



Dietary supplementation of guanidinoacetic acid for sows and their progenies: Performance, blood parameters and economic viability at nursery phase



I.B. Mendonça^a, P.H. Watanabe^{a,*}, B.A.N. Silva^b, M.M. Boiago^c, J.C. Panisson^d, T.S. Andrade^a, A.C.N. Campos^a, M.A.S.P. Mello^b

^a Animal Science Department/Departamento de Zootecnia, Universidade Federal do Ceará, Fortaleza, CE 60356-001, Brasil

^b Institute of Agricultural Sciences/Instituto de Ciências Agrárias, Universidade Federal de Minas Gerais, Montes Claros, MG 39404-547, Brasil

^c Animal Science Department/Departamento de Zootecnia, Universidade do Estado de Santa Catarina, Chapecó, SC 89815-630, Brasil

^d Animal Science Department/Departamento de Zootecnia, Universidade Federal do Paraná, Curitiba, PR 80035-050, Brasil

ARTICLE INFO

Keywords:

Creatine kinase
Creatinine
Guanidinoacetate

ABSTRACT

The aim of this study was to evaluate the effects of guanidinoacetic acid supplementation for sows and their litter on performance, blood parameters and economic viability of piglets at nursery phase. A total of 80 high-prolific mixed-parity sows from 3rd and 4th parity were randomly distributed between two treatments: control diet and diet supplemented with 0.1% guanidinoacetic acid. Sows were fed with the dietary treatments during the gestation and lactation. Piglets were weaned at 23 days of age and then distributed in a randomized block design, in a 2 × 2 factorial arrangement, considering two diets for the sows during gestation and lactation (control diet and diet supplemented with 0.1% GAA) and two diets for the piglets at nursery phase (control diet and diet supplemented with 0.1% GAA). Each treatment consisted of six replicates, being the pen with 40 animals considered as experimental unit. No interaction between guanidinoacetic acid supplementation for sows during the gestation and lactation and for their progenies was observed ($P > 0.05$) on performance and blood levels of creatinine and creatine kinase of the piglets during the nursery phase. The isolated factors also did not influence ($P > 0.05$) these parameters. There was no interaction between guanidinoacetic acid supply for sows and their progenies on economic evaluation. Piglets that received dietary supplementation of 0.1% guanidinoacetic acid presented higher average feed cost per kilogram of body weight and cost index, and also lower economic efficiency index. Dietary supplementation of 0.1% guanidinoacetic acid for sows and their litters does not influence performance and blood parameters of piglets during the nursery phase, and is economically unfeasible.

1. Introduction

The current genetic selection programs used in pig farming seek prolific sows, with potential to produce numerous litters, resulting in greater number of weaned animals/female/year. However, this advance has generated some negative aspects, such as piglets with low birth weight and high weight variability within the litters (Wolf et al., 2008). In the subsequent phases, these animals generally present worse performance, with reduction in daily weight gain, lower weights at weaning and nursery phase, with consequent increase in slaughter age (Gondret et al., 2006).

Aiming to solve these inherent failures in pig farming advances, many researches involving the nutrition of sows and their litter have been performed, with focus on nutritional additives that aim to improve

their performance. Among these additives, the guanidinoacetic acid (GAA) has stood out because it acts as an arginine-sparing compound, which can be used in others body functions. In this sense, the increased availability of arginine in the body can promote a greater vascularization in the placenta and mammary gland of pregnant and lactating sows, through the synthesis of nitric oxide, providing greater transfer of nutrients to its progenies and, consequently, increasing their weight (Mateo et al., 2008; Moreira et al., 2018).

Furthermore, arginine plays an essential role in the maximization of body development in piglets, because it acts directly on protein turnover, promoting a greater anabolism and attenuating catabolism (Kim and Wu, 2004; Wu et al., 2007).

The GAA also provides a higher creatine content in the liver and muscles, since it participates in the synthesis of this compound (Liu

* Corresponding author.

E-mail address: pedrowatanabe@ufc.br (P.H. Watanabe).

<https://doi.org/10.1016/j.livsci.2019.07.011>

Received 3 December 2018; Received in revised form 1 July 2019; Accepted 7 July 2019

Available online 08 July 2019

1871-1413/ © 2019 Elsevier B.V. All rights reserved.

et al., 2015; Mcbreairty et al., 2015; Ostojic et al., 2016). A higher content of this protein in the body can indirectly promote an increase in muscle mass, because it stimulates an influx of water into the muscle cells, inducing protein synthesis and reducing proteolysis (Janicki and Buzala, 2013).

