLEMENTATION IN MATERNAL DIET*

X.F. Yang, J.F. Qin, L. Wang, K.G. Gao, C.T. Zheng, L. Huang, Z.Y. Jiang♦

Institute of Animal Science, Guangdong Academy of Agricultural Sciences, Guangzhou, 510640, P. R. China
♦Corresponding author: jiangzy@gdaas.cn

Abstract

Glutamine plays an important role in neonatal growth and health. It is unknown whether supplementing the lactating sows' diet with glutamine will benefit the growth performance and intestinal development of suckling piglets through increasing content of milk glutamine. A total of 24 lactating sows (Large White) were fed diets supplemented with/without 1% glutamine throughout the 21-d lactation. Feed intake of the sows was recorded, blood and milk samples were collected. Piglets were weighed at birth and weaning, one piglet randomly selected from each litter was sacrificed for morphological analysis of the small intestine. Average daily feed intake of the sows did not differ between control and glutamine groups. Concentrations of total protein and urea nitrogen in sows' serum was increased by glutamine at d 14 of lactation (P<0.05). Contents of glutamine in both plasma and milk of sows were significantly increased by glutamine supplementation throughout lactation (P<0.01). Concentrations of proline, citrulline, valine, isoleucine, leucine, and arginine in sows' plasma were increased by glutamine supplementation (all P<0.05). Milk yield was increased by glutamine supplementation at d 14 and 21 of lactation (P<0.05). Supplementing the lactating sows' diet with glutamine increased average daily gain (P=0.006), weaning weight (P=0.032), as well as villous height and ratio of villous height:crypt depth in duodenum of the suckling piglets (both P<0.05). Collectively, supplementing lactating sows' diet with 1% glutamine significantly improved the growth performance of suckling piglets through elevating milk yield and glutamine content in the milk.

Key words: glutamine, lactating sows, suckling piglet, intestinal development

The importance of milk glutamine for suckling piglets is generally appreciated (Remillard et al., 1998; Reeds and Burrin, 2001). Accounting for approximately 20%

*The present study was financially supported by National Basic Research Program of China (2013CB127304), China Agriculture Research System (CARS-35), and Guangdong International Science and Technology Cooperation Program (2013B050800016).

of all amino acids in the circulation, glutamine functions as a nitrogen and amine carrier among tissues and organs, and is also widely considered to be the most important glycogenic amino acid (Souba and Wilmore, 1985; Stumvoll et al., 1999). Glutamine is mainly metabolized in intestinal and immune cells as an energy source and substrate for biosynthesis of citrulline, pyrimidines and purines (Wu et al., 2016). Glutamine is also important in the regulation of acid-base balance and thus prevents metabolic acidosis (Wu et al., 1997; Boza et al., 2000; Hulsewe et al., 2004). It has been demonstrated that glutamine is necessary in the critically ill to stimulate DNA synthesis and increase mucosal mass when endogenous supply of glutamine is insufficient (Lacey and Wilmore, 1990). Oral administration of glutamine (0.5 g/kg BW; twice daily) to 7- to 21-d-old sucking piglets increases their growth performance by 12% (Haynes et al., 2009), indicating that augmenting glutamine content beyond that obtained from milk is beneficial for improving growth performance of the young pigs.

The content of free glutamine in sows' milk increases the most among all free amino acids during lactation, and becomes the most abundant free amino acid in milk during late lactation (Wu and Knabe, 1994; Wu et al., 2010). Increased export of glutamine into milk, however, exacerbates mobilization of tissue protein in sows (Clowes et al., 2005), which will further compromise milking and reproductive performance of the sows as well as growth performance and health status of the piglets. Supplementing the lactating sows' diet with a mixture of glutamine and glutamate has been shown to increase content of glutamine in the milk (Manso et al., 2012; Aquino et al., 2014). It is likely that supplementing lactating sows' diet with glutamine may therefore improve growth of suckling piglets. The present study was designed to investigate the effect of supplementing lactating sows' diet with glutamine on intestinal development and growth performance of suckling piglets.

