CESAR AUGUSTO POSPISSIL GARBOSSA

ARGININA E RACTOPAMINA NA NUTRIÇÃO DE PORCAS GESTANTES: EFEITOS SOBRE O DESENVOLVIMENTO FETAL E PÓS-NATAL DAS PROGÊNIES

LAVRAS – MG

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Tese apresentada à Universidade Federal de Lavras, como parte das exigências do Programa de Pós-Graduação em Zootecnia, área de concentração em Produção e Nutrição de Não Ruminantes, para a obtenção do título de Doutor.

Orientador

Dr. Vinícius de Souza Cantarelli

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APROVADA em 11 de agosto de 2014.

Dr. Allan Paul Schinckel	PURDUE University/USA
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“O caminho para se conseguir a felicidade é fazendo as outras pessoas felizes.”

“...the real way to get happiness is by giving out happiness to other people.”

Robert Baden-Powell
(Fundador do escotismo).

RESUMO

Cem porcas foram divididas em quatro tratamentos, dieta controle, dieta controle mais 1,0% de inclusão de L-arginina (Arg), dieta controle acrescida de 20 ppm de ractopamina-HCL (Rac) e a dieta controle com a inclusão de ambos (Arg + Rac). As porcas foram blocadas de acordo com a sua ordem de parte e linhagem genética. As progênies das fêmeas foram avaliadas desde o nascimento até o abate. O tratamento Arg + Rac teve um maior número de leitões natimortos (P <0,014). O peso ao nascer dos leitões de porcas alimentadas com Rac foi 11% maior (P <0,031) quando comparado aos leitões do tratamento controle. A distribuição no peso ao nascer foi melhorada pelo tratamento com Rac e Rac + Arg, uma maior percentagem de leitões foi observada com peso de nascimento superior a 1,6 kg (P <0,079). O CV do peso na desmama da progênie de matrizes alimentadas com Rac durante a gestação teve tendência (P <0,080) a ser menor. O diâmetro da fibra muscular do músculo semitendíneo dos leitões das fêmeas que receberam Arg, Rac e Arg+Rac aumentou (P <0,0001), quando comparado com o controle e, como consequência, o número de fibras por mm² diminuiu (P <0,0001). Na fase de creche o peso final da progênie de porcas que receberam Arg e Rac foram maiores (P <0,010) quando comparados com os animais do grupo controle. No início da fase de terminação 1 o peso dos animais do tratamento das porcas que receberam Arg foi maior do que os animais do tratamento Arg + Rac. O peso de carcaça quente foi maior (P <0,0001) para a progênie das fêmeas que receberam Arg e Rac em relação ao controle. A compacidade de carcaça foi maior (P <0,0211) para a progênie das fêmeas que receberam Arg comparada com a progênie de fêmeas que receberam Arg + Rac. O índice de bonificação (IB) apresentou tendência (P = 0,061) a ser maior para os animais do grupo Rac em comparação com os outros grupos. Não foram observados efeitos significativos para o lucro líquido, os suínos de fêmeas que receberam Arg foram 0,9% mais rentáveis do que o controle. Considerando-se o IB os animais do tratamento Rac obtiveram um lucro líquido 2,3% maior, o que representa US$1,93 dólares a mais por animal, quando comparado com os animais do grupo controle. Demonstrou-se com o estudo que a utilização de arginina e ractopamina para porcas gestantes são tecnologias aplicáveis na produção de suínos, melhorando a qualidade da progênie. A associação de ambas não diferiram do grupo controle, porém mais testes devem ser feitos para avaliar e levar a uma melhor compreensão do uso dessas tecnologias nos sistemas de produção de suínos modernos.

Palavras-chave: Porca. β-adrenérgico. Fibras musculares. Gestação. Progênie.

ABSTRACT

One hundred sows were divided in four experimental treatments, control diet, control diet plus 1.0% inclusion of L-Arginine (Arg), control diet plus 20 ppm of ractopamine-HCL (Rac) and the control diet with inclusion of both (Arg+Rac). Sows were blocked according to their parity and genetic line. The progeny of the sows were evaluated from the birth to the slaughter. The Arg+Rac treatment had a greater number of stillborn piglets (P<.014). Piglet birth weight from sows fed Rac were 11 % greater (P < .031) than piglets of the control treatment. The distribution at birth weight was improved by the treatment with Rac and Rac+Arg, a greater percentage of piglets were observed with birth weight greater than 1.6 kg (P < .079). The CV progeny weight at weaning of sows had a tendency to be lesser to sows fed Rac during gestation (P < .080). The *semitendinosus* muscle-fiber diameter of the piglets from the sows that received Arg, Rac, and Arg+Rac increased (P < .0001) when compared with the control and as consequence the fiber number per mm² decreased (P < .0001). In the nursery phase the final weight of the progeny from sows fed Arg and Rac were greater (P < .010). when compared with the animals of the control group. At the beginning of the Finisher 1 phase the weight of the pigs of the treatment from sows received that Arg was greater than pigs of the Arg+Rac. Hot carcass weight was greater (P < .0001) for progeny of the sows that received Arg and Rac compared to the control. Carcass compacity were greater (P < .0211) for the progeny of the sows that received Arg compared with the progeny of sows that received Arg+Rac. The bonification index (BI) had a tendency (P = .061) to be greater for the pigs of the Rac group compared to other groups. No significant effects were observed for the net income, pigs from sows that received Arg were 0.9% more profitable than the control. If the BI is considered the pigs of the Rac treatment had a 2.3% greater net income which represents US$ 1.93 dollars more per pig when compared with the pigs of the control diet. The trial showed that the utilization of arginine and ractopamine for gestating sows are applicable technologies in the swine production, improving the progeny quality, the association of both did not differ from the control group, however more trials should be made to evaluate and lead to a better understanding of the use of these technologies in the modern swine production systems.
Key words: pigs, β-agonist, muscle fiber, gestation, progeny

Keywords: Sow. β-adrenergic. Muscle fiber. Gestation. Progeny.

SUMÁRIO

PRIMEIRA PARTE

1 INTRODUÇÃO

A nutrição de fêmeas suínas tem evoluído consideravelmente nos últimos anos. Essa evolução deve-se principalmente à necessidade que os nutricionistas tiveram de adequar os programas nutricionais ao potencial genético e a capacidade de produção das matrizes atualmente disponíveis no mercado. Ainda assim, os desafios continuam, pois a hiperprolificidade dessas fêmeas, mesmo sendo economicamente favorável, aumenta a variabilidade do peso dos leitões ao nascimento e favorece a ocorrência de leitões menores.

O aumento da variabilidade dos leitões ao nascimento pode comprometer o desenvolvimento, pois animais com baixo peso ao nascer competem com menos sucesso pelo alimento, especialmente durante a lactação. Somado a isso, esses animais possuem menor taxa de crescimento, pois o potencial de crescimento pós-natal do músculo de animais de baixo peso é limitado pela hipertrofia de suas fibras musculares. Nesse sentido, são necessárias tecnologias que possam diminuir a variabilidade dos leitões e incrementar a quantidade e tamanho das fibras musculares.

Uma tecnologia que pode ser utilizada estrategicamente com esse objetivo na fase de gestação é a utilização da ractopamina, a qual pode através dos receptores β-adrenérgicos presentes nos vasos sanguíneos favorecer vasodilatação e um maior aporte sanguíneo aos fetos. Outros fatores que podem contribuir para os seus efeitos de aumento de peso da progênie estão relacionados a um efeito direto de incremento muscular nos tecidos dos leitões através da maior retenção de nitrogênio e ativação dos receptores β-adrenérgicos da placenta.

Outra tecnologia promissora para melhorar o desempenho dos leitões ao nascimento é a suplementação da arginina para matrizes em gestação, os efeitos da arginina parecem ser devidos à sua participação em regular a angiogênese, desenvolvimento vascular, funções da artéria umbilical e placenta, o que propicia mais nutrientes e oxigênio da porca para os fetos e assim contribuindo para o seu desenvolvimento.

Estudos que associam essas duas tecnologias são inexistentes na literatura, sendo necessário o desenvolvimento de pesquisas nessa área, para verificar a possível aplicabilidade em sistemas de produção de suínos comerciais. Assim, objetivou-se com este trabalho avaliar o efeito da inclusão de ractopamina e suplementação de arginina sobre o desempenho reprodutivo de matrizes suínas gestantes de alta produção e os efeitos sobre as suas progênies do nascimento até o abate.

2 REFERENCIAL TEÓRICO

2.1 Fases gestacionais

A nutrição da fêmea suína gestante pode ser dividida em fases distintas com relação a eventos e exigências nutricionais, principalmente, pelo fato das linhagens maternas contemporâneas possuírem maior potencial para crescimento de tecido magro, o que está associado com alterações no metabolismo em geral, sendo necessário reavaliar as exigências nutricionais e as técnicas de manejo nutricional, para otimizar o aproveitamento de nutrientes por parte dessas fêmeas modernas (FOXCROFT et al., 2005).

De acordo com Jindal et al. (1996), o manejo nutricional no início da gestação tem como objetivo intensificar a sobrevivência embrionária e suprir adequadamente a formação da placenta e anexos fetais. Alguns estudos mostram uma relação entre a composição da dieta durante o período pré-ovulatório e posterior sobrevivência e desenvolvimento do embrião (BAIDOO et al., 1992; KIRKWOOD; BAIDOO; AHERNE, 1990; ZAK et al., 1997a, 1997b). Apesar de terem sido detectados efeitos da composição da dieta fornecida pré-ovulatória associado ao desenvolvimento de oócitos e folículos, bem como efeitos residuais sobre a sobrevivência e o desenvolvimento embrionário.