Studies evaluating the use of GAA in pig diets are scarce and the results have been variable (He et al., 2018; Jayaraman et al., 2018; Teixeira et al., 2017; Wang et al., 2012). In addition, no information about the possible implications of this additive for pregnant and lactating sows and for their progenies on piglets development at nursery phase is provided, and whether the dietary addition of GAA is economically viable in pig industry. Therefore, the objective of this study was to evaluate the effects of dietary supplementation of 0.1% GAA for sows and their litter on performance, blood parameters and economic viability of piglets at nursery phase.

2. Material and methods

All methods involving animal handling were performed in accordance with the protocol approved by the Committee of Ethic in Animal Research of the Federal University of Ceará and followed guidelines stated in the Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching (FASS, 2010).

The study was performed in the facilities of a commercial farm, located in the Southern region of Brazil, in Santa Catarina state, during the period between December 2017 and May 2018.

2.1. Animals and experimental design

A total of 80 multiparous sows (3rd and 4th parity order) of a high-prolificacy commercial genetic line (Landrace × Large White), were selected considering body weight and backfat thickness. The initial mean body weight and backfat thickness of the sows were 191.84 kg and 13.68, respectively. After 24 h of artificial insemination, sows were randomly distributed between two dietary treatments: control diet and diet supplemented with 0.1% GAA. GAA was incorporated into the diet by adding the commercial feed additive (CreAMINO®, > 96% GAA; Evonik Industries).

The sows were housed individually in crates equipped with semi-automatic feeder and nipple drinker. The feed level was fixed in a daily amount of 2.2 kg from insemination to 49 days of gestation, 2.1 kg from 50 to 84 days and 2.75 kg from 85 to 109 days of gestation. From 110 days of gestation until farrowing 2.0 kg of the lactation feed were daily provided for sows. After farrowing, sows were then submitted to a step-up feeding regime to stimulate gradual feed intake increase up to day 7 post-farrowing, starting with 2 kg on day 1 post-farrowing and reaching 8 kg on day 7. The allowance increased by 1 kg each day. After day 7, sows were fed 2 kg + 0.5 kg/piglet/day. The diets were formulated (Table 1) to meet the nutritional requirements of sows in gestation and lactation phases, according to the recommendations contained in the lineage manual and nutritional composition of feedstuffs by Rostagno et al. (2017). Water was available *ad libitum* throughout the experimental period.

After birth, piglets were handled for umbilical-cord treatment. As necessary, cross-fostering was conducted within the first 48 h after birth to standardize litter size among the sows from the same treatments. During the lactation period, piglets had no access to creep feed and water was available *ad libitum* through a bite-ball nipple drinker. A juggler equipped with infrared lights provided supplemental heat for the piglets.

At 23 days of age, the litters were weaned, weighed and from the initial dietary treatments were distributed in a randomized block design in a 2 × 2 factorial arrangement, considering the two dietary treatments for sows during gestation and lactation (control diet with 0 or 0.1% GAA) and two dietary treatments for piglets at nursery phase (control diet with 0 or 0.1% GAA), totaling 4 treatments with 6

Table 1

Calculated and analyzed nutritional composition of experimental diets for sows (as fed basis, %)^a.

Ingredients	Gestation	Lactation
Corn, grain	79.51	63.14
Soybean meal 45%	15.13	26.54
Meat and bone meal	1.50	2.43
Soybean oil	0.50	4.49
Dicalcium phosphate	0.88	0.39
Limestone	0.99	0.96
Salt	0.53	0.46
L-Lysine	0.10	0.47
DL-Methionine	0.00	0.17
L-Threonine	0.02	0.13
Choline chloride, 60%	0.14	0.12
Premix ^b	0.70	0.70
Total	100.00	100.00
Nutritional composition		
Metabolizable energy (kcal/kg)	3231	3450
Crude protein (%)	13.9	19.0
Ether extract (%)	3.8	7.5
Total available calcium (%)	0.70	0.80
Available phosphorus (%)	0.50	0.50
Sodium (%)	0.20	0.20
Lysine digestible (%)	0.70	1.20
Methionine digestible (%)	0.20	0.40
Threonine digestible (%)	0.50	0.80
Tryptophan digestible (%)	0.10	0.20
Isoleucine digestible (%)	0.60	0.80
Arginine digestible (%)	0.90	1.20
Valine digestible (%)	0.70	0.90

^a GAA was incorporated into the diet by adding the commercial feed additive.

