# The Confusions and Suggestions in Application of Arginine in Sow Production

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## Abstract

Arginine (Arg) supplementation to a gestation diet in sows has been shown to be effective in improving female reproductive performance and conceptuses development. However, there are no clear recommodations about the dose, period and duration of Arg supplementation in diet of gestating sows. In this review, we discuss current knowledge of Arg application and its influence on sow gestation; emphasizing how the dose, period and duration of Arg supplementation may affect the number and body weight (BW) of piglets born alive (BA). Based on the results of previous studies and the actual level of Arg in commecial diets for gestating sows, we suggest dietary Arg supplementation with a dose of 0.1-0.2% from early gestation until day 114 of gestation.

## Background

As a precursor for ornithine, nitric oxide, and creatine synthesis, Arg is one of the functional amino acids that signals embryonic and fetal development (Wu et al., 2009). The nitric oxide results in an increase in blood flow to the placenta and an improve ment in delivery of essential nutrients from maternal to fetal blood (Wu and Meininger, 2002). Polyamines have been shown to have positive effects on embryogenesis and placental growth (Reynolds and Redmer, 2001). Most of the previous studies have shown that supplementation of Arg benefits the reproduction of the gestating sows(Palencia et al., 2018). However, there was lack of a uniform methodolgy in these studies. Some of the previous studies for evaluating the effect of Arg in gestating sows were investigated in the early-gestation period (Bérard and Bee, 2010; Li et al., 2010; Li et al., 2015) or over the entire gestation period (Mateo et al., 2007; Bass et al., 2011; Gao et al., 2012; Che et al., 2013; Luise et al., 2020). Additionally, a high level of supplementary Arg (0.8%) was used . However, application of low supplemental Arg (0.1%-0.3%) has also been reported (Guo et al., 2016; Bieliński et al., 2017; Hong et al., 2020; Luise et al., 2020). Controveries in the dose, period and duration of Arg supplementation have been major obstacles in large scale adoption of Arg supplementation in gestation sows.

## Effectiveness of Arg in sow during gestation

two most important outcomes obtained from the use of Arg in the diets of gestating sows, are improvements in the number and the BW of total piglets BA (Table 1 and 2). Regarding the number of total piglets alive, 16 pertainant studies were used in the evaluation of which six reported a significant (37.5%) improvement with this parameter. The remaining trials (62.5%), there were no significant effect. However, from 24 results derived from 16 trials, 19 reporting a positive effect on BA, improvements ranging from 0.1 to 2.03 pigs per litter, with an average increase of 1.13 BA piglets. Results in three studies (Dallanora et al., 2017; Nuntapaitoon et al., 2018; Hines et al., 2019) actually reported a decrese in the number of piglet alive ranging from 0.10 to 1.0 with Arg supplementation in gestating sow. BW of live piglets was also measured in these16 trials. Six trials (37.5%) reported significant increase when supplementing Arg. The remaining ten trials (62.5%) reported no significant differences in BW. Similary, the majority (81.25%) indicated that Arg supplementation has a postive effect, 1.15 and 0.07 kg increase in total BA or average piglets BW, respectively. Only two studies showed a negligible decrease in body weigh of piglet alive (Dallanora et al., 2017; Bieliński et al., 2017). Overall, Arg supplementation in the diets of gestating sows benefited the numbers and BW of piglets BA in 79.17% and 81.25% of trials, of which 37.5% showed a statistically significant improvement.