Material and methods

Animals and diets

The protocol for the present research was approved by the Animal Experimental Committee of the Institute of Animal Science, Guangdong Academy of Agricultural Sciences.

A total of 24 gestating sows (Large White) with similar expected farrowing dates were assigned according to parity (parity 3 to 5) into 2 treatments (12 sows each). All sows were transferred into a farrowing house with temperature control, adequate lying area and free access to water 7 d before expected delivery. Experimental diets supplemented with 1% glutamine or 1.22% alanine (isonitrogenous control) were provided to sows 1 d before parturition through weaning at 21 d of lactation. The diets (Table 1) were formulated using primarily corn and soybean meal, based on NRC (1998) requirements.

Table 1. Composition and nutrient levels of the experimental diets (as-fed basis)

Ingredients contents (%)	Control	Glutamine
Corn	51.54	51.86
Soybean meal	24.50	24.50
Fish meal	4.00	4.00
Wheat bran	8.00	8.00
Soybean oil	5.20	5.10
Limestone	0.90	0.90
Calcium phosphate	1.20	1.20
L-Glutamine	-	1.00
Alanine	3.66	2.44
Premix[1]	1.00	1.00
Total	100.00	100.00
Nutrient levels[2]		
DE (MJ/kg)	14.02	14.02
CP (%)	22.30	22.32
EF (%)	8.09	8.00
Ca (%)	0.85	0.85
Available P (%)	0.44	0.44
Lys (%)	1.04	1.04
Met+Cys (%)	0.58	0.59
Thr (%)	0.72	0.72
Trp (%)	0.22	0.22
Arg (%)	1.26	1.26
Val (%)	0.88	0.88
Gln+Glu (%)	3.26	4.24

[1]Provided per kg of diet: vitamin A – 25,000 IU; vitamin D_3 – 3,000 IU; vitamin E – 65 mg; vitamin K – 5 mg; thiamine – 5 mg; riboflavin – 12.5 mg; niacin – 50 mg; D-pantothenic acid – 25 mg; pyridoxine – 5 mg; choline chloride – 750 mg; vitamin B_{12} – 37.5 µg; folic acid – 2.15 mg; biotin – 0.10 mg; cobalt – 0.15 mg (as $CoSO_4 \cdot 7H_2O$); copper – 8 mg (as $CuSO_4 \cdot 5H_2O$); manganese – 35 mg (as MnO_2); iron – 60 mg (as $FeSO_4 \cdot 7H_2O$); zinc – 60 mg (as ZnO); iodine – 0.35 mg (as KI); and selenium – 0.3 mg (as Na_2SeO_3).

[2]Value for crude protein (CP) was analyzed; other values were calculated from the China Feed-database (2009, http://www.chinafeeddata.org.cn/).

Feeding and sample collection

Daily feed intake of each sow was recorded to calculate average daily feed intake (ADFI). Milk yield was measured from 09:30 through 21:30 at d 7, 14, and 21 of lactation, using 4 randomly selected sows from each treatment; measurement was done by the standard weigh-suckle-weigh method.

Litter size of each sow was adjusted to 10 piglets within 48 h of parturition by cross-fostering. No creep feed was offered to piglets during the experiment. Body weight (BW) of each piglet at birth and at weaning was recorded to calculate average daily gain (ADG).

Chemical analyses

Blood was sampled from the marginal ear vein of each sow, at 09:00 (2 h after feeding), on d 1, 7, 14 and 21 of lactation. Plasma and serum were collected and stored at –80°C for subsequent analyses. Milk was collected at 08:00 on d 1, 7, 14 and 21 of lactation from 4 randomly selected sows per treatment. The entire udder was completely milked, 20 units of oxytocin was injected when needed. Aliquots of the well-mixed milk were stored at –80°C until analyzing.