Já Foxcroft e Town (2004) afirmam que a formação de fibras musculares primárias e secundárias ocorre em período intermediário da gestação. No entanto, estudos realizados por Ji et al. (2005) e McPherson et al. (2004) sugerem trabalhar de forma diferenciada os níveis nutricionais a partir dos 70 dias de gestação, em função da intima ligação com o desenvolvimento de fibras musculares dos fetos e formação do complexo mamário, visando ao melhor desempenho da leitegada ao nascer e vida reprodutiva futura da fêmea. Dessa forma é proposta a divisão da gestação em três fases: inicial, da cobertura

até os 21 dias; intermediária, dos 22 dias aos 75 dias; e fase final, dos 76 dias até o parto.

A terceira fase da gestação é caracterizada pelo maior desenvolvimento da glândula mamária (76 a 90 dias) e pelo crescimento mais acentuado do feto (a partir dos 91 dias). Nessa fase a necessidade de ganho proteico e reserva energética torna-se maior quando comparado aos dois períodos anteriores, resultando em aumento das exigências nutricionais da matriz, pois o crescimento fetal é acelerado no terço final da gestação (JI et al., 2005; MCPHERSON et al., 2004) e proteína extra é necessária para esse momento, especialmente se ainda estiver ocorrendo crescimento corporal da fêmea jovem. De acordo com Shields, Mahan e Maxson (1985), as fêmeas são muito mais sensíveis à suplementação proteica nessa fase em comparação com outras fases. A demanda de proteína pode ser suprida através de dietas contendo fontes de ingredientes vegetais ou animais e complementada com a adição de aminoácidos industriais (KIM et al., 2009).

Resumidamente, podemos dizer que no primeiro terço da gestação, as necessidades nutricionais são ligeiramente superiores às necessidades de mantença. No segundo terço, o principal objetivo de um programa nutricional é garantir o desenvolvimento corporal das fêmeas em crescimento e a recuperação das condições corporais das matrizes, devido à mobilização na lactação anterior. Nesse período o acompanhamento permanente da condição corporal dos animais é de extrema importância. Já o terço final de gestação é o período em que há o maior desenvolvimento fetal e das glândulas mamárias. Por isso, para cada fase deve ser dada uma atenção diferenciada.

2.2 Miogênese

A nutrição de fêmeas suínas tem evoluído consideravelmente nos últimos anos. Essa evolução deve-se principalmente à necessidade que os nutricionistas tiveram de adequar os programas nutricionais ao potencial genético e nível de produção das matrizes atualmente disponíveis no mercado.

O músculo esquelético constitui o principal componente da carcaça de animais destinados à produção de carne. O potencial de crescimento pós-natal do músculo de animais de baixo peso ao nascimento é limitado pela hipertrofia de suas fibras musculares. A hipertrofia é atingida quando as fibras alcançam seu máximo tamanho, portanto o tamanho do músculo é determinado com a compleição da hiperplasia (HANDEL; STICKLAND, 1988). Em mamíferos o desenvolvimento do músculo pode ser dividido em três fases: embrionária (miogênese primária), fetal (miogênese secundária) e pós-natal (miogênese pós-natal) (WIGMORE; STICKLAND, 1983). Durante a fase fetal a miogênese secundária é responsável pela formação da maioria das fibras musculares (DU; ZHU, 2009). Para a fase da miôgense secundária é necessário um grande número de fibras musculares, assim essa é suscetível ao estresse como a subnutrição da porca, a qual pode reduzir o número de fibras musculares do feto (ZHU et al., 2008). O desenvolvimento do músculo esquelético possui baixa prioridade na partição de nutrientes, tornando-se mais suscetível à flutuação de nutrientes (ZHU et al., 2008). Devido à característica de formação bifásica das fibras musculares existem períodos críticos para o desenvolvimento muscular no feto durante a gestação (WIGMORE; STICKLAND, 1983).

O baixo peso dos leitões ao nascer parece estar associado à redução do número de fibras musculares estabelecidas ainda no útero (WIGMORE; STICKLAND, 1983). Esse efeito é mantido no período pós-natal (HANDEL; STICKLAND, 1988) envolvendo, provavelmente, todos os músculos esqueléticos do corpo (STICKLAND; GOLDSPINK, 1973).

Avaliando o efeito do baixo peso ao nascer sobre as características musculares após o nascimento, Handel e Stickland (1987) verificaram uma correlação entre o baixo peso ao nascer e a redução no número de fibras musculares, mas concluíram que essa associação não foi consistente.

A principal causa do baixo peso ao nascer é a “subnutrição” uterina. Isso pode ser explicado pela distribuição dos fetos nos cornos uterinos, definindo uma diferenciação no aporte nutricional (DWYER; STICKLAND, 1991). Animais refugos normalmente são provenientes de placenta com menor peso e reduzido fluxo sanguíneo, comparado com leitões irmãos de maior peso, indicando uma diferença no aporte nutricional (DWYER; STICKLAND, 1991; POND; MANER, 1977).

A população inicial de fibras primárias se desenvolve por volta de 35 a 55 dias de gestação, através da fusão dos mioblastos para formar os miotubos primários, então a segunda geração de miotubos surge entre os dias 55 a 90-95 de gestação, originando a massa muscular principal. As fibras secundárias se formam envolta dos miotubos primários, usando-os como moldura. Acredita-se que o número total de fibras seja determinado definitivamente aos 90-95 dias de gestação. Existem alguns pesquisadores que sugerem a formação de uma terceira geração de fibras, as quais aparecem próxima ao nascimento de suínos. De acordo com Picard et al. (2002), as fibras terciárias somente estão presentes em animais de médio e/ou grande porte.

Powell e Aberle (1980) sugerem que ao nascimento existe uma relação de crescimento mais lento e menos eficiente de leitões leves comparados com seus irmãos mais pesados e que esses animais leves mostraram um menor número de fibras musculares, principalmente fibras secundárias (HANDEL; STICKLAND, 1987; WIGMORE; STICKLAND, 1983).

Handel e Stickland (1988) avaliaram o peso ao nascimento, o número de fibras musculares do músculo semitendíneo de suínos, sua relação com a taxa de

crescimento e o peso ao abate. Concluíram que animais com baixo peso ao nascer não são destinados a serem pequenos ao abate, desde que apresentem o mesmo número de fibras musculares que animais de maior peso ao nascimento. Os autores consideraram o número de fibras musculares um indicador do potencial de crescimento do suíno. É importante salientar também que o maior crescimento dos leitões, durante a gestação, ocorre no último mês, entre 85 a 115 dias (SOBESTIANSKY et al., 1998), o que não coincide com o período de hiperplasia das fibras musculares (36 a 90 dias de gestação Figura 1).

Suínos de baixo peso ao nascer competem com menos sucesso pelo alimento, especialmente durante a lactação. Portanto, esses animais podem apresentar uma baixa taxa de crescimento, mesmo possuindo um número adequado de fibras musculares. Por isso, a necessidade de uniformizar o tamanho dos animais durante seu crescimento (HEMSWORTH; WINFIELD; MULLANEY, 1976).

Para pesos vivos equivalentes, suínos com alto número de fibras musculares apresentaram menor diâmetro de suas fibras, comparados com animais com baixo número de fibras (DWYER; FLETCHER; STICKLAND, 1993), por apresentarem uma maior quantidade de fibras, possuem maior capacidade de crescimento muscular e consequentemente desempenho superior durante a fase produtiva apresentando carcaças mais pesadas ao abate.

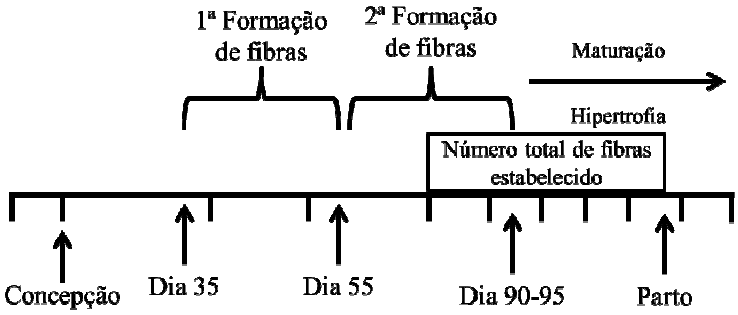

Figura 1 Representação esquemática do desenvolvimento da fibra muscular em suínos

Fonte: Adaptado de Wigmore e Stickland (1983)

Alvarenga et al. (2013), estudando leitões de baixo e alto peso ao nascer, verificaram que animais de alto peso apresentavam maior diâmetro das fibras musculares, no entanto menor número de fibras musculares por mm^2, os animais de baixo peso tiveram um desempenho inferior durante a sua vida e carcaças com menor peso, reafirmando a importância de se buscar leitões com maior peso ao nascimento, maior diâmetro e número total de fibras musculares.

2.3 Recursos para incrementar fibras musculares

Vários estudos estão relacionados aos diferentes métodos para incrementar a quantidade e diâmetro das fibras musculares com o objetivo de levar a um incremento no desempenho subsequente dos animais, melhorando o aporte nutricional das fêmeas,

Dwyer e Stickland (1991), no intuito de aumentar o número de fibras musculares de leitões através de um melhor aporte nutricional da progenitora,

verificaram melhores resultados quando o tratamento foi realizado antes do aparecimento das fibras secundárias (25 a 50 dias de gestação), período que aumentou de 9 a 13% o número de fibras comparado com o grupo controle. Como resultado observaram melhora na taxa de crescimento no ganho de peso e na conversão alimentar dos animais nos períodos mais tardios do crescimento até 80 kg de peso vivo, entretanto, os autores acreditaram que a causa não foi devido à melhora no aporte nutricional diretamente, mas sim aos efeitos indiretos da nutrição sobre os fatores de crescimento.