### Table 1. Effect of dietary Arg level and feeding stages during gestation on total piglets born alive

| Control | Arg treatment | Change | Period | Dose (%) | Arg content of basal diet (%) | Reference |
|---|---|---|---|---|---|---|
| 9.37 | 11.40* | +2.03 | 30-114 | 0.83 | 0.72 | Mateo et al.,2007 |
| 13.59±0.37 | 13.92±0.37 | +0.33 | 30-114 | 0.83 | 0.93 | Bass et al.,2011 |
| 9.26 | 10.76 | +1.50 | 90-114 | 0.83 | 0.72 | Wu et al.,2012 |
| 9.78 | 10.87 | +1.09 | 90-114 | 0.83 | 0.81 | Liu et al.,2012 |
| 11.25 | 12.35* | +1.10 | 22-114 | 0.83 | 0.88 | Gao et al.,2012 |
| 10.19±0.48 | 10.58±0.50* | +0.40 | 30-90 | 0.83 | 0.73 | Che et al., 2013 |
| | 11.81±0.47* | +1.62 | 30-114 | | | |
| 13.8 | 14.9 | +1.10 | 77-114 | 25.5 g/head/d | 0.77 | Quesnel et al., 2014 |
| 11.43 | 13.24 | +1.81 | 1-14 | 1.08 | 0.85 | Li et al., 2015 |
| | 12.98 | +1.55 | 15-30 | | | |
| | 13.00 | +1.57 | 1-30 | | | |
| 8.65 | 9.8* | +1.15 | 30-114 | 0.1 | 0.61 | Guo et al.,2016 |
| 14.3 | 13.3 | -1.0 | 25-80 | 1.0 | 1.05 | Dallanora et al., 2017 |
| 11.7 (Primiparous) | 13.0* | +1.3 | 28-114 | 0.3 | 0.9 | Bieliński et al., 2017 |
| 13.8 (Multiparous) | 13.8 | 0 | 28-114 | 0.3 | | |
| 12.3±0.4 | 12.2±0.5 | -0.1 | 85-114 | 0.4 | 1.28 | Nuntapaitoon et al.,2018 |
| | 13.2±0.5 | +0.9 | 85-114 | 0.83 | | |
| 13.2 | 12.8 | -0.4 | 15-45 | 1.0 | 0.65 | Hines et al.,2019 |
| | 12.9 | -0.3 | 15-114 | | | |
| | 13.3 | +0.1 | 85-114 | | | |
| 12.8 | 14.0 | +1.2 | 70-114 | 0.28 | 0.72 | Hong et al., 2020 |
| | 13.9 | +1.1 | 70-114 | 0.79 | | |
| 15.43 | 16.20 | +0.77 | 85-114 | 1.0 | 0.98 | Moreira et al., 2020 |
| 12.58 | 13.40* | +0.82 | 1-114 | 0.25 | 0.72 | Luise et al., 2020 |

*Different from the control group (P > 0.05)

### Table 2. Effects of dietary Arg level and feeding stages during gestation on BW of piglets born alive

| Kg | Control | Arg treatments | Change | Period | Dose(%) | Arg content of basal diet (%) | Reference |
|---|---|---|---|---|---|---|---|
| Litter weight of all piglets BA | 13.19 | 16.38* | +3.19 | 30-114 | 0.8 | 0.72 | Mateo et al.,2007 |
| | 14.12 | 16.26* | +2.14 | 90-114 | 0.8 | 0.81 | Liu et al.,2012 |
| | 15.82 | 17.52* | +1.7 | 22-114 | 0.8 | 0.88 | Gao et al.,2012 |
| | 14.81±0.69 | 15.30±0.53 | +0.49 | 30-90 | 0.81 | 0.73 | Che et al., 2013 |
| | | 16.91±0.70* | +2.1 | 30-114 | | | |
| | 16.32 | 17.43 | +1.11 | 1-14 | 1.08 | 0.85 | Li et al., 2015 |
| | | 18.14 | +1.82 | 15-30 | | | |
| | | 17.69 | +1.37 | 1-30 | | | |
| | 16.8 | 16.7 | -0.1 | 25-80 | 0.8 | 1.05 | Dallanora et al., 2017 |
| | 1.36 | 1.39 | +0.03 | 15-45 | 1.0 | 0.65 | Hines et al.,2019 |
| | | 1.39 | +0.03 | 15-114 | | | |
| | | 1.37 | +0.01 | 85-114 | | | |
| | 18.47 | 19.01 | +0.54 | 70-114 | 0.28 | 0.72 | Hong et al., 2020 |
| | | 20.69 | +1.12 | | 0.79 | | |
| | 17.81 | 18.19 | +0.38 | 1-114 | 0.25 | 0.72 | Luise,2020 |
| Average BW of piglets BA | 1.41 ± 0.02 | 1.42 ± 0.02 | +0.01 | 30-114 | 0.8 | 0.93 | Bass et al.,2011 |
| | 1.46 | 1.62* | +0.16 | 90-114 | 0.8 | 0.72 | Wu et al.,2012 |
| | 1.46 | 1.53 | +0.07 | 77-114 | 25.5 g/head/d | 0.77 | Quesnel et al., 2014 |
| | 1.25 | 1.25 | 0 | 30-114 | 0.1 | 0.61 | Guo et al.,2016 |
| | 1.26 (Primiparous) | 1.25 | -0.01 | 28-114 | 0.3 | 0.9 | Bieliński et al., 2017 |
| | 1.23 (Multiparous) | 1.22 | -0.01 | | | | |
| | 1.43±0.01 | 1.53±0.02* | +0.1 | 85-114 | 0.4 | 1.28 | Nuntapaitoon et al.,2018 |
| | | 1.48±0.02 | +0.05 | 85-114 | 0.8 | | |
| | 1.411 | 1.382 | +0.029 | 85- | 1% | 0.98 | Moreira et al., 2020 |