Concentrations of selected free amino acids (glutamine, proline, citrulline, valine, isoleucine, leucine, ornithine and arginine) in milk and plasma of sows were measured using an automatic amino acid analyzer (Hitachi 8800, Tokyo, Japan) in accordance with the manufacturer's instructions. A Milkoscan FT 120 (Foss Electric, Hillerød, Denmark) was used to measure milk composition (lactoprotein, milk fat, lactose, and non-fat solids) following the manufacturer's instructions. Total protein, urea nitrogen and albumin in serum were determined by an automatic biochemistry analyzer (Synchron CX5, Beckman Coulter, Brea, CA).

Intestinal morphology of suckling piglets

One randomly selected piglet per sow (n = 12) was euthanatized with an overdose of i.v. sodium pentobarbital on d 21, segments (1 to 2 cm) at the middle of the duodenum, jejunum and ileum were collected and fixed in 10% neutral buffered formalin. Samples were further processed and stained with hematoxylin and eosin, as described by Nabuurs et al. (1993). Villous height and crypt depth were measured using an image processing and analysis system (Optimus version 6.5 software, Media Cybernetics, North Reading, MA) and ratio of villous height : crypt depth was calculated.

Data analysis and statistics

All data are presented as means with pooled SEM. Each sow was taken as the experimental unit with multiple within-sow measurements, e.g. piglet weight, being averaged. The effect of glutamine supplementation was analyzed using Student's t test (SAS Inst. Inc., Cary, NC). Probability values less than 0.05 were considered to be statistically significant.

Results

Feed intake and biochemical variables in blood of lactating sows

ADFI of the sows did not differ between the glutamine-supplemented and control pigs (4.48 vs. 4.43 kg, $P>0.05$). Contents of total protein ($P=0.006$) and urea nitrogen ($P=0.043$) in serum were significantly increased by glutamine supplementation at d 14 of lactation (Table 2). Contents of albumin in serum did not differ between glutamine-supplemented and control sows throughout the experiment.

Concentrations of free amino acids in plasma of lactating sows, as affected by glutamine supplementation, are shown in Table 3. Compared with the controls, di-

etary glutamine supplementation increased the concentration of glutamine in the plasma of sows at d 1, 7, 14, and 21 of lactation (all P<0.01). Concentrations of proline (at d 1 and 21, both P<0.001), citrulline (at d 7, P=0.043), valine (at d 1, P=0.001), isoleucine (at d 1 and 21, both P<0.05), leucine (at d 1 and 21, both P<0.05) and arginine (at d 21, P<0.000) in sows' plasma were also increased by glutamine supplementation when compared with the controls.

Table 2. Effect of dietary glutamine supplementation on biochemical variables in the serum of sows at d 1, 7, 14 and 21 of lactation

Variables	Treatment		Pooled SEM	P-value
	control	glutamine		
Total protein (g/L)				
d 1	64.638	82.628	9.260	0.183
d 7	85.600	92.570	2.693	0.081
d 14	83.430	94.655	2.634	0.006
d 21	84.676	91.700	3.331	0.150
Albumin (g/L)				
d 1	18.196	18.415	1.032	0.882
d 7	18.618	19.930	1.316	0.488
d 14	18.554	18.030	1.041	0.725
d 21	18.436	18.990	1.216	0.750
Urea nitrogen (mmol/L)				
d 1	6.968	7.858	0.461	0.186
d 7	9.346	9.710	0.715	0.722
d 14	8.620	10.578	0.644	0.043
d 21	9.284	9.988	0.886	0.580

Data are means with pooled SEM, n = 12.

Table 3. Effect of dietary glutamine supplementation on concentrations of free amino acids in the plasma of sows at d 1, 7, 14 and 21 of lactation

AA (nmol/mL)	Treatment		Pooled SEM	P-value
	control	glutamine		
1	2	3	4	5
Glutamine				
d 1	218.699	450.698	21.012	<0.001
d 7	346.530	527.710	34.429	0.001
d 14	435.990	905.440	40.478	<0.001
d 21	551.400	1359.300	121.664	0.000
Proline				
d 1	209.050	482.430	36.528	<0.001
d 7	393.200	507.050	47.458	0.104
d 14	418.220	606.400	70.603	0.073
d 21	418.980	754.930	61.280	<0.001

Table 3 – contd.