Dwyer, Fletcher e Stickland (1993) verificaram ainda que houve correlação positiva entre o ganho diário de peso e a relação fibras secundárias:primárias no período de 25 a 80 kg de peso vivo. Também existiu correlação negativa entre a conversão alimentar e o número de fibras musculares. Os autores concluíram que o peso ao nascer teve correlação positiva com a taxa de crescimento somente nos estágios mais iniciais do crescimento do suíno e, no período mais tardio do crescimento, após 70 dias, o maior crescimento dos animais pareceu ser determinado pelo número de fibras musculares, ou seja, em animais que apresentavam maior quantidade de fibras no momento do nascimento foi verificado um melhor desempenho.

Os mecanismos pelos quais os hormônios agem sobre o incremento muscular fetal ainda não são bem conhecidos. É possível que exista uma grande relação entre os diferentes hormônios ligados ao crescimento e as substâncias denominadas de repartidores de nutrientes. Essas substâncias são assim nominadas devido à sua capacidade de redirecionar a distribuição de nutrientes em função da alteração do metabolismo da célula. Dessa forma, os nutrientes utilizados para a produção de tecido adiposo seriam dirigidos para aumentar a deposição de tecido muscular (RICKS; BAKER; DALRYMPLE, 1984).

2.4 Arginina

A arginina (Arg) é um aminoácido condicionalmente essencial produzido no organismo, porém em quantidade insuficiente para todas as necessidades (FLORA FILHO; ZILBERSTEIN, 2000). A síntese endógena de arginina atende à cerca de 50% das necessidades diárias desse aminoácido em suínos jovens, sendo a produção pelo organismo importante na regulação da homeostasia desse aminoácido em neonatos e suínos em crescimento (FLYNN; WU, 1996).

Em adultos, a síntese endógena de Arg ocorre no intestino delgado e rins (REYES; KARL; KLAHR, 1994) através do eixo intestino-renal (MORRIS JÚNIOR, 2002). Assim, a citrulina é absorvida pelo intestino delgado e transportada através da circulação até os rins, onde será captada e utilizada para a produção de Arg (DHANAKOTI et al., 1990). É importante que esses substratos sejam fornecidos pela dieta, pois a captação de glutamato ou prolina da circulação arterial pelo intestino delgado não é expressiva (WU et al., 2009).

A Arg desempenha múltiplos papéis no metabolismo animal servindo de substrato para a síntese de proteína, como intermediária no ciclo da ureia e como precursora na síntese de vários compostos metabólicos importantes incluindo a prolina, ornitina, poliaminas e óxido nítrico (KIM et al., 2007; WU; MORRIS, 1998).

A importância da arginina para a gestação da porca foi estudada por Mateo et al. (2007). Os autores verificaram que a suplementação com arginina no início da gestação elevou o número de nascidos vivos. Nos estudos dos mesmos autores a suplementação da ração de gestação com 1,0% de L-arginina a partir dos 30 dias até o parto, aumentou não somente o número, mas também o peso da leitegada (nascidos vivos) ao nascimento.

Os efeitos da arginina parecem ser devidos à sua participação em regular a angiogênese e desenvolvimento vascular e funções da artéria umbilical e placenta providenciando mais nutrientes e oxigênio da porca para os fetos (LIU et al., 2012).

O fluxo sanguíneo e a angiogênese são regulados pelo óxido nítrico derivado da Arg (LACASSE; PROSSER, 2003; MEININGER; WU, 2002). O óxido nítrico (ON) é uma molécula gasosa simples, altamente lipofílica. O óxido nítrico é o maior vasodilatador das células endoteliais (WU; MEININGER, 2000), e desempenha papel importante na regulação do fluxo sanguíneo placentário e, portanto, na transferência de nutrientes e oxigênio da mãe para o feto (BIRD; ZHANG; MAGNESS, 2003). Além disso, o ON é um importante mensageiro intercelular nos mamíferos superiores. O mecanismo de sinalização intercelular é, em geral, realizado através de receptores de membrana celular na célula alvo e, habitualmente, são transmembranosos em contato com citoplasma e desencadeando uma “cascata” de sinais intracelulares que interfere no metabolismo celular. Pelas suas características químicas de alta difusibilidade, a sinalização do ON é exercida diretamente em nível intracelular, sem receptores transmembranosos. Devido à sua penetração intracelular sem intermediários membranosos, o organismo utiliza o ON em funções fisiológicas em que é necessária uma resposta rápida (FLORA FILHO; ZILBERSTEIN, 2000).

2.5 Ractopamina

Entre os repartidores de nutrientes, existe a ractopamina, um agonista beta-adrenérgico da classe das fenetanolaminas, sintético com comprovada eficiência na produção de carne, proporcionando menor deposição de tecido adiposo e maior porcentagem de carne magra na carcaça (GARBOSSA et al., 2013).

A absorção da RAC ocorre no intestino delgado dos suínos, uma vez que a alcalinidade do meio reduz sua ionização (PALERMO NETO, 2002), apresentando pico plasmático entre uma a três horas após a ingestão da substância (SMITH, 1998).

A ractopamina tem sido considerada uma substância segura nas doses recomendadas considerando os limites máximos de resíduos (LMR) admitidos em tecidos comestíveis. Cerca de uma hora após a interrupção do fornecimento não se encontram mais concentrações da substância ativa, em tecidos comestíveis, capazes de provocar efeitos farmacologicamente importantes em uma pessoa de 60 kg (PALERMO NETO, 2002).

Os receptores beta-adrenérgicos são divididos quanto à sua resposta em α ou β, o mecanismo pelo qual os receptores beta-adrenérgicos ativados aumentam a taxa de lipólise está relacionado à ação da enzima proteína quinase A (PKA), segundo Fain e Garcia-Sainz (1983). A ativação dos beta-receptores é realizada com a participação das proteínas G, que ativam a adenilciclase, a qual converte a adenosina trifosfato em monofosfato (AMPc). O AMPc, que age como um sinalizador intracelular, liga-se à subunidade da PKA, ativando-a, essa por sua vez, é responsável pela fosforilação de muitas enzimas que aumentam a taxa de lipólise (MOODY; HANCOCK; ANDERSON, 2000).

O mecanismo de ação dos agonistas beta-adrenérgicos está sujeito a dois processos de regulação. O primeiro seria o número de receptores ou a densidade desses receptores na membrana celular, enquanto que o segundo mecanismo de regulação seria a habilidade desses receptores de interagirem com proteínas G para alterar a função celular (BIRNBAUMER et al., 1985).

Nos suínos a RAC parece se ligar principalmente aos receptores dos subtipos β1 e β2 (SILLENCE, 2004), entretanto apresentam aparentemente efeitos mais consistentes quando ligados aos receptores β2, já que Mills et al. (2003), utilizando células cultivadas *in vitro*, observaram que o aumento da

formação do segundo mensageiro AMPc é mais eficiente quando da ligação do ABA ao receptor β2 em relação ao receptor β1.

Alguns estudos indicam que a estimulação "*in vitro*" do músculo esquelético por agonista beta-adrenérgico, através da modulação na concentração de AMPc, está envolvida na regulação da diferenciação desse tecido (CURTIS; ZALIN, 1981). Um aumento na concentração de AMPc foi observado durante o desenvolvimento do músculo esquelético de embriões de frangos (ZALIN; MONTAGNE, 1975). Portanto, há indícios que a administração de um agonista beta-adrenérgico durante a gestação possa afetar, através da concentração de AMPc, o desenvolvimento pré-natal do músculo esquelético (KIM et al., 1994).

Em estudo realizado por Karadas et al. (2007) avaliando o efeito de agonistas β-adrenérgicos em artérias umbilicais *in vitro* foi verificado que esses tiveram a capacidade de aumentar o AMPc levando a uma vasodilatação, o que pode contribuir para um maior fluxo sanguíneo destinados aos fetos.

Outro fator que pode contribuir para a utilização de Rac para matrizes suínas está ligado ao fato de que essa substância tem a capacidade de aumentar a retenção de nitrogênio, ou seja, podendo contribuir para que seja sintetizado uma maior quantidade de tecido muscular nos fetos durante a fase de formação desse tecido (CANTARELLI et al., 2009).

A ação hipertrófica da ractopamina sobre o músculo esquelético pode ser mediada pelo IGF-I (Insulin-like Growth Factor-I), que aumenta a síntese proteica (ROE; HARBER; BUTTERY, 1989) e parece ser importante na regulação do número de fibras musculares, porque é responsável pela proliferação e diferenciação dos mioblastos (ENGERT; BERGLUND; ROSENTHAL, 1996; EWTON; FLORINI, 1980; FLORINI; EWTON; MAGRI, 1991; ROSENTHAL; CHENG, 1995). Entretanto, Grant et al. (1993) observaram que o tratamento com ractopamina, por um período de 4 semanas,

não aumenta a concentração de RNAm responsável pela produção de IGF-I no fígado.

Em alguns experimentos conduzidos por Hoshi et al. (2005a, 2005b) em que estudaram a utilização de ractopamina dos 25 aos 50 dias de gestação, não verificaram aumento no peso de nascimento, tamanho do músculo, e fibras musculares, porém o peso de carcaça e o desempenho da progênie provenientes dessas fêmeas foi superior. Gatford et al. (2009) também avaliaram o efeito da suplementação de 20 ppm de ractopamina para porcas dos 25 aos 50 dias de gestação e observaram um aumento no peso médio ao nascer e incremento no diâmetro das fibras musculares.