^b Premix: vitamin A (1500000 IU/kg), vitamin D (226.667 IU/kg), vitamin E (6667 IU/kg), vitamin K3 (333.30 mg/kg), vitamin B1 (333.30 mg/kg), vitamin B2 (1167 mg/kg), vitamin B6 (416.60 mg/kg), vitamin B12 (5333.30 mg/kg), niacin (6000 mg/kg), pantothenic acid (3333.30 mg/kg), folic acid (400 mg/kg), biotin (32 mg/kg), manganese (8333.30 mg/kg), zinc (18.33 g/kg), iron (13.33 g/kg), copper (2333.30 mg/kg), iodine (266.70 mg/kg), selenium (100 mg/kg).

replicates each, considering the pen with 40 animals (20 male and 20 female) as experimental unit. The criterion adopted for the formation of the blocks was the initial weight of the piglets, with average weight of the light and heavy piglets of 4.9 ± 0.2 kg and 6.8 ± 0.3 kg, respectively.

At nursery phase, the piglets were housed in a shed, equipped with an automatic temperature and humidity control system, aiming at the maximum thermal comfort of the animals. The shed was composed of 60 collective pens, with maximum capacity of 50 animals each, being provided with automatic feeder and nipple drinker.

2.2. Performance trial

During the nursery phase, water and feed were available *ad libitum* to piglets. Feed were formulated (Table 2) considering the nutritional composition of feedstuffs and the nutritional requirements of piglets in the following periods: pre-initial I (23 to 28 days of age), pre-initial II (29 to 36 days of age), initial I (37 to 53 days of age) and initial II (54 to 63 days of age), according to Rostagno et al. (2017).

At the beginning and end of each period, piglets were weighed, as well as the amount of feed supplied and refusals daily collected. From the data obtained, performance parameters were analyzed regarding average daily feed intake (ADFI), average daily gain (ADG) and feed conversion ratio (FCR).

2.3. Blood biochemical analysis

For serum parameters evaluation, blood samples were collected in

Table 2

Calculated and analyzed nutritional composition of experimental diets for piglets at nursery phase (as fed basis, %)^a.

Ingredients	Pré-initial I	Pré-initial II	Initial I	Initial II
Corn, grain	30.88	38.89	46.06	54.74
Soybean meal 45%	22.60	23.20	27.70	29.00
Meat meal	5.00	5.00	5.00	2.65
Cookie meal	7.00	7.00	5.00	3.00
Soybean oil	4.90	4.60	4.70	5.00
Dicalcium phosphate	0.50	0.46	0.70	1.00
Limestone	0.20	0.34	0.30	0.90
Salt	0.00	0.08	0.34	0.47
L-Lysine	0.57	0.65	0.64	0.64
DL-Methionine	0.28	0.26	0.24	0.22
L- Tryptophan	0.18	0.20	0.19	0.17
L-Threonine	0.13	0.16	0.17	0.17
Choline chloride, 60%	0.06	0.06	0.06	0.04
Dairy product PI ^b	25.70	17.1	0.00	0.00
Dairy product II ^c	0.00	0.00	6.90	0.00
Premix ^d	2.00	2.00	2.00	2.00
Total	100.00	100.00	100.00	100.00
Nutritional composition				
Metabolizable energy (kcal/kg)	3500	3450	3450	3430
Crude protein (%)	22.7	22.3	21.6	20.2
Ether extract (%)	7.8	7.8	8.1	8.1
Total available calcium (%)	0.80	0.85	0.85	0.85
Available phosphorus (%)	0.75	0.72	0.72	0.65
Sodium (%)	0.32	0.27	0.25	0.23
Lysine digestible (%)	1.69	1.63	1.51	1.39
Methionine digestible (%)	0.55	0.55	0.53	0.48
Threonine digestible (%)	1.08	1.04	0.97	0.90
Tryptophan digestible (%)	0.33	0.32	0.30	0.28
Isoleucine digestible (%)	0.93	0.90	0.88	0.82
Arginine digestible (%)	1.38	1.37	1.38	1.30
Valine digestible (%)	1.12	1.08	1.00	0.93

^a GAA was incorporated into the diet by adding the commercial feed additive.

^b Dairy product pré-initial (21.64% crude protein).

^c Dairy product initial 1 (12% crude protein).