1	2	3	4	5
Citrulline				
d 1	62.370	89.890	9.649	0.056
d 7	70.870	184.820	37.518	0.043
d 14	132.620	110.600	21.728	0.481
d 21	150.090	119.310	25.713	0.407
Valine				
d 1	236.390	464.240	43.691	0.001
d 7	390.620	501.600	66.042	0.247
d 14	498.000	489.000	92.985	0.946
d 21	432.800	613.100	91.897	0.179
Isoleucine				
d 1	105.840	173.590	18.166	0.015
d 7	163.300	182.5100	26.961	0.619
d 14	175.180	196.190	37.974	0.699
d 21	136.410	279.160	36.571	0.011
Leucine				
d 1	147.630	299.260	26.154	<0.001
d 7	277.300	305.160	41.369	0.639
d 14	288.600	339.150	61.339	0.566
d 21	244.560	465.000	58.700	0.014
Ornithine				
d 1	125.240	192.050	29.165	0.120
d 7	203.270	209.750	24.640	0.854
d 14	167.720	229.570	46.301	0.355
d 21	176.080	224.180	24.696	0.182
Arginine				
d 1	94.260	151.040	34.534	0.257
d 7	185.440	186.920	39.305	0.979
d 14	171.670	270.870	39.767	0.092
d 21	121.630	354.520	38.836	<0.001

Milk yield and composition, and contents of free amino acids in milk of lactating sows

As shown in Table 4, milk yield at d 14 and 21 was greater in sows fed the glutamine-supplemented diet, compared with control sows (both $P<0.05$). However, there was no significant difference between sows supplemented with glutamine and controls in milk composition (contents of lactoprotein, milk fat, lactose, or non-fat solids) throughout the experimental period.

Concentrations of free amino acids in milk are presented in Table 5. Content of glutamine in milk of glutamine-treated sows was significantly higher than in the controls at d 1, 7, 14, and 21 of lactation (all $P<0.01$). With the exception of valine and leucine, which were significantly decreased by glutamine-supplementation at d 21 (both $P<0.05$), the concentrations of proline, isoleucine, ornithine, and arginine in sows' milk were essentially unaffected by glutamine treatment.

Table 4. Effect of dietary glutamine supplementation on milk yield and composition of sows at d 1, 7, 14 and 21 of lactation

Variables	Treatment		Pooled SEM	P-value
	control	glutamine		
Milk yield (kg)				
d 1	-	-	-	-
d 7	6.263	6.708	1.261	0.805
d 14	9.510	12.850	1.089	0.041
d 21	10.360	12.500	0.680	0.037
Lactoprotein (%)				
d 1	16.250	15.050	0.811	0.307
d 7	5.330	5.870	0.296	0.210
d 14	5.570	5.210	0.203	0.223
d 21	4.670	4.970	0.200	0.300
Milk fat (%)				
d 1	4.750	4.300	0.675	0.642
d 7	6.490	9.770	1.136	0.053
d 14	7.510	8.275	0.661	0.422
d 21	7.150	8.710	0.609	0.084
Lactose (%)				
d 1	3.770	3.930	0.248	0.653
d 7	6.170	5.280	0.384	0.116
d 14	5.210	5.880	0.470	0.324
d 21	6.410	5.580	0.309	0.071
Non-fat solids (%)				
d 1	21.730	20.050	1.047	0.269
d 7	11.530	11.410	0.726	0.908
d 14	10.390	11.350	0.548	0.229
d 21	11.050	10.810	0.266	0.530

Table 5. Effect of dietary glutamine supplementation on concentrations of free amino acids in the milk of sows at d 1, 7, 14 and 21 of lactation*

AA (nmol/mL)	Treatment		Pooled SEM	P-value
	control	glutamine		
1	2	3	4	5
Glutamine				
d 1	132.130	313.100	22.421	<0.001
d 7	2088.300	4519.700	101.131	<0.001
d 14	2439.100	3664.100	214.982	0.001
d 21	2298.900	3947.000	154.156	<0.001
Proline				
d 1	99.880	85.200	52.103	0.844
d 7	214.080	223.930	51.143	0.893
d 14	118.600	140.530	36.737	0.677
d 21	211.00	243.100	30.699	0.468

Table 5 – contd.