Embora sejam poucos os trabalhos que tratam das relações dos beta-adrenérgicos com o desenvolvimento fetal, os resultados indicam que os períodos de tratamento mais extensos não são necessariamente os responsáveis pelos melhores efeitos. Esse comportamento pode ser explicado pelos estudos conduzidos por Moody, Hancock e Anderson (2000), os quais descrevem que os receptores beta diminuem a sensibilidade aos agonistas após exposição por períodos longos. O processo de dessensibilização ocorre através da fosforilação da região C-terminal dos beta-receptores. Essa fosforilação induz as proteínas G a se ligarem a outras proteínas, resultando na desativação dos receptores (PIPPIG et al., 1993).

De acordo com e Sanches et al. (2010), See, Armstrong e Weldon (2004) e Weber et al. (2006) há maior ganho de peso em animais suplementados com RAC. Schinckel, Richert e Herr (2002) observaram aumento em 10 a 12% no ganho de peso diário quando a ractopamina é administrada durante cinco semanas para um ganho de 40 kg antes do abate. Marinho et al. (2007a, 2007b) e Rikard-Bell et al. (2009), verificaram que houve melhor conversão alimentar para animais recebendo RAC. Cantarelli et al. (2009), verificaram que a

suplementação de 5 ppm de RAC na dieta de suínos em terminação melhora as características de carcaça e torna viável economicamente a produção.

3 CONSIDERAÇÕES GERAIS

As matrizes suínas atuais são mais precoces, possuem maior peso corporal e são mais produtivas, com potencial de produção, em alguns sistemas, de 35 leitões desmamados/ano. Entretanto, tem-se observado um aumento na incidência de leitões com baixo peso ao nascimento, o que diminui a viabilidade desses animais, elevando, assim, as taxas de mortalidade nas fases iniciais de produção.

O desenvolvimento de leitões com baixo peso ao nascimento (0,8 – 1,1 kg) tende a ser mais lento e menos eficiente que animais com pesos superiores (2,0 – 2,5 kg). Isso se deve principalmente ao processo competitivo constante que os coloca em contínua desvantagem, e não necessariamente porque apresentam um número reduzido de fibras musculares secundárias comparados com animais de maior peso.

Durante o desenvolvimento pré-natal, sabe-se que o número de fibras musculares secundárias do leitão pode ser afetado pelo ambiente uterino. Em geral, influências nutricionais e hormonais podem incrementar o número de fibras musculares e, consequentemente, aprimorar o desenvolvimento pós-natal dos animais.

Dentre as alternativas de manipulação de crescimento fetal, a utilização da ractopamina associada a aminoácidos funcionais tem despertado a atenção dos pesquisadores, a partir do reconhecimento de funções metabólicas importantes e diretamente relacionadas às funções reprodutivas das matrizes.

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SEGUNDA PARTE

ARTIGO–Ractopamine and arginine fed for sows improves the progenies quality

Normas do Journal of Animal Science

ABSTRACT: One hundred sows were divided in four experimental treatments, control diet, control diet plus 1.0% inclusion of L-Arginine (Arg), control diet plus 20 ppm of ractopamine-HCL (Rac) and the control diet with inclusion of both (Arg+Rac). Sows were blocked according to their parity and genetic line. The progeny of the sows were evaluated from the birth to the slaughter. The Arg+Rac treatment had a greater number of stillborn piglets (P<.014). Piglet birth weight from sows fed Rac were 11 % greater (P < .031) than piglets of the control treatment. The distribution at birth weight was improved by the treatment with Rac and Rac+Arg, a greater percentage of piglets were observed with birth weight greater than 1.6 kg (P < .079). The CV progeny weight at weaning of sows had a tendency to be lesser to sows fed Rac during gestation (P < .080). The *semitendinosus* muscle-fiber diameter of the piglets from the sows that received Arg, Rac, and Arg+Rac increased (P <

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.0001) when compared with the control and as consequence the fiber number per mm² decreased (P < .0001). In the nursery phase the final weight of the progeny from sows fed Arg and Rac were greater (P < .010) when compared with the animals of the control group. At the beginning of the Finisher 1 phase the weight of the pigs of the treatment from sows received that Arg was greater than pigs of the Arg+Rac. Hot carcass weight was greater (P < .0001) for progeny of the sows that received Arg and Rac compared to the control. Carcass compacity were greater (P < .0211) for the progeny of the sows that received Arg compared with the progeny of sows that received Arg+Rac. The bonification index (BI) had a tendency (P = .061) to be greater for the pigs of the Rac group compared to other groups. No significant effects were observed for the net income, pigs from sows that received Arg were 0.9% more profitable than the control. If the BI is considered the pigs of the Rac treatment had a 2.3% greater net income which represents US$ 1.93 dollars more per pig when compared with the pigs of the control diet. The trial showed that the utilization of arginine and ractopamine for gestating sows are applicable technologies in the swine production, improving the progeny quality, the association of both did not differ from the control group, however more trials should be made to evaluate and lead to a better understanding of the use of these technologies in the modern swine production systems.

Keywords: pigs, β-agonist, muscle fiber, gestation, progeny.

INTRODUCTION

Modern sows are more prolific and produce progeny with increased genetic potential for lean growth. For this reason, modern sows have increased nutrient requirements during gestation (Ball and Moehn, 2013), as the number of piglets increase, the placental blood flow per fetuses decreases (Père and Etiene, 2000). Due to this increased prolificacy, intrauterine growth retardation has become a more common problem (Bérard et al., 2010). Large litter sizes can be affected by limited uterine capacity leading to decreased fetal growth, increased fetal death, and reduced litter size at birth (Vallet et al., 2002). As the number of piglets per litter increases, the variability in birth weight increases, while their mean birth weight decreases (Quiniou et al., 2002). The within-litter birth weight variation is economically important because it is positively correlated with pre-weaning mortality (Wolf et al., 2008), and greater variation in slaughter weight.

Adequate maternal nutrition, especially adequate amounts of protein and specific amino acids, is very important with prolific sows. Essential amino-acids play crucial roles in the development and growth of the placenta and the fetuses (Wu et al., 2004). Arginine is an amino acid that plays multiple roles in animal metabolism as a precursor of various important metabolic molecules as nitric oxide (NO) and polyamines (Mateo et al., 2007). Increased NO concentrations can increase blood flow (Wu and Meininger, 2000), therefore increasing the transference of essential nutrients from maternal to fetal blood (Bird et al., 2003). Past research has observed positive effects of supplementing L-arginine to gestating sows, including enhanced fetal survival, increased myofiber

formation, and increased number of piglets born alive (Mateo et al., 2007; Bérard et al., 2010). Another technology that can increase fetal and progeny development is the utilization of β_2-adrenergic agonists. Kim et al. (1994) found that feeding sows with salbutamol in the first third of pregnancy increased muscle size and altered muscle fiber types of progeny. Past trials (Hoshi et al., 2005a,b) evaluated the effect of feeding ractopamine (Rac) to sows from day 25 to 50 of gestation, and reported greater progeny growth rate and carcass weight for progeny of sows fed Rac. A similar trial (Gatford et al., 2009) evaluated the effects of feeding Rac to sows in the same stage of gestation and reported a 9% increase of 9% in fetal weight.

The objective of this research was to verify the effect of inclusion of ractopamine, arginine, and the association of both compounds on performance of sows and their offspring from birth to slaughter.

MATERIAL AND METHODS

This experiment involved two stages: reproduction (gestation and lactation of sows) and production (progeny performance from weaning to slaughter). The experiment was carried out between June of 2013 and February of 2014 at Arapé, a commercial farm with 2,500 sows in Formiga, Minas Gerais State, Brazil.

All procedures and housing adopted in this trial were approved by the "Ethic Committee on Animal Use" of Federal University of Lavras under protocol #099/12, Lavras – Brazil.

Reproduction stage

This stage was carried out on gestation and farrowing facilities of a Commercial Farm, Minas Gerais State, Brazil.

Animals and housing

One hundred sows were individually housed in gestating crates, until the 53rd day of gestation. Afterwards, they were group housed in pens with of 15 animals each until day 110 of gestation, and were transferred to farrowing crates. Sows had *ad libitum* access to water during the entire gestation and lactation phases.

Experimental design

The four dietary treatments groups were: Control: control diet; Arg: control diet + supplementation of 1.0% of L-Arg from day 25 to 53

of gestation; Rac: control diet + addition of 20 ppm of HCl-Rac from day 25 to 53 of gestation; Arg+Rac: control diet + supplementation of 1.0% of L-Arginine + 20 ppm of HCl-Rac from day 25 to 53 of gestation. The feeding period of the gestation dietary treatments was targeted as the pre-hyperplasia stage (25 to 50 days of gestation), the time of secondary muscle cell development for piglets (Dwyer et al., 1994), and as recommended by Hoshi et al. (2005a).

Experimental procedure

All sows were checked for estrus once daily in the morning and inseminated twice with unfrozen semen during estrus (18-24 h apart), using semen from hybrid boars with the same genetic background. At day 25 of gestation, sows were blocked according to their genetic line (DanBred - DB90 or Agroceres PIC - Camborough 25) and parity, and start date for the experimental period. Sows were fed once a day during the entire gestation period with the gestation diet presented in Table 1. From breeding to 28 days of gestation sows were fed 2.3 kg per day, from 29 to 90 days of gestation 1.8 kg per day, from day 91 to 110 days of gestation 2.8 kg per, day from 111 days of gestation to the previous day of farrowing the sows were fed 2.6 kg per day. The Rac and Arg supplements were top-dressed on the sows feed day 25 to day 53 of gestation.

During lactation, sows were given *ad libitum* access to feed with the lactation diet presented in Table 1.