^d Premix (per kg of the premix): vitamin A, 5000 IU; vitamin D3, 800 IU; vitamin E, 30,000 mg; vitamin K 3200 mg; riboflavin 4000 mg; vitamin B3, 20,000 mg; vitamin B6, 2000 mg; vitamin B12, 16,000 mcg; pantothenic acid, 14,000 mg; Cu, 6600 mg; Fe, 15,000 mg; manganese, 6000; selenium, 36 mg; zinc, 18,000 mg.

three animals per experimental unit, based on the piglets mean weight of each replicate at 23, 36 and 63 days of age. A total of 5 ml of blood were collected in each animal by puncturing the jugular vein, using sterilized needles and plain tubes. After collection, samples were centrifuged at 2000 g for 15 min at room temperature and the serum obtained was stored in 1.5 ml Eppendorf tubes at -20°C for subsequent determination of the creatinine and creatine kinase parameters.

The methodology employed for the determination of creatinine and creatine kinase was enzymatic colorimetric, using commercial kits (Labtest Diagnóstica S.A.) and a semiautomatic analyzer (BIO-2000 spectrophotometer, Bioplus[®]).

2.4. Economic viability

Economic viability of GAA dietary supplementation was determined considering piglets performance and feed cost, calculated based on the prices (US\$/kg) of feedstuffs during the experimental period at Santa Catarina state (Table 3). The average feed cost per kilogram of body weight (FCBW) was calculated according to the feed cost, feed intake and weight gain of the piglets in each period. The economic efficiency index (EEI) and the cost index (CI) were calculated according to equations proposed by Fialho et al. (1992), as follow:

$$\text{EEI} = \text{LCei} \times 100/\text{CTei}$$

$$\text{CI} = \text{CTei} \times 100/\text{LCei}$$

Table 3

Feedstuffs cost of experimental diets.

Ingredients	Cost (US\$/kg) ^a
Corn, grain	0.17
Soybean meal 45%	0.37
Meat meal	0.25
Cookie meal	0.19
Soybean oil	0.73
Dicalcium phosphate	0.56
Limestone	0.05
Salt	0.04
L-Lisina HCL	1.93
DL-Metionina	3.02
L-Triptofano	12.97
L-Treonina	2.27
L-Lysine	2.40
DL-Methionine	1.76
L- Tryptophan	1.33
L-Threonine	4.74
Guanidinoacetate acid	7.66

^a Cost calculated using the prices of the feedstuffs during the experimental period at Santa Catarina (Brazil).

In what: LCei = lowest feed cost per kilogram of body weight observed among treatments; CTei = cost of treatment i considered.

2.5. Statistical analysis

Performance data, blood biochemical evaluation and economic viability were submitted to analysis of variance by General Linear Models (GLM) procedure, and means were compared by Tukey test at 5% of probability by Statiscal Analysis System (SAS - University Edition), which were evaluated the periods I (23 to 28 days of age), II (23 to 36 days of age), III (23 to 53 days of age) and total (23 to 63 days of age).

3. Results

There were no interaction ($P > 0.05$) between GAA supplementation for sows during the gestation and lactation phases and for their progenies on average daily feed intake, average daily gain and feed conversion ratio of piglets during the nursery phase (Table 4). In addition, no significant differences were observed ($P > 0.05$) on piglets performance considering GAA dietary supplementation for sows or piglets.

There were no effects ($P > 0.05$) of interaction between GAA supplementation for sows and their piglets on serum concentrations of creatinine and creatine kinase of piglets during the nursery phase (Table 5). The GAA dietary supplementation alone for sows or piglets also did not influence ($P > 0.05$) blood parameters of animals.

Regarding on economic evaluation (Table 6), no interaction effects were observed between GAA supplementation for sows and their progenies. However, in periods III (23 to 53 days of age) and total (23 to 63 days of age), there was an effect ($P < 0.05$) of the GAA dietary supplementation for piglets during the nursery phase on average feed cost per kilogram of body weight, economic efficiency index and cost index. Piglets that received GAA supplemented diet presented a higher average feed cost per kilogram of body weight and cost index, besides a lower economic efficiency index.

4. Discussion

The effects of dietary supplementation of GAA for pregnant and lactating sows on their progenies have not yet been elucidated in the literature. It is known that when supplied in the diet, GAA is rapidly absorbed in the gastrointestinal tract, being transported to the liver, where it receives a methyl group of S-adenosyl-L-methionine, producing creatine (Dilger et al., 2013; Gualano et al., 2010; Janicki and

Table 4

Effects of dietary supplementation of guanidinoacetic acid for sows and their progeny on piglets performance at nursery phase.