1	2	3	4	5
Valine				
d 1	44.300	52.680	17.406	0.737
d 7	106.350	98.880	11.144	0.640
d 14	57.250	60.480	11.687	0.847
d 21	71.350	49.000	7.361	0.043
Isoleucine				
d 1	7.000	12.675	4.110	0.340
d 7	31.350	45.575	6.859	0.157
d 14	23.800	22.475	4.136	0.823
d 21	47.800	42.230	12.124	0.748
Leucine				
d 1	75.650	57.350	23.300	0.584
d 7	112.230	154.500	16.773	0.089
d 14	74.650	79.130	14.921	0.834
d 21	231.980	85.270	9.784	<0.001
Ornithine				
d 1	-	-	-	-
d 7	55.300	65.620	9.654	0.458
d 14	55.270	62.900	15.723	0.735
d 21	57.280	124.170	26.173	0.084
Arginine				
d 1	-	-	-	-
d 7	208.950	218.300	14.529	0.654
d 14	133.950	160.60	25.708	0.471
d 21	164.050	127.070	29.133	0.379

*Citrulline was undetectable.

Growth performance and intestinal development of suckling piglets

Compared with the controls, supplementing the lactating sows' diet with glutamine significantly increased ADG (120% that of controls, P=0.006) and weaning weight (5.32 vs. 6.04 kg, P=0.032) of suckling piglets (Table 6). Glutamine supplementation significantly increased villous height and ratio of villous height:crypt depth in duodenum (both P<0.05), crypt depth in duodenum and ileum (both P<0.05) of suckling piglets, compared to their control counterparts (Table 7). The ratio of villous height:crypt depth was decreased by glutamine treatment in ileum (P=0.002).

Table 6. Effect of supplementing glutamine in lactating sows' diet on growth performance of suckling piglets

Variables	Treatment		Pooled SEM	P-value
	control	glutamine		
Birth weight (kg)	1.361	1.430	0.077	0.533
Weaning weight (kg)	5.315	6.036	0.222	0.032
ADG (kg/d)	0.198	0.237	0.009	0.006

Table 7. Effect of supplementing glutamine in lactating sows' diet on intestinal morphology of suckling piglets

Variables	Treatment		SEM	P-value
	control	glutamine		
Villous height (μm)				
duodenum	309.10	438.70	29.97	0.006
jejunum	301.30	302.80	20.64	0.959
ileum	392.00	297.70	38.60	0.098
Crypt depth (μm)				
duodenum	218.30	242.10	6.99	0.025
jejunum	168.00	168.50	10.61	0.974
ileum	116.70	158.50	7.28	<0.001
Villus:Crypt*				
duodenum	1.45	1.82	0.12	0.040
jejunum	1.84	1.81	0.16	0.896
ileum	3.40	1.73	0.34	0.002

*Villous height:Crypt depth.

Discussion

The data obtained in the present study showed that supplementing the lactating sow's diet with 1% glutamine increased milk yield and content of free glutamine in milk, which is presumed to account for improved growth performance and development of the intestinal mucosa of the suckling piglets. The beneficial effects of elevated milk glutamine on suckling piglets are consistent with previous studies for piglets offered diets supplemented with glutamine (Wu et al., 1996; Wang et al., 2008; Haynes et al., 2009; Cabrera et al., 2013).