Farrowing process was observed for data recording. Twenty four hours after birth, litter size number was standardized by cross-fostering to 12 piglets, corresponding to their treatment.

Sows had backfat depth recorded at days 25 and 53 of gestation, and at farrowing. Backfat depth was measured at the P2 position using an ultrasound scanner (Lean Meater, Renco Corporation, Minneapolis, Minnesota, USA).

After each farrowing the weight of the placenta, number of piglets born alive, stillbirth, and mummified were recorded. Each pig was individually weighed and tagged according to their mother's treatment. Pre-weaning deaths as the weaning individual pig weights and number weaned per litter was recorded.

At farrowing 12 male piglets of each treatment with the average birth weight of the litter were euthanized, to harvest *semitendinosus* muscle. A complete transverse slice 1 cm thick was taken from the muscle, the samples were frozen in liquid nitrogen at -196°C, and were at -80°C. In order to determine muscle fiber number and area, samples were cut in 10 µm thickness by using cryostat and H&E (hematoxylin-eosin) stained. For each section, 6 fields were captured at 20x resolution for later counting of muscle fibers using random-systematic sampling, starting in the upper lefthand quadrant and capturing fields with constant horizontal and vertical spacing. All fibers were counted in an area of 0.0768 mm^2 per field using ImageJ IJ 1.46r (Rasband and Ferreira, 2012). Muscle fiber number (fiber number/mm^2) was calculated as the mean number of fibers per mm^2. Fiber diameter of fibers was measured at 40x resolution using ImageJ IJ 1.46r for 40 fibers per field and 6 fields per *M. semitendinosus*

(total 240 fibers per piglet). The animals that were euthanized had the brains and liver weight recorded, to evaluate the brain:liver ratio.

After weaning, the pigs were fed the same series of diets up to slaughter. All the piglets were mixed sex housed in pens for 45 pigs for 39 days grouped according to the treatment received by the sow (6 replicates per treatment of approximately 45 animals per replicate). After this period, the pigs were transferred to the growing barn and housed in pens for 20 animals for 38 days (12 replicates per treatment of approximately 20 animals per replicate). For the Finisher phase the animals were transferred to the finishing barn with pens of 16 pigs each for a period of 40 days (15 replicates per treatment of approximately 16 animals per replicate).

Feed intake and body weight data of the pigs were recorded to slaughter. During the nursery phase had *ad-libitum* access to feed. The feeding program was divided in three diets pre-starter during 17 days, Starter I during 12 days, and Starter II during 10 days. In the grower and finisher phase the feeding program were divided in five diets, being liquid fed by a computerized feeding system (WEDA, Germany) the amounts fed were determined by the growing-finishing feed intake curve of the commercial farm that consider the age of the animals to increase the feed amount. The grower feeds were: Grower 1 fed during 12 days, Grower 2 fed during 12 days, and Grower 3 fed during 14 days. The finisher diets were: Finisher 1 fed during 20 days and Finisher 2 that had 6.0 ppm of Rac and a greater amount of crude protein and Lysine to allow a greater growth of the pigs fed Rac this feed were fed until the animals went to slaughter. Diets composition and nutritional values are presented in Table

2. Intakes were recorded weekly and pigs were group weighted at age in days 60, 98, 118, and 138 post-weaning.

Growth and carcass data

Body weight (BW) and feed consumption were assessed in order to evaluate growth performance criteria, average daily gain (ADG), average daily feed intake (ADFI), gain to feed ratio (G:F), in the nursery, grower and finisher phases. On day 121 post-weaning, one male pig with the greatest body weight of each replicate was selected to be slaughtered, the pigs were fasted for 12 hours, weighed, and then shipped to a commercial facility to be slaughtered according to the Brazilian legislation (BRASIL, 2000). After being electrically stunned, the pigs were exsanguinated and eviscerated. The carcasses were weighed before and after chilling for 24 hours. Muscle pH was measured in the *Longissimus dorsi* muscle at the last rib of the left-side carcass 45 minutes after slaughter (pH 45 min) and after 24 hours of cooling at 4 °C (final pH).

Backfat thickness at tenth rib (BF) was measured as well as loin depth (LD) with an electronic caliper (Neiko 01407A Stanless Steel). Longissimus muscle area (LMA) was evaluated by drawing the outline of the muscle at the tenth rib on a paper and then scanning and measuring the area through ImageJ IJ 1.46r (Rasband and Ferreira, 2012). The carcass length was measured; carcass compacity was calculated by the relation between carcass length and cold carcass weight.

Color was examined in the *Longissimus dorsi* muscle 24 hours after slaughter using a portable Minolta colorimeter model CR-400, with

integrating sphere and angle of view 10º, i.e., and illuminant D65. The components L* (lightness), a* (red-green component), and b* (yellow-blue component) are expressed using the CIELAB color system (Konica Minolta Holdings, 1998). Measurements were obtained by moving the device in three different positions, in such a way that almost the entire muscle surface was sampled. The average reading was used for statistical analysis. Chroma (C*) and hue angle (h*) were evaluated as color cariables being calculated by the equations suggested by Ramos and Gomide (2007) where C* = (a*2 + b*2)1/2 and h* = tan-1 (b*/a*).

The carcass meat yield (CMY) and the bonus index (BI) were estimated by equations described by Guidoni (2000): CMY = 65.92 – (0.685 * BT) + (0.094 * LD) – (0.026 * HCW) where CMY = carcass meat yield (%), BT = backfat thickness (mm), LD = loin depth (mm) and HCW = hot carcass weight (kg) and BI = 23.6 + 0.286 * HCW + CMY where BI = bonus index (%).

Gross income was calculated using a equation suggest by Fávero et al. (1997): GI (US$) = (BI*[price paid for the kg of live weight of the swine (US$)/0,7145])*HCW.

Feed costs (F_{cost}) were determined for the pigs during the entire period of the trial as the following formula: F_{cost} (US$) = total feed consumption of each diet (kg) * price of each diet (US$) using February 2014 prices.

The price to acquire each pig at weaning was US$ 45.00. The total cost (T_{cost}) was calculate by the sum of the feed cost (F_{cost}) plus the cost to acquire each animal (A_{cost}) plus the cost to feed the sows with the products (S_{cost}), as the following formula: $T_{cost}= F_{cost}+ A_{cost} + S_{cost}$.

Net income (NI) was calculated by subtracting the gross income by the total cost, as the following formula:NI (US$) = GI (US$) - T_{cost} (US$)

Table 1. Dietary composition, as formulated, of gestation and lactation diets used in the experiment.

Ingredients (%)	**Gestation**	**Lactation**
Corn	76.500	53.500
Soybean, 46%	17.500	23.500
Yeast	1.000	2.500
Biscuit meal	-	10.000
Soybean oil	-	3.000
Sugar	-	2.500
Phosphate	1.820	1.400
Dicalcium limestone	0.700	0.600
Sodium chloride	1.190	1.350
Vitamin premix	0.350	0.300
Mineral premix	0.120	0.100
DL-Methionine 99	0.025	0.050
L-Lysine 78	0.075	0.250
L-Threonine 98	0.040	0.065
Cooper Sulfate 25%	0.025	0.025
Tart-450[1]	0.300	0.300
Co-Factor III	0.030	0.020
Organic Zinc[3]	0.030	0.030
Organic Selenium[4]	0.010	0.010
Vitamin E 50%	0.005	0.010
Biotine 2%	0.010	0.010
Choline 60%	0.070	0.055
Adsorbent[6]	0.200	0.200
Sodium Bicarbonate	-	0.200
AgSweet 500	-	0.015
Phytase 500	-	0.010
Total	100	100
Calculated Values		
Metabolizable energy, kcal/kg	3,191	3,450
Crude protein, %	14.290	17.204
Lysine, %	0.802	1.129
Methionine, %	0.254	0.306
Threonine, %	0.630	0.745
Arginine, %	0.892	1.410
Phosphorus, %	0.659	0.590
Calcium, %	0.800	0.800
Crude fiber, %	3.329	3.392
Fat, %	2.977	6.406
Ash, %	5.236	5.215

[1]Blended Organic Acids, Sanphar, Brazil; [2]Bioplex, Alltech inc; [3]SelPlex, Alltech inc; [4]Starfix, Alltech inc.

Table 2. Dietary composition, as formulated, pre-starter, starter, weaner grower and finisher diets used in the experiment.