*Different from the control group (P > 0.05)

## Arg dose for gestating sows

Regarding the optimum dietary L-Arg concentration there has not been a precise dose-response experiment reported to estimate Arg level for reproduction of the gestating sow. Two studies were conducted with three Arg levels (Nuntapaitoon et al.,2018; Hong et al., 2020). Relativly high level of basal diet Arg (1.28%) was used in Nuntapaitoon et al. (2018) reporting an increase of piglets BA with a high supplementation of Arg (0.8%) compared with control-fed sows. In contrast, Hong et al. (2020) proved that low dose of Arg (0.28%) also resulted in an increase in number and BW of piglets BA. Additionally, a higher dose of supplemental Arg (0.79%) further increased the litter weight of all piglets BA. Regretfully, an optimal dietary Arg cannot be concluded from these two studies due to the number of treatments and levels of Arg supplementation chosen by the researchers.

The common adopted level of Arg (1% of a 83% pure product) was first suggested by Mateo et al (2007). They choose based on their previous study since it increased the plasma Arg concentration in pregnant sows by 70% at 2 h post-feeding (Figure 1). This indicated that Arg provided through dietary supplementation can be delivered to the body successfully for further metabolism (Wu et al., 2007). Therefore, most of the reported trials have been conducted with very high Arg additions. In these trials, free Arg level ranging from 0.4% to 1.08% and with 0.83% as the most frequent tested level, besides basal dietary Arg (Mateo et al.,2007; Bass et al.,2011; Liu et al.,2012; Gao et al.,2012; Wu et al.,2012;Che et al., 2013; Quesnel et al., 2014; Li et al., 2015; Dallanora et al., 2017; Nuntapaitoon et al.,2018; Hines et al.,2019; Moreira et al., 2020). However, Li et al. (2010) reported embryo mortality significantly increased as Arg supplementation increased from 0.4 to 0.8% between 0 and 25 days of gestation. This report suggest that higher Arg addition may be harmful in early gestation. On the other hand, considering the market cost of L-arginine, dietary arginine below 1% supplementation need to be investigated (Hong et al., 2020). Four studies using lower supplemental Arg levels (0.1%-0.3%) reported an increase in the number of piglets BA (Guo et al., 2016; Bieliński et al., 2017; Hong et al., 2020; Luise et al., 2020). However, Nuntapaitoon et al. (2018) using lower dose of Arg (0.4%) had no effect on the number of piglets BA but significantly increased their BW.

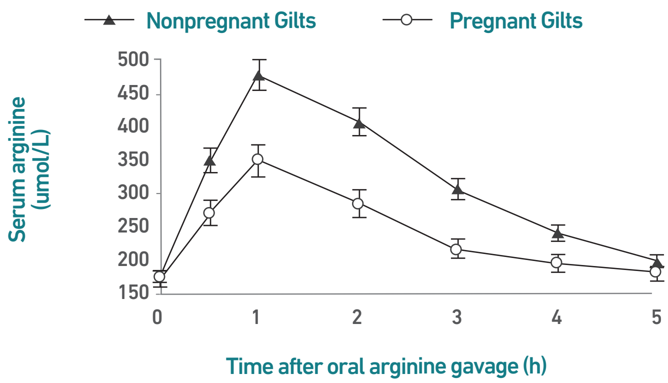


**Figure 1. Concentrations of Arg in serum of nonpregnant and pregnant gilts after oral administration of Arg (50 mg Arg/kg BW) (Wu et al., 2007)**