Accounting for approximately one-half of the whole body pool of free amino acids (Souba and Wilmore, 1985; Stumvoll et al., 1999), glutamine is the most abundant amino acid in blood and intracellular fluids. At low dietary levels, most ingested glutamine is catabolized by the visceral tissues and fails to enter the peripheral circulation; the large pool of glutamine within the body is essentially synthesized *de novo* (Squires and Brosnan, 1983; Hankard et al., 1995; Wu et al., 2007; Wu et al., 2013). In the present study, plasma concentration of glutamine was markedly increased by dietary supplementation with 1% glutamine in lactating sows, which is consistent with findings in weaning piglets (Wang et al., 2008) and rats (Boza et al., 2001). Manso (2012) reported that compared with the negative control, dietary supplementation with 2.5% AminoGut, Ajinomoto (a commercial glutamine product, which was indicated to contain 10% free glutamine and 10% glutamic acid) significantly increased plasma content of glutamine plus glutamate at 21 d post-farrowing in lactating gilts, while supplementation with 2.5% L-glutamine did not have such effect in the gilts. We also found in a pilot study that, compared with dietary supplementation of 1% glutamine, 3% glutamine tended to have no better effect in increasing plasma glutamine content (unpublished data). These results suggest that the glutamine ef-

fects were concentration-dependent and appeared to diminish when a high level of glutamine was used.

Intestinal uptake of glutamine is mediated by discrete sodium-dependent and sodium-independent glutamine transport systems, located in the brush border membrane (Wilde and Kilberg, 1991; Broer, 2008). Upon entering enterocytes, glutamine is either metabolized intracellularly or is released across the basolateral membrane as free amino acid or metabolites to reach the portal and then systemic circulations (Watford, 1994; Arnaud et al., 2004). It would be reasonable to infer that the abundant glutamine present in intestinal lumen in supplemented animals increases the absorption or uptake of glutamine. Under normal conditions, most of the glutamine in blood of mammalian species is endogenously synthesized. Attempts to determine the turnover rate of glutamine in the body have yielded values of 1,300 to 3,800 μmol/kg/h in rats and 180 to 500 μmol/kg/h in humans (Squires and Brosnan, 1983; Kreider et al., 1997). The large amount of endogenous glutamine emphasizes the importance of *de novo* glutamine synthesis. Therefore, both endogenous and exogenous sources of glutamine contribute to the glutamine pool in blood and changes in either will cause fluctuations. The objective of the present study was to increase milk glutamine by maternal dietary supplementation. The strategy was clearly effective, with the increase of glutamine in sows' milk reflecting the change in concentration of glutamine in plasma. This outcome was consistent with Aquino et al. (2014) who also found that supplementing lactating sows' diet with a mixture of glutamine and glutamate lead to increased milk glutamine throughout lactation.

In the present study, dietary glutamine supplementation also increased the concentrations of other amino acids in sows' plasma, particularly those of proline, citrulline, valine, isoleucine, leucine and arginine. There is evidence that the small intestine can take up and use glutamine while releasing arginine, alanine, citrulline, glutamate and proline into the circulatory system (Wu et al., 1994). The effect of glutamine supplementation on other amino acids in milk was much less evident than in plasma. Indeed, concentrations of valine and leucine in milk were significantly decreased in glutamine-treated sows. The high level of glutamine in plasma and milk may suppress the secretion of leucine by the mammary gland since the two amino acids share a common transport system in the cell membrane and each inhibits transport of the other (Lynch and McGivan, 1987; Pacitti et al., 1993). It is presumed that the increased milk consumed by the piglets (expressed as sows' milk yield) may result in identical amounts of valine and leucine transported to the piglets, as no adverse effect was induced by the lower concentrations of blood valine and leucine on growth performance of the suckling piglets. Nevertheless, net fluxes of free amino acids in both blood and milk of the sows needed to be determined to better show the changes introduced by glutamine supplementation. Despite the changes in concentrations of milk glutamine, valine and leucine, milk proximate composition was not influenced by dietary glutamine supplementation, whereas Aquino et al. (2014) reported that milk fat content was increased by supplementation of AminoGut, Ajinomoto. It is a limitation that concentrations of other amino acids, especially that of glutamate, were not included in the present study. Full spectrum of amino acids should be presented in further studies to better clarify the mechanism of amino acids functioning.

Conclusion

Supplementation of 1% glutamine into lactating sow's diet increased plasma and milk glutamine, which resulted in enhanced growth performance of the suckling piglets.