Ingredients (%)	Pre-Starter	Weaner		Grower			Finisher	
		I	II	I	II	III	I	II
Corn	0.140	42.28	62.88	64.63	69.17	72.89	77.08	75.99
Soybean, 46%	20.00	24.00	28.00	28.50	25.50	22.00	18.50	19.50
Yeast	2.500	2.500	1.000	-	-	-	-	-
Biscuit meal	12.50	5.000	-	-	-	-	-	-
Soybean oil	1.000	1.000	1.000	-	-	-	-	-
Sugar	5.000	5.000	-	-	-	-	-	-
MBM[1]	3.500	2.500	3.000	5.000	3.500	3.500	3.000	3.000
PBPM[2]	4.000	3.000	2.000	-	-	-	-	-
Pre-gelatinized corn	24.00	-	-	-	-	-	-	-
Concentrate[3]	10.00	-	-	-	-	-	-	-
Concentrate[4]	5.000	-	-	-	-	-	-	-
Concentrate[5]	-	5.000	-	-	-	-	-	-
Dried whey[6]	10.00	7.500	-	-	-	-	-	-
Sodium chloride	0.200	0.400	0.500	0.460	0.500	0.500	0.500	0.500
Vitamin premix	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300
Mineral premix	0.100	0.100	0.100	0.100	0.090	0.080	0.070	0.060
DL-Methionine 99	0.250	0.200	0.100	0.080	0.060	0.020	-	-
L-Lysine 78	0.475	0.350	0.300	0.250	0.245	0.225	0.205	0.245
L-Threonine 98	0.195	0.130	0.100	0.090	0.090	0.075	0.065	0.095
L-Tryptophan	0.065	0.045	0.015	0.010	0.010	0.005	0.005	0.005
Cooper Sulfate 25%	0.050	0.050	0.050	0.045	0.040	0.035	0.035	0.035
Zinc Oxide 79%	0.275	0.200	0.225	0.140	0.140	0.120	-	-
Tart-450[7]	0.300	0.300	0.300	0.300	0.300	0.200	0.200	0.200
Colistin Sulfate 50%	0.035	0.030	0.025	-	-	-	-	-
Bio Plus 2B[8]	0.040	0.040	0.040	-	-	-	-	-
Enradin F80[9]	0.025	0.020	0.020	-	-	-	-	-
Choline 60%	0.020	0.010	-	-	-	-	-	-
Doxiciclyn 50%	-	-	-	0.050	-	-	-	-
Surmax 200[10]	-	-	-	-	0.010	0.010	0.010	0.005
Halquinol 60%	-	-	-	-	0.030	0.025	0.020	0.020
Tiamuline 45%	-	-	-	0.030	-	-	-	-
AgSweet 500	0.030	0.030	0.030	-	-	-	-	-
Phytase 500[12]	-	0.010	0.010	0.010	0.010	0.010	0.010	0.010
Ractopamine 2%[11]	-	-	-	-	-	-	-	0.030
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Calculated values								
ME[12], kcal/kg	3,439	3,328	3,250	3,197	3,224	3,246	3,268	3,264
CP[13], %	21.963	21.495	20.987	20.521	18.766	17.329	15.913	16.304
Lysine, %	1.598	1.486	1.369	1.307	1.190	1.079	0.968	1.021
Lactose, %	14.80	7.625	0.000	0.000	0.000	-	-	-
Phosphorus, %	0.697	0.598	0.602	0.683	0.577	0.552	0.527	0.533
Calcium, %	0.939	0.779	0.728	0.811	0.692	0.652	0.614	0.623
Crude fiber, %	2.646	3.205	3.823	3.895	3.763	3.600	3.445	3.482
Fat, %	5.553	4.617	4.139	3.364	3.275	3.382	3.380	3.367
Ash, %	6.588	5.622	5.022	5.445	4.738	4.449	4.085	4.137

[1]Meat and bone meal; [2]Poultry by-products meal [3]Conc. Focus 2791 S Pr; [4]Conc. Focus 2792 S Pr; [5]Conc. Focus 2793 S In; [6]Dried whey, 12% of crude protein; [7] Blended Organic Acids, Sanphar, Brazil; [8] Probiotic, Chr. Hansen A/S, Denmark; [9]Enramycin 8%, MSD Saúde Animal, Brazil; [10]Avilamycin 20%, Elanco, Brazil; [11] Ractopamine 2%, Ourofino Saúde Animal, Brazil; [12]Metabolizable energy; [13]Crude protein;

Statistical analysis

All variables measured were tested for normality before analysis, and any variable that failed to follow normal distribution was transformed through the proc Rank procedure of SAS. The sows performance data were analyzed as a block design considering genetic line and parity as random factors by ANOVA using proc Mixed procedure of SAS, least-square means were compared using the Tukey test with P,0.05 being considered significant and levels of P,0.10 referred to as tendencies. Progeny performance was analyzed as a block design considering initial weight of each phase as random factor. Carcass data were analyzes as block design considering final live weight as random factor. The data was evaluated by ANOVA using proc Mixed procedure of SAS, least-square means were compared using the Tukey test with P,0.05 being considered significant and levels of P,0.10 referred to as tendencies. In the tables, data are reported as least-square means and the pooled s.e.m.

RESULTS AND DISCUSSION

Sow Performance. The sows´ reproductive performance for each treatment is presented in table 3. None of the treatments affected backfat thickness at any period of evaluation (P>0.05). According to Houde et al. (2010) fluctuations in back fat thickness during the reproductive cycle should be avoided, as it is associated with declining reproductive performance over subsequent parities. However if we observe the

difference in percentage between the evaluation at day 53 and 25 it shows that sows receiving Rac could be in greater catabolism than the sows of the treatments, as the nutritional management of the farm provided less nutrients than recommended by Rostagno et al. (2011). Catabolic sows during the gestation could have an impaired fetal growth manifested as reduced birth weight of the offspring (Rehfeldt et al., 2011) besides it the colostrum yield is compromised (Decaluwé et al., 2013). Considering that if the diets were adjusted, or the fed amount were greater, probably the results of sows receiving Rac would be better.

During the 28 days of arginine supplementation, the diets were not isonitrogenous. However, over the entire treatment feeding period, crude protein intake was only 1.31% greater for sows fed the Arg treatments Pond et al. (1992) reported that even after severe dietary protein restriction (13% vs. 0.5%) of the sows during gestation neither fetus survival at day 44 of gestation, nor litter size at birth differed. Therefore, the supplementation with L-arginine during 28 days probably did not affect the fetal survival rate.

The number of pigs born (total and alive) and the percentage of mummified piglets were not affected by the treatments (Table 3). However, the number of stillborn piglets were approximately three times greater for Arg and Rac treatments and five times greater for the Arg+Rac treatment than the control treatment ($P<.01$). This could be associated with the fact that sows receiving Rac, Arg, and both had a numerically greater number of total piglets born, and according to Van Der Lende and Van Rens (2003), around 100 days of gestation fetal mortality can increase due to limited uterine space. The greater number of

piglets born per sow increased farrowing time, which is another factor that contributes to the greater number of stillborn (Muirhead and Alexander, 1997; Canario et al., 2006). Other aspect that could increase the number of stillborns is the greater number of mummified piglets According to Mengeling et al. (2000) the presence of mummies can increase the total farrowing time and the farrowing time between piglets. Added to thus a greater piglet body birth weight leads to a longer time of farrowing, this is another trait that can clue to a greater number of stillborn (Van Dijk and Van Rens, 2005). In this trial, the individual piglet birth weight at farrowing was greater for all treatments compared to the sows of the control group. The greater percentage of piglets with birth weights greater than 1.6 kg was greater for sows of the Rac and Rac+Arg treatments than the Arg and Control treatments.

Litter birth weights were numerically greater (10.6%) for sows Arg Rac, Arg+ Rac groups compared to the control, but the difference was not statistically significant ($P>0.05$) (Table 3). However, evaluating the individual birth weight of the piglets from sows fed Rac, they were 11 % heavier ($P < .031$) than piglets not fed Rac. Similar results were found by Gatford et al. (2009) after feeding 20 ppm of Rac from day 25 to 50 of gestation.

Feeding Rac during gestation can have direct effects on fetal muscle development (Hoshi et al., 2005a; Gatford et al., 2009) as past research found that sows fed 20 ppm during early to mid-gestation had improved progeny performance and muscle development of the piglets.

Zalin and Montagne (1975), demonstrate greater concentrations of cAMP during the development of the skeletal muscle of chicks. Feeding a

beta-adrenergic agonist can affect the prenatal development of the skeletal muscle.

Sows placenta expresses beta-adrenergic receptors, and Rac as a beta agonist can regulate the Na^+ transfer in sows placenta, as shown *in vitro* by Sibley et al. (1986). These authors demonstrated a possible a possible direct effect of Rac on the placenta. Also, beta-adrenergics can increase blood flow to the fetuses, via the receptors present in the smooth muscle cells of the blood vessels elevating the cAMP causing vasodilation, as shown in exposed in human umbilical arteries *in vitro* (Karadas et al., 2007). As shown by Cantarelli et al. (2009), Rac increases nitrogen retention, which can contribute to a greater amount of protein synthesis in the fetus, therebye increasing the formation of muscle tissues.

Ractopamine can act via alteration of sow metabolism, is known that it can increase the skeletal muscle deposition in finishing pigs (Garbossa et al., 2013), and thus may increase nutrient availability toward fetal growth. But no effect was observed in plasmatic concentrations of total protein, total lipids, creatinine, urea, and glucose of sows receiving Rac (Hoshi et al., 2005b; Gatford et al., 2009).

Individual birth weights of pigs from the treatments Arg and Arg+Rac were 4.15% and 9.32% greater than control pigs. Similar results were observed by Mateo et al. (2007). The effects of arginine appear to be due to its involvement in regulating angiogenesis and vascular development and functions of the umbilical vein and placenta providing more nutrients and oxygen to the fetuses (Liu et al., 2012).

Arginine is a precursor of nitric oxide (NO) and it is a highly lipophilic simple gaseous molecule synthesized by endothelial cells,

macrophages and certain group of neurons in the brain. According to Lacasse et al. (1996), NO is a potent vasorelaxant of vascularization of the mammary gland. Nitric oxide is the major vasodilator endothelial cells (Wu and Meininger, 2000) and plays an important role in regulating placental blood flow and therefore the transfer of oxygen and nutrients to the fetus (Bird et al., 2003). In addition, NO is an important intercellular messenger in greater mammals. The mechanism of intercellular signaling is generally accomplished via cell membrane receptors on the target cell, and usually is in contact with transmembrane and cytoplasmic triggering a "cascade" of intracellular signals that interfere with cell metabolism. By their chemical characteristics of high diffusibility of NO signaling is exerted directly on intracellular level without transmembrane receptors. Due to its intracellular penetration without membranous intermediates, the body uses NO in physiological functions in which a rapid response is required (Flora Filho and Zilberstein, 2000).