Parameters ^a	Sup. Sows (SS) ^b		Sup. Piglets (SP) ^d		RSD (%) ^e	P-value SS	SP	SS*SP ^f
	0% GAA ^c	0,1% GAA	0% GAA	0,1% GAA				
Period I (23 to 28 days of age)								
ADFI, kg	0.173	0.183	0.177	0.179	10.82	0.1182	0.9891	0.3672
ADG, kg	0.103	0.107	0.098	0.110	11.16	0.9113	0.1912	0.2366
FCR	1.80	1.76	1.81	1.74	11.47	0.5441	0.4665	0.1075
Period II (23 to 36 days of age)								
ADFI, kg	0.266	0.282	0.271	0.277	8.05	0.5467	0.5822	0.3464
ADG, kg	0.207	0.215	0.214	0.208	9.83	0.5835	0.4856	0.4040
FCR	1.33	1.37	1.34	1.36	9.63	0.1460	0.6982	0.5370
Period III (23 to days of age)								
ADFI, kg	0.429	0.448	0.440	0.437	4.92	0.2251	0.2292	0.2502
ADG, kg	0.328	0.340	0.346	0.323	5.91	0.5667	0.1409	0.6913
FCR	1.31	1.32	1.29	1.34	4.09	0.5713	0.4688	0.6334
Total period (23 to 63 days of age)								
ADFI, kg	0.547	0.569	0.558	0.559	4.99	0.5019	0.7097	0.1783
ADG, kg	0.410	0.425	0.425	0.410	4.33	0.4424	0.8996	0.3644
FCR	1.34	1.36	1.33	1.37	3.72	0.1733	0.6791	0.6013

^a ADFI: average daily feed intake. ADG: average daily gain. FCR: feed conversion ratio.^b Guanidinoacetate acid supplementation for sows during gestation and lactation phases.^c Guanidinoacetate acid.^d Guanidinoacetate acid supplementation for piglets at nursery phase.^e Relative standard deviation.^f Interaction between guanidinoacetate acid supplementation for sows and their progenies; Means followed by different letters on the same line differ from each other by Tukey test ($P < 0.05$).

Buzala, 2013). The higher content of this protein in the body promotes a negative feedback on arginine:glycine amidinotransferase, inhibiting the endogenous synthesis of GAA and, consequently, the use of its precursors, the amino acids arginine and glycine (Baker, 2009; Wyss and Kaddurah-Daouk, 2000). In view of this, it was expected that dietary supplementation of GAA for sows during gestation and lactation could positively affect the performance of their progenies due to the greater amount of arginine available in the organism of these females, which could favor nitric oxide synthesis, and therefore, the nutrients transfer to the piglets through the placenta and mammary gland. However, in the present study, the absence of significant effects of GAA supplementation for the sows on piglets performance may have occurred, because even with the correct use of dietary additives, it is difficult to guarantee the expected effects on the progeny from the supplementation of sows, due to the individual variability of absorption, transport and utilization of nutrients in the body (Wu et al., 2004).

In piglet nutrition, the increased availability of arginine and creatine from the dietary supplementation of GAA may favor the performance maximization of these animals, as these compounds promote a greater protein anabolism. However, in the present study, no significant

differences were observed on ADFI, ADG and FCR of piglets, corroborating with Teixeira et al. (2017), who also found no effects of GAA supplementation during the nursery phase on animal performance. However, the data obtained differ from those reported by Jayaraman et al. (2018), when providing GAA in pig diets from weaning to finishing, observed a higher ADG and G:F during starter, grower, finisher and the overall period (30 to 180 days of age).

The lack of more evident results of GAA dietary supplementation on ADG and FCR in the present study may have occurred because the diets provided to the piglets at nursery phase meet or exceed their arginine requirements, since contained feedstuffs with high levels of these amino acids, such as meat meal and dairy products. In addition, no differences were observed in ADFI of piglets, because GAA does not have flavoring properties capable of stimulating a greater intake by the animals.

Regarding blood parameters, it was observed that the values are within the range expected for pigs, which are from 1.0 to 2.7 mg/dL and 2.4 to 22.5 IU/L for creatinine and creatine kinase, respectively (Kaneko et al., 2008; Meyer et al., 2004).

The concentrations of blood biochemical parameters can also be used as indicative of the productive performance of the animals

Table 5

Effects of dietary supplementation of guanidinoacetic acid for sows and their progeny on blood parameters of the piglets at nursery phase.