Acknowledgements

We gratefully acknowledge Dr. W. B. Currie (Cornell University, Ithaca, NY) for suggestions on manuscript presentation.

References

Aquino R.S., Dutra W.M., Manso H.E.C.C., Manso Filho H.C., Kutschenko M., Nogueira E.T., Watford M. (2014). Glutamine and glutamate (AminoGut) supplementation influences sow colostrum and mature milk composition. Livest. Sci., 169: 112–117.

Arnaud A., Ramirez M., Baxter J.H., Angulo A.J. (2004). Absorption of enterally administered N-acetyl-l-glutamine versus glutamine in pigs. Clin. Nutr., 23: 1303–1312.

Boza J.J., Moennoz D., Bournot C.E., Blum S., Zbinden I., Finot P.A., Ballevre O. (2000). Role of glutamine on the *de novo* purine nucleotide synthesis in Caco-2 cells. Europ. J. Nutr., 39: 38–46.

Boza J.J., Turini M., Moennoz D., Montigon F., Vuichoud J., Gueissaz N., Gremaud G., Pouteau E., Piguet-Welsch C., Finot P.A., Ballèvre O. (2001). Effect of glutamine supplementation of the diet on tissue protein synthesis rate of glucocorticoid-treated rats. Nutrition, 17: 35–40.

Broer S. (2008). Amino acid transport across mammalian intestinal and renal epithelia. Physiol. Rev., 88: 249–286.

Cabrera R.A., Usry J.L., Arrellano C., Nogueira E.T., Kutschenko M., Moeser A.J., Odle J. (2013). Effects of creep feeding and supplemental glutamine or glutamine plus glutamate (Aminogut) on pre- and post-weaning growth performance and intestinal health of piglets. J. Anim. Sci. Biotechnol., 4: 29.

Clowes E.J., Aherne F.X., Baracos V.E. (2005). Skeletal muscle protein mobilization during the progression of lactation. Am. J. Physiol. Endocrin. Metab., 288: E564–E572.

Hankard R.G., Darmaun D., Sager B.K., D'Amore D., Parsons W.R., Haymond M. (1995). Response of glutamine metabolism to exogenous glutamine in humans. Am. J. Physiol., 269: E663–670.

Haynes T.E., Li P., Li X., Shimotori K., Sato H., Flynn N.E., Wang J., Knabe D.A., Wu G. (2009). L-glutamine or L-alanyl-L-glutamine prevents oxidant- or endotoxin-induced death of neonatal enterocytes. Amino Acids, 37: 131–142.

Hulsewe K.W., van der Hulst R.W., van Acker B.A., von Meyenfeldt M.F., Soeters P.B. (2004). Inflammation rather than nutritional depletion determines glutamine concentrations and intestinal permeability. Clin. Nutr., 23: 1209–1216.

Kreider M.E., Stumvoll M., Meyer C., Overkamp D., Welle S., Gerich J. (1997). Steady-state and non-steady-state measurements of plasma glutamine turnover in humans. Am. J. Physiol., 272: E621–627.

Lacey J.M., Wilmore D.W. (1990). Is glutamine a conditionally essential amino acid? Nutr. Rev., 48: 297–309.

Li N., Liboni K., Fang M.Z., Samuelson D., Lewis P., Patel R., Neu J. (2004). Glutamine decreases lipopolysaccharide-induced intestinal inflammation in infant rats. Am. J. Physiol. Gastr. L., 286: G914–921.

Lynch A.M., McGivan J.D. (1987). Evidence for a single common Na+-dependent transport system for alanine, glutamine, leucine and phenylalanine in brush-border membrane vesicles from bovine kidney. Biochim. Biophys. Acta, 899: 176–184.

Manso H., Filho H., Carvalho L., Kutschenko M., Nogueira E., Watford M. (2012). Glutamine and glutamate supplementation raise milk glutamine concentrations in lactating gilts. J. Anim. Sci. Biotechnol., 3: 2.