There are two obvious concerns with these studies: (1) Basis for recommended free Arg level. As the baseline level of plasma Arg in pregnant gilts is about 180 μmol/L (Figure 1), levels of plamsa Arg above 300 μmol/L are sufficient according to Mateo et al (2007). But in fact, the concentration of plasma Arg in all the studies excceded 300 μmol/L after a period of feeding, except for Guo et al. (2016) in which 0.1% free Arg was supplemented thus resulting in plasma Arg levels of 242 and 258 μmol/L at day 70 and 90 during gestation, respectively (Table 3). (2) Level of basal dietray Arg. In the previous studies, only supplemental Arg was considered or disscussed. A greater amount of free Arg were supplemented to a control diet with low basal Arg (0.72% or below) to expect a significant result (Mateo et al., 2007; Wu et al., 2012; Che et al., 2013; Dallanora et al., 2017; Hines et al., 2019; Hong et al., 2020; Luise et al., 2020). In the other studies, the basal diet already contained higher content of Arg (0.93%-1.28%) from feed ingedient (Bass et al.,2011; Dallanora et al., 2017; Nuntapaitoon et al.,2018; Lusie et al., 2020 ).

**Table 3. Concentration of plasma Arg at 2 hour after feeding supplementary Arg to gestating sows**

| Timing | Feeding stage | Dose of free Arg (%) | Plasma Arg(μmol/L) | Reference |
|---|---|---|---|---|
| 30 | 30- | 0.00 | 202 | Mateo et al., 2007 |
| | | 0.80 | 203 | |
| 70 | | 0.00 | 194 | |
| | | 0.80 | 349 | |
| 110 | | 0.00 | 193 | |
| | | 0.80 | 341 | |
| 40 | 22-114 | 0.00 | 186 | Gao et al., 2012 |
| | | 0.80 | 348 | |
| 70 | | 0.00 | 177 | |
| | | 0.80 | 405 | |
| 90 | | 0.00 | 200 | |
| | | 0.80 | 401 | |
| 30 | Control | 0.00 | 238 | Che et al., 2013 |
| | 30-90 | 0.81 | 245 | |
| | 30-114 | 0.81 | 242 | |
| 90 | Control | 0.00 | 220 | |
| | 30-90 | 0.81 | 455 | |
| | 30-114 | 0.81 | 459 | |

| Timing | Feeding stage | Dose of free Arg (%) | Plasma Arg(µmol/L) | Reference |
|---|---|---|---|---|
| 110 | Control | 0.00 | 245 | Che et al., 2013 |
| | 30-90 | 0.81 | 286 | |
| | 30-114 | 0.81 | 466 | |
| 30 | 30- | 0.00 | 188 | Guo et al., 2016 |
| | | 0.10 | 196 | |
| 70 | | 0.00 | 196 | |
| | | 0.10 | 242 | |
| 90 | | 0.00 | 213 | |
| | | 0.10 | 258 | |
| 70 | 70-114 | 0.00 | 154.5 | Hong et al., 2020 |
| | | 0.28 | 255.0 | |
| | | 0.79 | 195.8 | |
| 90 | | 0.00 | 262.9 | |
| | | 0.28 | 349.1 | |
| | | 0.79 | 482.7 | |
| 110 | | 0.00 | 196.4 | |
| | | 0.28 | 301.2 | |
| | | 0.79 | 366.9 | |

## Supplementation period of Arg in gestating sows

Dietary Arg supplementation during sows pregnancy is an alternative solution to improve reproductive efficiency. The ideal time to supplement Arg is still uncertain, without consensus in the literature (Palencia et al., 2018). As shown in figure 2, more than adequate numbers of viable embryos enter the uterus on d 2 or 3 of gestation, but due to an asynchrony of development, 20 to 30% of conceptuses are lost by d 18. Additional numbers of conceptus loss occur between d 30 and 40 (15 to 20% loss) and during the last third of gestation (5 to 10% loss) as the competition for limited uterine space becomes critical (Ford et al., 2002). Supplementation of Arg at first pregnancy stage were confirmed to be determinant for embryos viability and survival, because it benefits embryo implantation, formation, vascularization, and placental growth (Li et al., 2014). Additionally, Wu and Meininger (2002) reported that dietary Arg improved the blood flow between the placenta and fetus, which affected nutrients and oxygen transfer to the fetuses. Thus, additional Arg supplementation specifically during late gestation was likely to improve placental growth and fetal development via the above mechanism, resulting in a linear increase in the total litter weight at birth.