The weight distribution at birth was improved by the treatment with Rac and Rac+Arg (Figure 1). A greater percentage of piglets had brith weights greater than 1.6 kg, this result as discussed above probably is not just due to the better nutrition to the fetuses. Considering the progeny of Arg treatment sows, these piglets did not have the same increased birth weight, and it is known that the main effect of Arg to increase the weight of piglets is through increased blood flow.

Placenta is the central organ in mediating the supply of substrates from the sow to the fetuses. So the placental efficiency affects nutrient transfer across the placenta (Rehfeldt et al., 2004). However, placental efficiency was not affected.

Brain to liver weight ratio was not affected by the treatments This ratio is an indicator of intrauterine growth retardation (IUGR) (Bauer et al., 1998). None of the piglets had a greater brain to liver weight ratio probably because the piglets chosen to be euthanized were the pigs with the average litter weight, and greater brain to liver ratios suggesting IUGR are more commonly observed in piglets with less than average birth weights (Burke et al., 2006).

The coefficient of variation (CV) of the litter at birth was similar for all treatments (Table 3). But, the CV of weaning weight for the sows fed Rac had a tendency to be smaller ($P < .080$). In contrast, Titus et al. (2013) showed that the CV at birth is a good predictor of the CV at 21 days. Decreasing the CV of within litter is extremely important because, as show by Kim et al. (2009) and Wolf et al. (2008), greater CV are related to lower survival rates, besides that variation at weaning can be a possible predictor of market weight variation (Titus et al., 2013). The lower CV at weaning is possibly related to the greater birth weight of the piglets because light litter-mates are usually outcompeted by the heavier litter-mates which nurse more effectively, directing a larger amount of hormones and nutrients involved in milk production to the respective teats (Grandison et al., 2005). The smaller piglets are more susceptible to starvation and crushing (Alonso-Spilsbury et al., 2007), as leading to low weight gain, which increases the variation within litters. The progeny of the sows that received Rac had a greater percentage (45%) of piglets with birth weights above 1.6 kg what can contribute to the reduction of the CV, as the lighter animals are more likely to die. As reported by Quesnel

(2011) small piglets take longer to consume fewer amounts of colostrum and are more susceptible to crushing by the sow.

Final weight and ADG of the piglets were numerically greater for the the ARG and Rac treatment at weaning (Table 3), however the performance of the progeny (final weight, average daily gain, number of piglets weaned, and mortality) were not affected (P > 0.05) by the experimental treatments. The results are similar to the results found by Hoshi et al. (2005a) that did not observed any differences nursery performance between control and Rac treatment.

Table 3.Effects of supplementing arginine and ractopamine, or both during 25 to 53 days of gestation for sows.

Item	Treatment				SEM	P Value
	Control	Arg	Rac	Arg+Rac		
Sows, n	23	23	22	22		
BF, mm						
Day 25 of Gestation	14.76	14.24	13.90	13.98	0.83	0.571
Day 53 of Gestation	14.34	13.95	12.78	12.98	0.70	0.183
Difference 53-25, %	3.49	4.78	-1.77	-1.04	1.98	0.060
Farrowing Performance	14.68	14.45	12.94	13.56	0.83	0.389
TB, n	13.28	14.53	13.44	13.81	0.64	0.367
BA, n	12.87	13.20	12.62	12.33	0.59	0.721
SB (%)	1.01A	3.86AB	3.32AB	5.53B	1.13	0.014
MM (%)	1.77	4.65	2.28	5.05	1.20	0.163
LW, kg	17.80	19.78	19.93	19.35	0.94	0.222
IW, kg	1.38B	1.43AB	1.53A	1.51AB	0.04	0.031
PE	5.32	5.81	5.81	6.24	0.61	0.803
Brain:liver Ratio	0.59	0.68	0.61	0.59	0.04	0.302
CV						
Birth(%)	19.88	20.57	19.17	20.69	1.57	0.681
Weaning(%)	16.82	16.44	13.10	16.78	1.30	0.080

Within a row means without a common capital letter differ by Tukey test (P < 0.05). Control = control diet during the whole gestation; Arg = control diet + supplementation of 1.0% of L-Arginine during days 25 to 53 of gestation; Rac = control diet + supplementation of 20 ppm of ractopamine during days 25 to 53 of gestation; Arg+Rac = control diet + supplementation of 1.0% of L-Arginine + 20 ppm of ractopamine during days 25 to 53 of gestation. BF = Back fat thickness; TB = Total born; BA = Born alive; SB = Stillborn; MM = Mummified; LW = Litter weight; IW = Individual weight; PE = Placental efficiency; CV = Coefficient of variation;

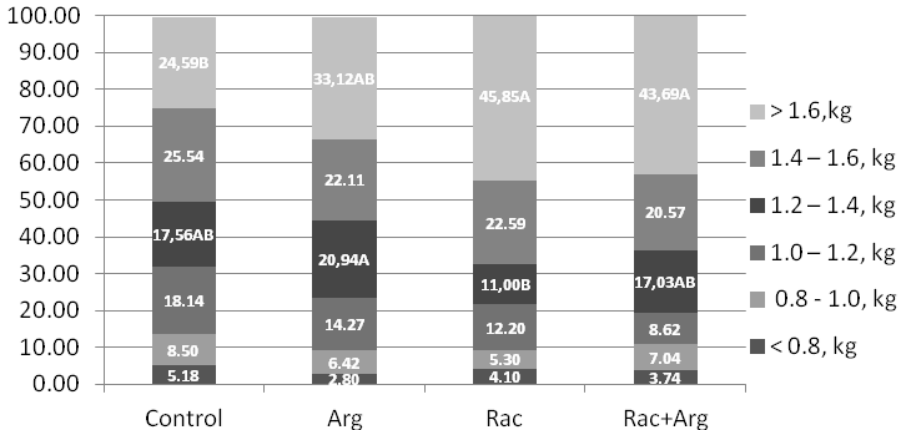

Figure 1 Effect of sows treatment on piglet distribution into birth weight classes. Means without a common capital letter differ by Tukey test ($P < 0.05$).

The *semitendinosus* muscle fiber number and fiber diameter data are shown in Table 4. Treatment of the sows decreased *semitendinosus* muscle fiber number 3.76%, 4.58%, and 4.70% comparing the Arg, Rac, and Arg+Rac to the control treatment, respectively. Muscle fiber diameter was also affected by the treatments ($P < 0.0001$) of the sows. The muscle fiber diameters were 16.99%, 16.34%, and 17.36% greater for the Arg, Rac and Arg+Rac pigs than the control pigs, respectively. Since the diameters were greater, the number of fibers per mm² decreased. These results are similar to those found by Alvarenga et al. (2013), that evaluated piglets with low (LBW) and high birth weight (HBW), demonstrating that pigs with HBW had a greater diameter and a lesser number of muscle fiber per mm², the same author suggests that a better post-natal performance is related with the increased fiber diameter. The

greater birth weight of the piglets could be associated with the increased fiber diameter (Nissen et al., 2004).

Table 4. Effects of supplementing arginine and ractopamine, or both during 25 to 53 days of gestation for sows on muscle fiber number (MF) and fiber diameter (FB) of the *semitendinosus* muscle of newborn piglets.

Item	Treatment				SEM	P Value
	Control	Arg	Rac	Arg+Rac		
MF, n/mm²	947.49A	911.81B	904.05B	902.92B	3.59	< .0001
FD, µm	32.35B	37.84A	37.63A	37.96A	0.55	< .0001

Within a row means without a common capital letter differ by Tukey test (P < 0.05). Control = control diet during the whole gestation; Arg = control diet + supplementation of 1.0% of L-Arginine during days 25 to 53 of gestation; Rac = control diet + supplementation of 20 ppm of ractopamine during days 25 to 53 of gestation; Arg+Rac = control diet + supplementation of 1.0% of L-Arginine + 20 ppm of ractopamine during days 25 to 53 of gestation. MF = Muscle fiber number per mm²; FD = Mean fiber diameter.

Progeny Performance. The results for the progeny performance are presented in Table 5. The results were divided into three phases: nursery, grower, and finisher. Finisher was divided in two phases because Finisher phase 2 was the moment that the pigs started to receive RAC in the fattening period.

In the nursery phase, the final weight was 9.7 % and 6.7 % greater (P < .010) for the progeny of sows fed Arg and Rac respectively than progeny of the control group (Table 5). Consequently, the final weight for these two groups were 8.3 % and 6.5 % greater. The results are different than those previously reported by Hoshi et al. (2005a) that fed 20 ppm of Rac for sows in different stages of gestation and did not found any difference between treatments. Kim et al. (1994), who studied the effects of salbutamol, a beta-adrenergic agonist and reported that sows treated during the first 38 days of gestation (pre-hyperplasia period) produced

pigs with greater weight gains when compared to the untreated control pigs Dwyer et al. (1993) reported that birth weight had a positive correlation with growth performance in the first phases, as observed in this trial. Other papers have found a positive correlation of birth weight with growth rates and better feed efficiency (Schinckel et al., 2010). Light weight piglets have less muscle fibers and satellite cells so had a lower growth potential (Lefaucheur, 2010).

For the Grower, Finisher 1, and Finisher 2 phases, despite the numerical differences (Table 5) no treatment effect was found for the overall performance (final body weight, ADG, ADFI, and FE) data. These growth performance were not found to be statistically different, to some extent due to the increased standard errors of the later measurements. However the initial weight for Finisher 1 phase for the Arg treatment was 4.2% greater ($P < .01$) than pigs of the Arg+Rac treatment. This statistical difference in the initial weight of Finisher 1 and not in the growing final weight for these treatments was caused as the number of replicates were increased when pigs were transferred from the growing to finishing barn.