Parameters	Sup. Sows (SS) ^a		Sup. Piglets (SP) ^c		RSD (%) ^d	P-value		SS*SP ^e
	0% GAA ^b	0,1% GAA	0% GAA	0,1% GAA		SS	SP	
23 days of age								
Creatinine, mg/dL	1.13	1.13	1.12	1.16	3.87	0.7479	0.2742	0.4938
Creatine kinase, UI/L	3.57	3.62	3.61	3.66	2.21	0.5793	0.1362	0.2956
36 days of age								
Creatinine, mg/dL	1.33	1.34	1.32	1.36	3.79	0.6572	0.3809	0.5738
Creatine kinase, UI/L	5.76	5.86	5.75	5.83	3.57	0.2683	0.2330	0.8120
63 days of age								
Creatinine, mg/dL	1.45	1.48	1.46	1.50	3.90	0.8755	0.362	0.8630
Creatine kinase, UI/L	6.82	6.83	6.80	6.88	2.64	0.7363	0.212	0.9096

^a Guanidinoacetate acid supplementation for sows during gestation and lactation phases.^b Guanidinoacetate acid.^c Guanidinoacetate acid supplementation for piglets at nursery phase.^d Relative standard deviation.^e Interaction between guanidinoacetate acid supplementation for sows and their progenies; Means followed by different letters on the same line differ from each other by Tukey test ($P < 0.05$).

Table 6

Effects of dietary supplementation of guanidinoacetic acid for sows and their progeny on the economic evaluation.

Parameters ^a	Sup. Sows (SS) ^b 0% GAA ^c	0,1% GAA	Sup. Piglets (SP) ^d 0% GAA	0,1% GAA	RSD (%) ^e	P-value SS	SP	SS*SP ^f
Period I (23 to 28 days of age)								
FCBW (US\$/Kg)	1.44	1.49	1.54	1.39	14.95	0.9549	0.0977	0.1741
EEL (%)	94.9	95.1	90.0	100.0	12.71	0.4309	0.0656	0.2046
CI (%)	107.2	103.4	110.7	100.0	14.95	0.9549	0.0977	0.1741
Period II (23 to 36 days of age)								
FCBW (US\$/Kg)	0.93	0.94	0.90	0.97	7.59	0.1391	0.0533	0.8517
EEL (%)	97.9	96.2	100.0	94.2	5.79	0.1078	0.0537	0.7185
CI (%)	102.6	104.6	100.0	107.3	7.59	0.1391	0.0531	0.8517
Period III (23 to 53 days of age)								
FCBW (US\$/Kg)	0.71	0.72	0.68b	0.74a	3.32	0.4454	<0.0001	0.5792
EEL (%)	96.1	96.0	100.0a	92.3b	3.34	0.4782	<0.0001	0.5904
CI (%)	104.1	104.2	100.0b	108.3a	3.33	0.4454	<0.0001	0.5792
Total period (23 to 63 days of age)								
FCBW (US\$/Kg)	0.64	0.65	0.63b	0.66a	3.09	0.9992	0.0006	0.8306
EEL (%)	97.4	97.3	100.0a	94.7b	3.11	0.9714	0.0006	0.8087
CI (%)	102.7	102.7	100.0b	105.5a	3.09	0.9992	0.0006	0.8306

^a FCBW: average feed cost per kilogram of body weight; EEL: economic efficiency index; CI: cost index.^b Guanidinoacetate acid supplementation for sows during gestation and lactation phases.^c Guanidinoacetate acid.^d Guanidinoacetate acid supplementation for piglets at nursery phase.^e Relative standard deviation.^f Interaction between guanidinoacetate acid supplementation for sows and their progenies; Means followed by different letters on the same line differ from each other by Tukey test ($P < 0.05$).

(Rotava et al., 2008) and creatinine content is highly correlated with the weight and amount of body muscle mass of the pigs (Cameron et al., 2003). Therefore, the use of diets with substances that increase protein deposition may lead to increased creatinine in the blood of these animals. Another molecule often described as an important indirect muscle marker is creatine kinase (Foschini et al., 2007). Individuals with larger muscle mass generally have higher blood concentrations of total creatine kinase (Brancaccio et al., 2007). In this sense, the absence of significant differences in GAA supplementation on creatinine and creatine kinase blood levels may have occurred because the requirement in amino acids was being met for maximum muscle deposition, as observed by the same animal performance of all treatments. The results obtained are in agreement with Teixeira et al. (2017), who also did not observe significant effects on the concentrations of these metabolites when supplementing up to 0.2% GAA for piglets at nursery phase. The authors attributed the absence of differences in animal weight gain to the maximum creatine kinase activity range, which is related to the protein anabolism peak, which occurs between 11 and 28 weeks of age. He et al. (2018) evaluating the GAA dietary supplementation at growing and finishing phases also found that there were no significant differences on creatinine and creatine kinase blood concentrations of pigs.