Nabuurs M.J.A., Hoogendoorn A., van der Molen E.J., van Osta A.L.M. (1993). Villus height and crypt depth in weaned and unweaned pigs, reared under various circumstances in the Netherlands. Res. Vet. Sci., 55: 78–84.

National Research Council (US) Subcommittee on Swine Nutrition (1998). Nutrient requirements of swine. National Academy Press, Washington.

Pacitti A.J., Inoue Y., Souba W.W. (1993). Characterization of Na(+)-independent glutamine transport in rat liver. Am. J. Physiol., 265: G90–98.

Reeds P.J., Burrin D.G. (2001). Glutamine and the bowel. J. Nutr., 131: 2505S–2508S.

Remillard R.L., Guerino F., Dudgeon D.L., Yardley J.H. (1998). Intravenous glutamine or limited enteral feedings in piglets: amelioration of small intestinal disuse atrophy. J. Nutr., 128: 2723S–2726S.

Souba W.W., Wilmore D.W. (1985). Gut-liver interaction during accelerated gluconeogenesis. Arch. Surg., 120: 66–70.

Squires E.J., Brosnan J.T. (1983). Measurements of the turnover rate of glutamine in normal and acidotic rats. Biochem. J., 210: 277–280.

Stumvoll M., Perriello G., Meyer C., Gerich J. (1999). Role of glutamine in human carbohydrate metabolism in kidney and other tissues. Kidney Int., 55: 778–792.

Wang J., Chen L., Li P., Li X., Zhou H., Wang F., Li D., Yin Y., Wu G. (2008). Gene expression is altered in piglet small intestine by weaning and dietary glutamine supplementation. J. Nutr., 138: 1025–1032.

Watford M. (1994). Glutamine metabolism in rat small intestine: synthesis of three-carbon products in isolated enterocytes. Biochim. Biophys. Acta, 1200: 73–78.

Wilde S.W., Kilberg M.S. (1991). Glutamine transport by basolateral plasma-membrane vesicles prepared from rabbit intestine. Biochem. J., 277: 687–691.

Wu G., Knabe D.A. (1994). Free and protein-bound amino acids in sow's colostrum and milk. J. Nutr., 124: 415–424.

Wu G., Borbolla A.G., Knabe D.A. (1994). The uptake of glutamine and release of arginine, citrulline and proline by the small intestine of developing pigs. J. Nutr., 124: 2437–2444.

Wu G., Meier S.A., Knabe D.A. (1996). Dietary glutamine supplementation prevents jejunal atrophy in weaned pigs. J. Nutr., 126: 2578–2584.

Wu G., Davis P.K., Flynn N.E., Knabe D.A., Davidson J.T. (1997). Endogenous synthesis of arginine plays an important role in maintaining arginine homeostasis in postweaning growing pigs. J. Nutr., 127: 2342–2349.

Wu G., Bazer F.W., Johnson G.A., Knabe D.A., Burghardt R.C., Spencer T.E., Li X.L., Wang J.J. (2010). Important roles for L-glutamine in swine nutrition and production. J. Anim. Sci., 89: 2017–2030.

Wu G., Wu Z., Dai Z., Yang Y., Wang W., Liu C., Wang B., Wang J., Yin Y. (2013). Dietary requirements of "nutritionally non-essential amino acids" by animals and humans. Amino Acids, 44: 1107–1113.

Wu M., Xiao H., Liu G., Chen S., Tan B., Ren W., Bazer F.W., Wu G., Yin Y. (2016). Glutamine promotes intestinal SIgA secretion through intestinal microbiota and IL-13. Mol. Nutr. Food Res., 60: 1637–1648.

Wu G.Y., Bazer F.W., Davis T.A., Jaeger L.A., Johnson G.A., Kim S.W., Knabe D.A., Meininger C.J., Spencer T.E., Yin Y.L. (2007). Important roles for the arginine family of amino acids in swine nutrition and production. Livest. Sci., 112: 8–22.

Received: 3 VII 2017
Accepted: 22 XI 2017