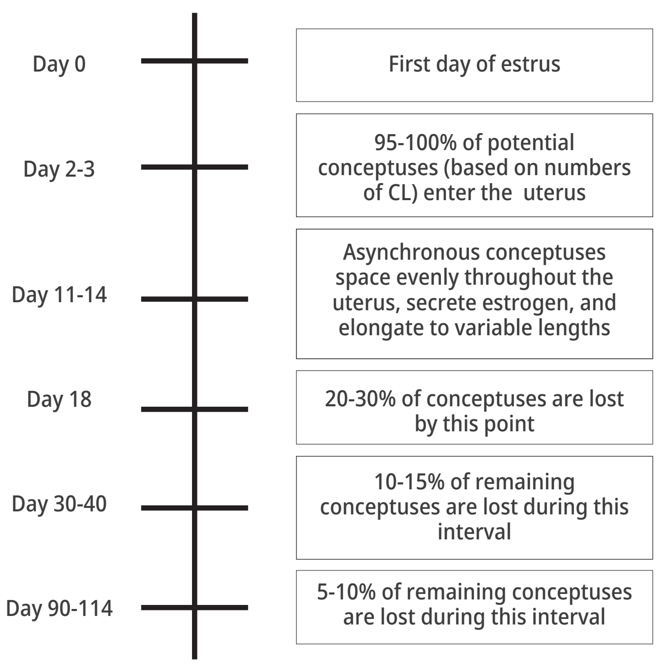


**Figure 2. A time line demonstrating the time periods of conceptus loss in the pig (Ford et al., 2002)**

On the basis of this mechansim, Li et al. (2015) supplemented Arg in the first third of gestation (d 1-30) and reported improved results for sow's reproductive efficiency. In addition, Bérard and Bee (2010) pointed out the influence of 26 g L-Arg HCl daily supplementation between 14 and 28 days of gestation on fetal myogenesis, positively affecting the primary phase of myofiber formation, and also increasing the number of viable fetuses and the total weight of fetuses at 75 days of gestation. On the other hand, some studies have shown that Arg supplementation would be effective in later pregnancy (Palencia et al., 2018), because an efficient placenta in late gestation is physiologically required for rapid fetal growth during the last 20 days of gestation (Wu et al., 2012; Liu et al., 2012; Nuntapaitoon et al., 2018; Moreira et al., 2020; Hong et al., 2020). Meanwhile, it has been reported that dietary Arg supplementation from early gestation until day 114 of gestation enhances sow placental growth, litter size, and weight (Mateo et al., 2007; Bass et al., 2011; Gao et al., 2012; Che et al., 2013; Luise et al., 2020). In addition, two studies examined whether Arg supplementation during different gestational stages impacts gilt's reproductive performance. Che et al. (2013) reported that litter performance in sows receiving Arg until day 114 of gestation is improved compared to sows receiving Arg only until day 90 of gestation. However, Hines et al. (2019) reported no positive effect of supplementing Arg during specific phases of gestation on the number of piglets BA.

## Suggestions

Based on the analysis of the current literatures, some suggestions are as following:
Dose of supplemental Arg: At least three factors should be considered including the optimal dietary Arg requirement for gestating sows, Arg content of basal diet, and the duration of Arg supplementation. Briefly, usage of high Arg dose (0.4-0.8%) in a short time or usage of low Arg dose (0.1-0.2%) over a longer time depending on basal dietary Arg Level.
Period of supplemental Arg: The expected objectives and cost-effectiveness of supplemental Arg in gestating sow a should be considered. Supplementation of Arg at first pregnancy stage is targeted for embryos viability and survival, and during late gestation to improve placental growth and fetal development. Taking these two factors into consideration, dietary Arg supplementation from early gestation until day 114 of gestation may be a better choice.

## Conclusion

It is well kown that Arg may benefit the reproduction effeciency of gestation sows, however, a series of systematic research trials are needed to investigate the effect of dose, timing and duration of Arg supplementation on reproduction efficiency of the gestating sow. Nevertheless, in light of some implications from most previous studies and the actual dietary level of Arg in commecial diets of gestating sows, we suggest dietary Arg supplementation using a low Arg dose (0.1-0.2%) from early gestation until day 114 of gestation.

## List of abbreviations

Arg, arginine; BA, born alive; BW, body weight

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