Considering that the total costs of pig farming are mostly related to animal feeding, the use of additives is applicable from the improvement in feed efficiency or from productive indexes. In this sense, it was observed that the supply of 0.1% GAA in the piglets diets during the nursery phase led to a higher FCBW and CI, besides a lower EEL. These results may be justified by the additional cost of the GAA inclusion in diet and by the absence of significant differences in ADFI and ADG of animals between treatments. Therefore, it can be stated that the dietary supplementation of 0.1% GAA for piglets at nursery phase is not an economically viable practice. However, more studies are needed to evaluate the use of this additive at higher levels or in diets without animal feedstuffs, which present lower levels of arginine.

5. Conclusion

Dietary supplementation of 0.1% GAA for sows and their progenies does not influence performance parameters and creatinine and creatine

kinase serum concentrations of piglets at nursery phase. The inclusion of this additive in piglet diets is economically unfeasible.

Conflict of interest

None.

Acknowledgements

The authors gratefully acknowledge CAPES(Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) for the financial support of this research.

References

- Baker, D.H., 2009. Advances in protein-amino acid nutrition of poultry. *Amino Acids* 37, 29–41. <https://doi.org/10.1007/s00726-008-0198-3>.
- Brancaccio, P., Maffulli, N., Limongelli, F.M., 2007. Creatine kinase monitoring in sport medicine. *Br. Med. Bull.* 81, 209–230. <https://doi.org/10.1093/bmb/ldm014>.
- Cameron, N.D., McCullough, E., Troup, K., Penman, J.C., 2003. Physiological responses to divergent selection for daily food intake or lean growth rate in pigs. *Anim. Sci.* 76, 27–34. <https://doi.org/10.1017/S1357729800053285>.
- Dilger, R.N., Bryant-Angeloni, K., Payne, R.L., Lemme, A., Parsons, C.M., 2013. Dietary guanidino acetic acid is an efficacious replacement for arginine for young chicks. *Poult. Sci.* 92, 171–177. <https://doi.org/10.3382/ps.2012-02425>.
- Federation of Animal Science Societies, 2010. *Guide for the Care and Use of Agricultural Animals in Research and Teaching*, 3rd ed. Federation of Animal Science Societies, Champaign, IL, USA.
- Fialho, E.T., Barbosa, H.P., Ferreira, A.S., Gomes, P.C., Giroto, A.F., 1992. Utilização da cevada suplementada com óleo de soja para suínos em crescimento e terminação. *Pesquisa Agropecuária Brasileira* 27, 1467–1475.
- Foschini, D., Prestes, J., Charro, M.A., 2007. Relação entre exercício físico, dano muscular e dor muscular de início tardio. *Revista brasileira cineantropometria e desempenho humano* 9, 101–106.
- Gondret, F., Lefaucheur, L., Juin, H., Louveau, I., Lebre, B., 2006. Low birth weight is associated with enlarged muscle fiber area and impaired meat tenderness of the longissimus muscle in pigs. *J. Anim. Sci.* 84, 93–103. <https://doi.org/10.2527/2006.84193x>.
- Gualano, B., Acquesta, F.M., Ugrinowitsch, C., Tricoli, V., Serrão, J.C., Junior, A.H.L., 2010. Efeitos da suplementação de creatina sobre força e hipertrofia muscular: atualizações. *Rev. Bras. Med. Esporte* 16, 219–223. <http://dx.doi.org/10.1590/S1517-86922010000300013>.
- He, D.T., Gai, X.R., Yang, L.B., Li, J.T., Lai, W.Q., Sun, X.L., Zhang, L.Y., 2018. Effects of guanidinoacetic acid on growth performance, creatine and energy metabolism, and carcass characteristics in growing-finishing pigs. *J. Anim. Sci.* 96, 3264–3273. <https://doi.org/10.1093/jas/sky186>.
- Janicki, B., Buzala, M., 2013. The role of creatine in the organism of pigs and its effect on