Table 5. Pre-weaning, nursery, grower, finisher 1 and finisher 2 progeny performance of sows treated with a control, arginine, ractopamine, or both during 25 phases to 53 days of gestation.

Item	Treatment				SEM	P Value
	Control	Arg	Rac	Arg+Rac		
Pre-weaning						
Initial, kg	1.39B	1.49A	1.48A	1.46A	0.05	<0.0001
Final, kg	5.59	5.82	5.89	5.61	0.19	0.471
ADG, g/d	193.8	198.6	201.9	192.5	0.80	0.799
WA(days)	21.69	21.97	21.82	21.25	0.33	0.422
PW, n	11.04	11.04	11.05	10.96	0.22	0.953
PM (%)	7.97	7.99	7.93	8.66	1.86	0.953
Nursery						
BW						
Initial, kg	5.63	5.89	5.93	5.63	0.49	0.525
Final, kg	20.72B	22.44A	22.06AB	20.81B	0.99	0.009
ADG, kg/d	0.387B	0.425A	0.413AB	0.388B	0.01	0.004
ADFI, kg/d	0.598	0.636	0.636	0.592	0.02	0.106
Gain:Feed	0.650	0.668	0.643	0.651	0.01	0.826
Grower						
BW						
Initial, kg	20.82	22.17	21.74	20.42	0.62	0.181
Final, kg	46.10	47.14	46.96	45.12	1.41	0.779
ADG, kg/d	0.665	0.657	0.658	0.654	0.03	0.987
ADFI, kg/d	1.50	1.57	1.52	1.51	0.03	0.434
Gain:Feed	0.441	0.420	0.432	0.429	0.02	0.805
Finisher 1						
BW						
Initial, kg	46.37AB	47.16A	46.19AB	45.26B	0.31	0.009
Final, kg	64.06	65.27	64.72	63.81	1.58	0.867
ADG, kg/d	0.885	0.906	0.909	0.891	0.07	0.992
ADFI, kg/d	2.47	2.46	2.47	2.43	0.06	0.941
Gain:Feed	0.363	0.370	0.368	0.365	0.03	0.998
Finisher 2						
BW						
Initial, kg	64.50	65.46	64.76	63.37	1.45	0.599
Final, kg	85.55	87.60	86.09	85.12	1.68	0.604
ADG, kg/d	1.055	1.103	1.068	1.082	0.03	0.786
ADFI, kg/d	2.63	2.56	2.58	2.55	0.05	0.740
Gain:Feed	0.401	0.430	0.415	0.425	0.01	0.422

Within a row means without a common capital letter differ by Tukey test ($P < 0.05$). Control = control diet during the whole gestation; Arg = control diet + supplementation of 1.0% of L-Arginine during days 25 to 53 of gestation; Rac = control diet +

supplementation of 20 ppm of ractopamine during days 25 to 53 of gestation; Arg+Rac = control diet + supplementation of 1.0% of L-Arginine + 20 ppm of ractopamine during days 25 to 53 of gestation. BW = Body weight; ADG = Average daily; WA = Weaning age; PW = Piglets weaned; PM = Preweaning mortality; ADFI = Average daily feed intake; FE = Feed efficiency.

Slaughter Evaluation. The carcass data are presented in Table 6. Body weight did not differ among treatments. However hot carcass weight was 3.8% and 2.1% greater ($P < 0.0001$) and cold carcass weight were 3.9% and 2.3% greater for the progeny of the sows that received Arg and Rac compared to the control progeny. These results are similar to those found by Hoshi et al. (2005a) who fed 20 ppm of Rac to sows in different stages of gestation and Kim et al. (1994), who studied the effects of salbutamol, and reported that sows treated during the first 38 days of pregnancy produced heavier pigs at slaughter.

No differences were seen for the parameters hot and cold carcass yield, muscle pH and temperature at 45 min and 24 hours of the carcass, backfat depth, fat area, muscle depth and loin muscle area (*Longissimus dorsi* muscle), carcass length, and the color components (L, a*, b*, c* and h*) of treated animals. However, mainly the progeny of sows fed Rac were numerically better when compared to the other groups (Table 6). These parameters showed that the use of these substances does not compromise pork quality.

Carcass compacity was 4.1% greater ($P < .0211$) for the progeny of sows that received Arg compared with the progeny of sows that received Arg+Rac. According to Yáñez et al. (2004), this is an important parameter to estimate objectively the conformation of the animals which can be used to evaluate the production of meat from pigs weighing similar weights, so animals that have greater values of carcass compacicity will

have a superior amount of meat of animals of the same weight with minors values.

Bonification index (BI) had a tendency (P = .061) to be grater for the pigs of the Rac group compared to other groups, this is linked to their numerically greater loin muscle area and smaller backfat thickness. The BI is a parameter of major importance, because it can lead to greater profitability to the producer as the packers pays more by the improved carcass quality.

Table 6.Progeny carcass characteristics of sows treated with a control, arginine, ractopamine, or both during 25 phases to 53 days of gestation.

Item	Treatment				SEM	P Value
	Control	Arg	Rac	Arg+Rac		
Pigs, n	18	18	18	18	-	-
BW, kg	100.89	102.85	101.48	99.92	1.65	0.620
HCW, kg	79.14BC	82.11A	80.78AB	77.24C	1.37	<0.0001
HCY, %	79.66	79.31	79.62	78.53	0.49	0.322
CCW, kg	77.01BC	80.04A	78.78AB	75.31C	1.34	<0.0001
CCY, %	77.53	77.32	77.64	76.58	0.48	0.378
pH, 45 min	6.18	5.95	6.176	6.17	0.12	0.788
pH, 24 Hrs	5.92	6.12	6.04	5.96	0.09	0.459
Tp 45 min °C	37.41	37.45	37.38	37.75	0.49	0.934
Tp 24 Hrs °C	5.19	4.76	4.79	5.13	0.26	0.298
BF, mm	12.62	14.15	11.74	13.93	0.85	0.126
LD, mm	59.42	62.01	62.80	62.43	1.74	0.496
LEA, cm²	50.49	49.57	51.72	51.59	1.19	0.457
FA, cm²	15.91	18.05	15.92	16.00	0.99	0.200
CL, cm	90.23	90.64	89.99	89.91	0.84	0.862
CC, kg/cm	0.856AB	0.881A	0.876AB	0.842B	0.01	0.021
CLY	60.79	56.99	61.71	60.21	0.62	0.163
BI	107.28	106.99	108.41	106.15	0.67	0.061
Color components						
L	49.63	49.09	49.24	51.33	1.05	0.297
a*	1.01	0.90	1.02	0.86	0.33	0.945
b*	10.14	10.09	9.83	10.49	0.51	0.800
c*	10.22	10.19	9.98	10.57	0.53	0.865
h*	84.49	86.03	85.37	85.96	1.72	0.909

Within a row means without a common capital letter differ by Tukey test (P < 0.05). Control = control diet during the whole gestation; Arg = control diet + supplementation of 1.0% of L-Arginine during days 25 to 53 of gestation; Rac = control diet + supplementation of 20 ppm of ractopamine during days 25 to 53 of gestation; Arg+Rac = control diet + supplementation of 1.0% of L-Arginine + 20 ppm of ractopamine during days 25 to 53 of gestation. BW = Body weight; HCW = Hot carcass weight; HCY = Hot carcass yield; CCW = Cold carcass weight; CCY = Cold carcass yield; Tp= Temperature; BF = Backfat thickness; LD = Loin depth; LEA = Loin eye area; FA = Fat area; CL = Carcass length; CC = carcasscompacity; CLY = Carcass lean yield; BI = Bonification index; L= lightness; a* = redness; b*= yellowish; c*= chroma; h*=Hue angle.

Economical Evaluation. The economic evaluation which evaluates the profitability per pig is presented in Table 7. The treatments had no significant effect for the parameters evaluated. Only total cost had a tendency to be greater (P = .057) for the Arg treatment being greater than the control treatment. No significant treatment effects were observed for the net income, however pigs from sows that received Arg were 0.9% more profitable than control pigs. Considering the bonification index basis no treatment differences were observed for the net income. However the pigs of the Rac treatment had a 2.3% greater net income which represents an extra US$ 1.93 dollars per animal.

Table 7.Total cost, gross income and net income per slaughtered animal of sows treated with a control, arginine, ractopamine, or both during 25 phases to 53 days of gestation.

Item	Tratment				SEM	P Value
	Control	Arg	Rac	Arg+Rac		
Live weight basis						
TC, US$	112.53	115.21	113.48	112.86	0.74	0.057
GI, US$	163.31	166.49	164.27	161.71	2.30	0.529
NI, US$	50.78	51.28	50.79	48.88	2.08	0.854
Bonification index basis						
GIBI, US$	195.68	197.53	198.56	188.91	3.53	0.326
NIBI, US$	83.15	82.32	85.08	76.05	3.30	0.250

Control = control diet during the whole gestation; Arg = control diet + supplementation of 1.0% of L-Arginine during days 25 to 53 of gestation; Rac = control diet + supplementation of 20 ppm of ractopamine during days 25 to 53 of gestation; Arg+Rac = control diet + supplementation of 1.0% of L-Arginine + 20 ppm of ractopamine during days 25 to 53 of gestation. TC = Total cost; GI = Gross income; NI = Net income; GIBI= Gross income considering bonification index; NIBI = Net income considering bonification index.

CONCLUSIONS

The trial showed that the utilization of arginine and ractopamine for gestating sows are applicable technologies in the swine production, improving the piglets quality, profitability, however the association of both did not have a sum effect not differing of the control treatment. More trials should be completed to evaluate and better understand the use of these technologies in the modern swine production systems.

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