- the quality of pork: a review. *Ann. Anim. Sci.* 13, 207–215. <https://doi.org/10.2478/aoas-2013-0003>.
- Jayaraman, B., La, K.V., La, H., Doan, V., Carpena, E.M., Rademacher, M., Channarayana, G., 2018. Supplementation of guanidinoacetic acid to pig diets: effects on performance, carcass characteristics, and meat quality. *J. Anim. Sci.* 96, 2332–2341. <https://doi.org/10.1093/jas/sky137>.
- Kaneko, J.J., Harvey, J.J., Bruss, M.L., 2008. Clinical biochemistry of domestic animals. *Clin. Biochem. Domest. Anim.* <https://doi.org/10.1016/B978-0-12-370491-7.X0001-3>.
- Kim, S.W., Wu, G., 2004. Dietary arginine supplementation enhances the growth of milk-fed young pigs. *J. Nutr.* 134, 625–630. <https://doi.org/10.1093/jn/134.3.625>.
- Liu, Y., Li, J.L., Li, Y.J., Gao, T., Zhang, L., Gao, F., Zhou, G.H., 2015. Effects of dietary supplementation of guanidinoacetic acid and combination of guanidinoacetic acid and betaine on postmortem glycolysis and meat quality of finishing pigs. *Anim. Feed Sci. Technol.* 205, 82–89. <https://doi.org/10.1016/j.anifeeds.2015.03.010>.
- Mateo, R.D., Wu, G., Moon, H.K., Carroll, J.A., Kim, S.W., 2008. Effects of dietary arginine supplementation during gestation and lactation on the performance of lactating primiparous sows and nursing piglets. *J. Anim. Sci.* 86, 827–835. <https://doi.org/10.2527/jas.2007-0371>.
- McBrearty, L.E., Robinson, J.L., Furlong, K.R., Brunton, J.A., Bertolo, R.F., 2015. Guanidinoacetate is more effective than creatine at enhancing tissue creatine stores while consequently limiting methionine availability in Yucatan miniature pigs. *PLoS ONE* 10, 1–11. <https://doi.org/10.1371/journal.pone.0131563>.
- Meyer, D.J., Harvey, J.W., Taibo, R.A., 2004. Veterinary laboratory medicine: interpretation & diagnosis. *Veterin. Lab. Med. Interpret. Diagn.* <https://doi.org/10.1111/j.1939-165X.2004.tb00372.x>.
- Moreira, R.H.R., Lanferdini, E., da Silva Fonseca, L., Chaves, R.F., Garbossa, C.A.P., Saraiva, A., Nogueira, E.T., de Abreu, M.L.T., 2018. Arginine improves nutritional quality of sow milk and piglet performance. *R. Bras. Zootec.* 47. <http://dx.doi.org/10.1590/rbz4720170283>.
- Ostojic, S.M., Ostojic, J., Drid, P., Vranes, M., 2016. Guanidinoacetic acid versus creatine for improved brain and muscle creatine levels: a superiority pilot trial in healthy men. *Appl. Physiol. Nutr. Metabol.* 41, 1005–1007. <https://doi.org/10.1139/apnm-2016-0178>.
- Rostagno, H.S., Albino, L.F.T., Hannas, M.I., Donzele, J.L., Sakomura, N.K., Perazzo, F.G., Saraiva, A., Teixeira, M.V., Rodrigues, P.B., Oliveira, R.F., Barreto, S.L.T., Brito, C.O., 2017. Tabelas Brasileiras Para Aves e suínos: Composição De Alimentos e Exigências Nutricionais, 4th ed. Editora UFV, Viçosa.
- Rotava, R., Zanella, I., Karkow, A.K., Dullius, A.P., Silva, L.P.D., Denardin, C.C., 2008. Bioquímica sanguínea de frangos de corte alimentados com subprodutos da uva. *Agrarian* 1, 91–104.
- Teixeira, K.A., Mascarenhas, A.G., de Carvalho Mello, H.H., Arnhold, E., da Silva Assunção, P., Carvalho, D.P., Lopes, S.G., 2017. Effect of diets with different levels of guanidinoacetic acid on newly weaned piglets. *Semina Ciências Agrárias* 38, 3887–3896. <http://dx.doi.org/10.5433/1679-0359.2017v38n6p3887>.
- Wang, L.S., Shi, B.M., Shan, A.S., Zhang, Y.Y., 2012. Effects of guanidinoacetic acid on growth Performance, meat quality and antioxidation in growing-finishing pigs. *J. Anim. Veterin. Adv.* 11, 631–636.
- Wolf, J., Žáková, E., Groeneveld, E., 2008. Within-litter variation of birth weight in hyperprolific Czech large white sows and its relation to litter size traits, stillborn piglets and losses until weaning. *Livest. Sci.* 115, 195–205. <https://doi.org/10.1016/j.livsci.2007.07.009>.
- Wu, G., Knabe, D., Kim, S.W., 2004. Arginine nutrition in neonatal pigs. *J. Nutr.* 134, 2783–2790.
- Wu, G., Fuller, W.B., 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. <https://doi.org/10.1016/j.livsci.2007.07.003>.
- Wyss, M., Kaddurah-Daouk, R., 2000. Creatine and creatinine metabolism. *Physiol. Rev.* 80, 1107–1213. <https://doi.org/10.1152/physrev.2000.80.3.1107>.